Challenges in the Management of Pediatric Bone & Joint Infections

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FORWARD

PREFACE

Every 1500 live births one child gets affected from bone and joint infection in India. Unless diagnosed promptly and treated adequately, these conditions leave behind a life long disability. Worldwide, there is an emerging trend towards either prevention or early identification of Pediatric osteoarticular infections. Vaccination against causative organisms are being developed and made universally available to reduce its incidence. Primary care physicians are trained to identify the red flags and treatment centers follow unique algorithms to fight against this non-yielding problem. Now is the time to introspect about where do we stand?

We are confronted with several challenges in the management of Pediatric bone & joint infections. Many of the referrals at tertiary centers are late, so that a curative intervention becomes a salvage procedure. The radiology and pathology services are utilized sub optimally, perhaps because of financial constrains in our country. Many physicians work as an independent unit rather than a comprehensive team, which frequently ends up in an inadequate treatment. Incidence of community acquired methicillin resistant staphylococcus aureus (CA-MRSA) is emerging in India & it is mandatory to take help from the Neonatologists and Pediatricians for proper anti-microbial therapy. Unless treated promptly, it can become a limb & life threatening condition. At instances, it looks that we over rely on the role of antibiotics. Surgical reduction of the load of pathogen is important to prevent permanent damage to the articular cartilage. Due to the lack of awareness and facilities in rural areas, there are many patients who have lost part of their bony architect as a result of a previous musculoskeletal infection. Treatment methodology of such complex issues is not well described in the world literature. In fact, we have to customize the treatment based on the local biology and economic status of the patient.

In this book, we have tried to include all the important aspects of a comprehensive management of bone and joint infection. It

comprises of lucid description of basic patho-anatomy of pediatric bone & joints, changing pattern of the pathology worldwide and current concepts in diagnosis of the condition. It also includes a Pediatrician's concern & perspective while managing osteoarticular infection. Surgical strategies of the primary and salvage procedures are also described in details. I am sure, that this book will become a good companion in your clinic as a ready reference source.

I am thankful to Dr. P.M. Vekariya, President, AOS and Dr. Jitendra Chaudhary, Secretary, AOS for giving me an opportunity to work on this project. I am obliged to Dr. William Cole, Dr. Andrew Howard and Dr. Michael Segbefia for spending their valuable time to contribute in this book. I am grateful to Dr.S M Tuli for pouring his life-long experience in a chapter. I heartily thank all the national authors for providing me with excellent quality of academic material based on their personal experiences. I appreciate Mr. Akshat Khokhani & his team for timely formatting & printing the book.

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I N D E X

CHAPTER 1

What are the challenges?

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Pediatric bone & joint infections are routine encounters in our clinical practice. There are many challenges in successfully treating these issues, right from early identification, timely referral, optimum use of pathology & radiology to confirm the diagnosis, appropriate anti-microbial therapy & prompt surgical intervention. All phases of management pose different challenges. A team approach is required for the optimum treatment of this non-yielding problem.

Magnitude of problem

The incidence of septic arthritis / osteomyelitis in India is approximately 1 in 1500 live births[1]. This incidence is higher than the Western world (1 in 15,000 live births in USA[2] & 1 in 5,000 in UK[3]). The probable reason for this high incidence is a high rate of systemic sepsis in Indian children. Neonatal bone & joint infection are seen as a part of systemic sepsis in about 76% of patients[1]. Vaccination against causative organisms like Haemophilus influenza type B & Streptococcus Pneumoniae is not universally available in India. In North America, successful vaccination has almost eliminated the H.influenza as the causative organism[4, 5].

Time of Referral

Neonatal infections are notorious for remaining non-evident till they enter the late stage. Diagnosis in a very sick baby is delayed due to relative immobility and attention to systemic illness. Especially, the shoulder & hip joints affections require a very high degree of suspicion to identify early in the course of septic arthritis. Any referral after 5-7 days of onset of symptoms ends up with

universally compromised long term results. This is due to the fact that the loss of glycosaminoglycans & collagen from the cartilage structure begins as early as 8 hours of bacterial inoculation in joint. (Fig-1)

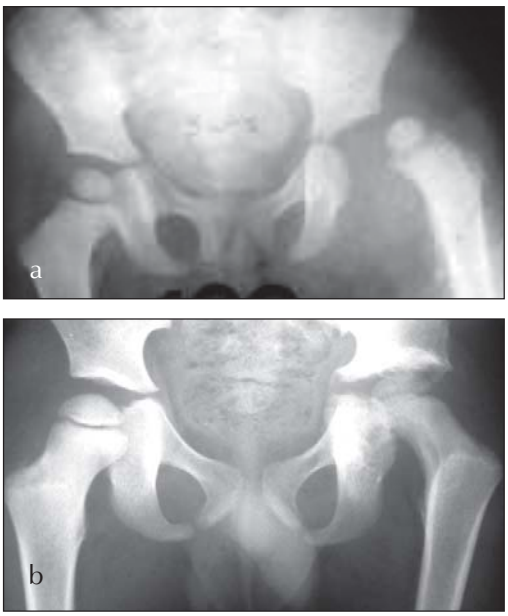
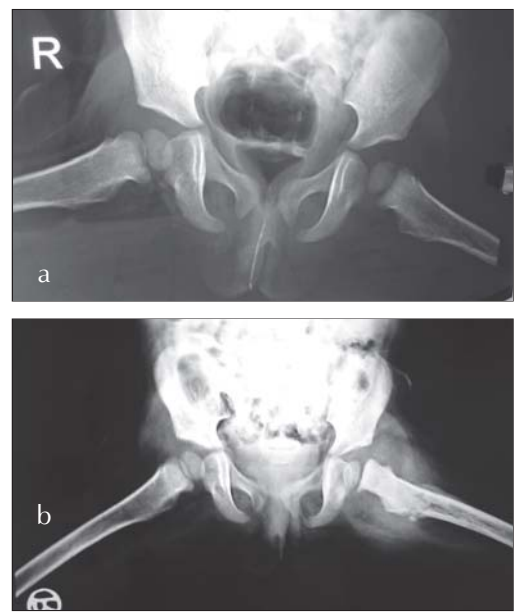


Fig.1 a. A 2 year old boy presented 10 days after the onset of symptoms.
b. Evident chondrolysis in left hip at one year follow up after treatment.

Diagnostic Challenges

Kocher et. al. developed a clinical prediction algorithm for septic arthritis based on four clinical variables: history of fever, non-weight-bearing, an erythrocyte sedimentation rate of ″40 mm/hr, and a seruam white blood-cell count of >12,000/mm3 (>12.0 □ 109/L)[6]. Although by using this algorithm, the author demonstrated 99 % predicted probability of the patient having septic arthritis, other studies showed only 60% [7]. We face the same diagnostic dilemma in our clinical practice. Many immuno-compromised children fail to have fever & may show lowered white blood cell count. The other two criterions are also seen in other conditions like juvenile idiopathic arthritis, osteomyelitis and tuberculous arthritis. This commonly leads to either over diagnosis or under diagnosis of the condition.

Suboptimal usage of imaging technology also contributes in a delayed diagnosis. Positive changes on x-ray suggest that the disease is already in its advanced stage. Hence to diagnose the condition in its early stage, optimum use of investigations like ultrasound and MRI should be done. Unfortunately, these latest techniques are not available at all centers or are costly for patients belonging to lower socio-economic class. (Fig.2) In children older then 2 years, 40 % of patients with osteomyelitis end up in septic joint, where the metaphysis is intra-articular. Such locations of osteomyelitis warrant regular



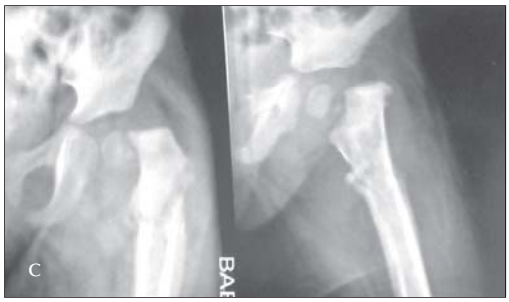


Fig.2 **a.** A 3 year old girl admitted to PICU due to Pneumonia complained of left hip pain on 5th day of admission. X-ray did not reveal any abnormality. **b.** X-ray on discharge from PICU shown osteomyelitis changes in proximal femur. Child was not further investigated. **c.** Two weeks later, x-ray which was taken to find the reason of increased pain, revealed a proximal femoral physeal separation. A timely ultrasound or MRI of the hip could have avoided the complication.

ultrasound screening of the adjacent joint[8].

Bone infection mimickers

Many conditions can mimic pediatric bone and joint infection, especially in its early course. Transient synovitis, idiopathic arthritis, tuberculous arthritis and rheumatic fever are the commonest conditions in differential diagnosis. A detailed history, appropriate clinical examination and reliable blood investigations can help confirming the diagnosis. The radiological picture of tumors like Ewing's Sarcoma and Leukemic infiltrates can also mislead the diagnosis of osteomyelitis. It is worth following the dictum: "Biopsy all infections and Culture all tumors." Osteomyelitis accompanying with Sickle cell anemia[9] and major vessels thrombophlebitis[10] demand a prompt treatment of the later conditions. Detailed information about the common differential diagnosis of bone infection is discussed elsewhere in the book. (Chapter:11)

Treatment Challenges

To treat patients with septic arthritis satisfactorily, it is imperative that they present in time. General knowledge about the requirement of urgent referral to the treatment centre is also essential. Timely referral & treatment can lead to normal functional outcome.

As discussed above, many patients with bone & joint infection have associated systemic illness. It is important to involve Neonatologists or Pediatricians timely for optimum treatment. A comprehensive team approach is desirable rather than functioning at an individual level in such patients.

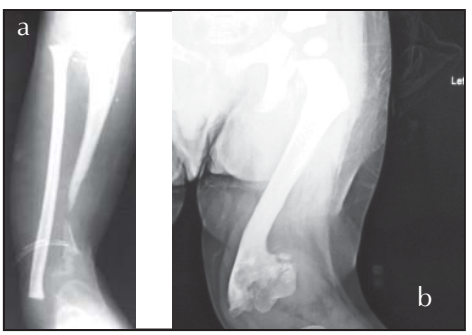
Controversies exist about the type & duration of antibiotic use. As the causative organism and its virulence are changing, we need to keep ourselves updated about the knowledge of most effective antibiotic therapy. Based on the latest review of literature, use of intravenous antibiotics till child improves clinically and starts weight bearing, followed by oral antibiotics for 4-6 weeks seems to be a standard regimen. The duration of antibiotics depends on the clinical recovery rather than a fixed time frame. Resolving blood markers are additional indicators about the duration & efficacy of antibiotic therapy. Complications related to long-term intravenous antibiotics should be avoided.

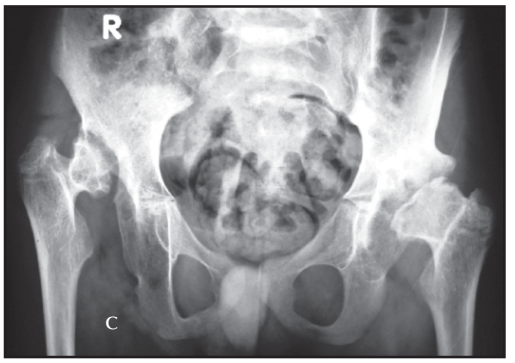
Increasing incidence of community associated methicillin-resistant

Staphylococcus aureus (CA-MRSA) induced musculoskeletal infection is of great concern. Orthopedic surgeons should be vigilant in recognition and treatment of CA-MRSA infections, as the disease spectrum is completely different. Unless prompt treatment through empiric antibiotic therapy, timely and repeated debridement and management of systemic sequelae are done, these can end up in limb & life- threatening situation.[11, 12]

With the advent of modern antibiotic therapy and better understanding of surgical clearance of intra-medullary infection in treatment of acute osteomyelitis, the occurrence of chronic osteomyelitis has reduced. But still we come across such difficult situations. Mcmurray rightly said: "last surgeon who removed the last sequestrum, cured the condition." In pediatric age group, many a times the local bone condition does not allow to remove the whole sequestrum, otherwise it would end up in an unstable situation predisposing it for a pathological fracture or an infected non-union in future. Chronic osteomyelitis remains a lasting & challenging problem all over the developing world.[13]

Challenges in treating sequelae of musculoskeletal infection





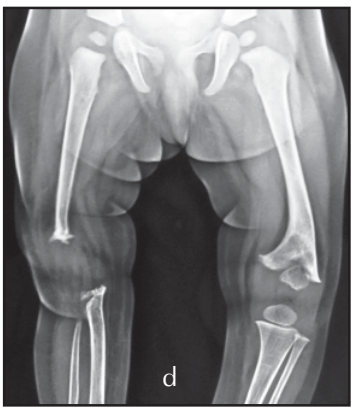


Fig.3 a. Infected non-union tibia **b.** Distal lateral femoral physeal arrest with resultant valgus deformity. **c.** Bilateral epiphyseal loss **d.** Right side total knee joint loss with left side distal femoral growth arrest.

We routinely are confronted with the complex salvage issues of previously affected musculoskeletal infections. This can be an infected non-union, a physeal arrest, a metaphyseal loss, a diaphyseal loss, an epiphyseal loss or a whole joint loss (Fig. 3). These problems are unique & require customizing the management based on the local biology (Fig.4). Surgeons from developing world should publish the literature regarding these specifically tailored

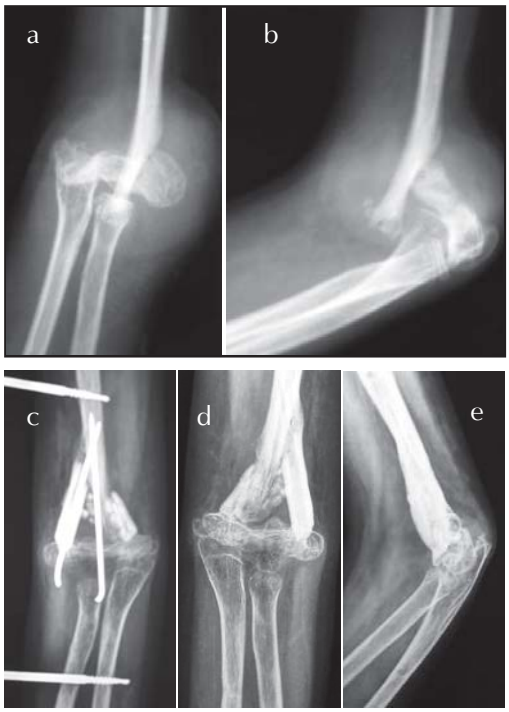


Fig. 4 a,b. Thirteen years old post-infective non-union of distal humerus with loss of Olecranon fossa and humeral metaphysis. Patient had movement at the pseudoarthrosis site but was not able to perform any functional activity. **c.** Reconstruction was performed using fibular strut graft to create lateral pillar of distal humerus. Medial pillar was created with the distal tapered sclerotic end of humeral diaphysis. A gap was left between two pillars to form an olecranon fossa. K-wire fixation was augmented with monolateral external fixator to give additional stability. **d,e.** Follow up images show well structured distal end humerus. Patient achieved good range of functional movement from the elbow after a second stage arthrolysis. (Courtesy: Dr.Nitingiri Goswami, Dr.Maulin shah)

treatment strategies, as they have huge experience of such difficult situations. There is a great need to craft a management algorithm for such not uncommon conditions.

Summary:

Pediatric bone & joint infections are challenging problems. Timely referral to the treatment centre & management through a comprehensive team approach are the keys to successful outcome & lasting bone and joint architect.

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CHAPTER 2

Relevant Pathoanatomy of Bone and Joint Infections

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Osteomyelitis

Understanding normal pediatric bone anatomy and physiology facilitates the management of osteomyelitis and septic arthritis.

The diaphysis of long bones consists of outer and a central medullary cavity. Cortex is relatively acellular while medullary cavity is filled with a rich reticuloendothelial (RE) system. On the other end, the metaphyseal region has a thin cortex and the medullary cavity is filled with trabecular bone. This trabecular area has relatively few RE cells. Because of lesser number of phagocytic cells in the metaphyseal region of the bone, infection in this area is more prone to occur.

Another reason why infection is more prone at the metaphyseal region is due to its vascular anatomy. Vessels beneath the physeal plate are small arterial loops which empty into the venous sinusoids. Because of difference in the diameter, turbulence can result which may be the cause of localization. In addition, it has been demonstrated that the endothelial wall of new metaphyseal capillaries have gaps that allow the passage of blood cells and, presumably bacteria.

Hematogenous osteomyelitis has a strong predilection for the most rapidly growing end of the large long bones, especially those of the lower extremity. This predilection may be explained by the observation that, in rapidly growing bones, the phagocytic cells are farther away from where the bacteria localize. Therefore, the inflammatory response takes longer to reach the bacteria, allowing an infection to become established.

Once the bacteria begin to multiply in the metaphysis adjacent to the physis, a process of bone resorption begins. Osteoblasts die and bone trabeculae are resorbed by numerous osteoclasts within 12 to 18 hours. Lymphocytes may release osteoclastic activating factor, and macrophages, monocytes, and vascular endothelial cells may all directly resorb both the crystalline and matrix components of the bone. In response to toxins and bacterial antigens, interleukin-1 and Prostaglandin E_2 are produced, which cause further bone resorption.

The accumulation of bacteria, inflammatory cells and chemicals causes thrombosis of medullary vessels. This further reduces the host's ability to fight infection. Purulent exudate accumulated in the metaphysis may exit out through the porous metaphyseal cortex to create a subperiosteal abscess. Periosteum covering metaphyseal and diaphyseal cortical bone is thick in children and so cannot be easily penetrated, but can be easily separated from bone. As the periosteum is elevated, the cortical bone loses its blood supply and becomes necrotic, forming a sequestrum. Because the periosteum receives its blood supply from outside, it retains its blood supply, remains viable and produces new bone. The new bone forming around the necrotic sequestrum is known as involucrum.

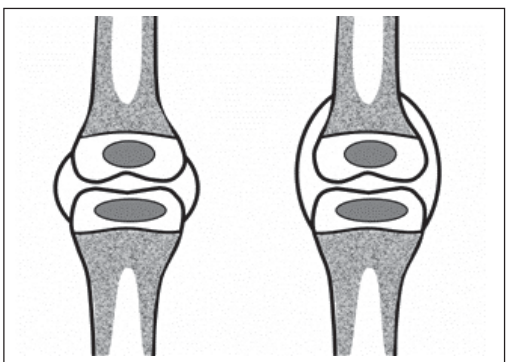

Figure 1

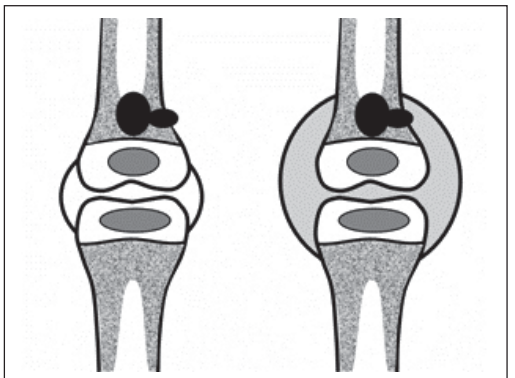

Figure 2

If the metaphysis is intra-articular at the site where infection breaches the metaphyseal cortex, infection will spread in to the joint and septic arthritis results. (Figure 1 and 2) This can take place at four locations in the older child:

- Proximal femur
- Proximal humerus
- Distal lateral tibia
- Proximal radius

Infection generally does not spread down the medullary cavity because the well-developed RE system of the diaphysis is able to prevent its expansion in this direction.

Because of the unique and changing anatomy of the interosseous blood supply, pathophysiology of osteomyelitis in the infant may vary from the pattern described above. Trueta first noted that before the ossific nucleus forms, the vessels from the

metaphysis penetrate directly into the cartilaginous ephysis[1]. Because of this blood supply pattern, the initial bacterial localization may occur in the cartilage epiphysis precursor instead of metaphyseal area. From here the infection may spread to the joint, causing septic arthritis as well as physeal injury and growth alteration. As the ossific nucleus develops, a separate blood supply to this epiphysis develops and the metaphyseal vessels crossing the developing physeal plate disappear. When the physeal plate is formed, it provides a temporary barrier to the spread of infection from metaphysis to epiphysis.

Infection can also affect the growth plate and may produce limb length discrepancy or angular deformity.

Septic Arthritis

Septic arthritis can occur from the primary seeding of the synovial membrane, secondarily from infection in the adjacent metaphyseal bone or directly from infection in the adjoining epiphysis. In the hip, shoulder, ankle, and elbow, the joint capsule overlaps a portion of the adjoining metaphysis, and if a focus of osteomyelitis breaks through the soft metaphyseal bone, it can directly seed the joint and lead to concurrent septic arthritis. (Figure 3) Additionally, in the hip, vessels cross the epiphysis until the age of approximately eighteen months, and this provides a direct route for infection to spread from the metaphysis to the hip joint. (Figure 4) Just as in bone, it is likely that transient bacteremia results in bacteria entering the joint, but, in almost all cases, the joint has the ability to clear itself of bacteria and avoid infection. However, when the inoculum is large, or when virulent pathologic bacteria such as S. aureus are less effectively cleared, clinical infection may result. Distinct histologic characteristics of a synovial joint affect the pathophysiology of septic arthritis. Joint synovium does not have a basement membrane and secretes fluid that is essentially a transudate of serum. The remaining interior joint surface is covered with articular cartilage, creating an environment favorable to bacterial proliferation, similar to a culture tube.

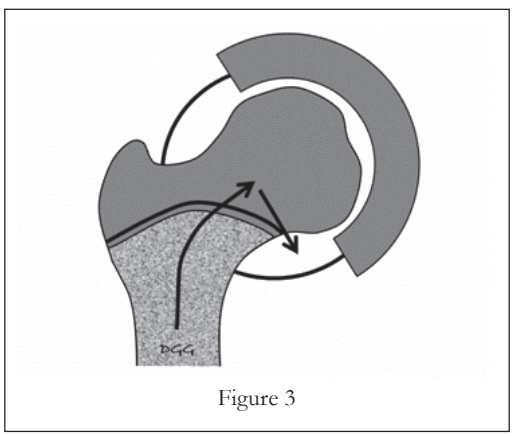

Figure 3

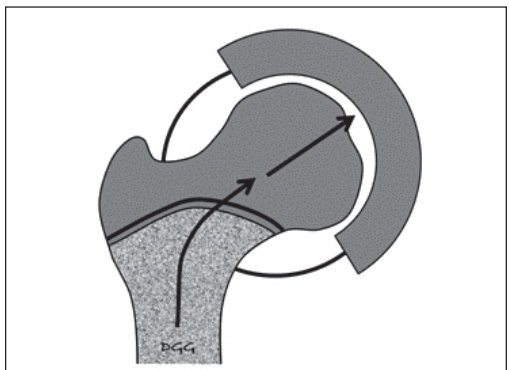

Figure 4

The main goal of the treating doctor is to

interrupt and reverse the process of articular cartilage damage. Understanding of this process will facilitate optimal treatment. When septic arthritis occurs, bacteria rapidly gain access to the joint cavity and within a matter of hours cause synovitis and formation of fibrinous exudate followed by areas of synovial necrosis.

Proteases, peptidases, and collagenases are released from the leukocytes and synovial cells. These enzymes break down the cellular and extracellular structure of cartilage[2,3]. The loss of glycosaminoglycans is the first measurable change in articular cartilage, occurring as early as 8 hours after bacteria are introduced into the joint[4]. Loss of glycosaminoglycans softens the cartilage and may cause it to be susceptible to increased wear. Collagen destruction follows and is responsible for visible change in cartilage appearance[5,6,7]. Once catalytic enzymes are released into the joint, the presence of living bacteria is not necessary for cartilage destruction to continue.

Elevation of the intracapsular pressure, thrombosis causes impairment of the intracapsular vascular supply which may also play a role in the articular destruction. In certain joints like hip, infection distends and softens joint capsule and may cause joint subluxation or dislocation. (Figure 5 to 7)

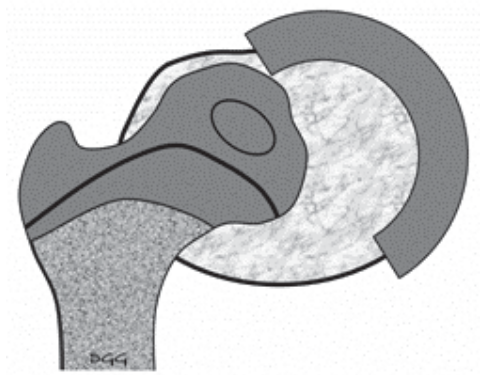

Figure 5

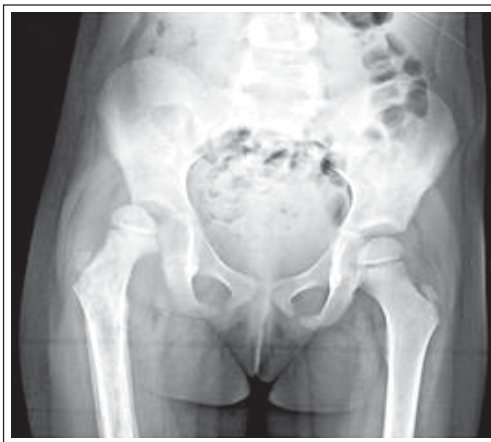

Figure 6

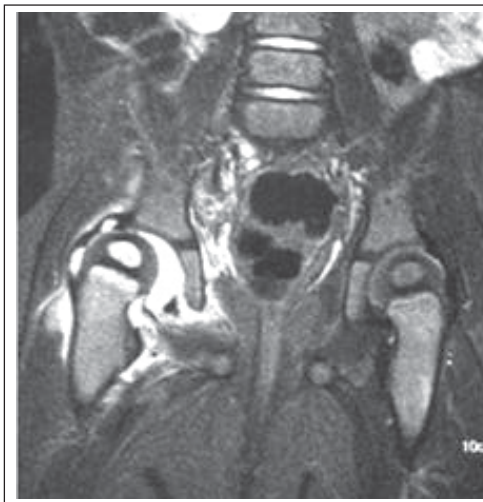

Figure 7

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CHAPTER 3

Changing Patterns of Septic Arthritis in Childhood

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Introduction

Acute bacterial arthritis, usually called septic arthritis, continues to be an important condition throughout childhood[1]. It has been known for many decades that late presentation as well as late or inadequate treatment are associated with advanced systemic and local pathology. The latter problems are well illustrated by delayed treatment of septic arthritis of the hip that may result in dislocation, avascular necrosis, loss of the femoral head, growth plate arrest, coxa breva, coxa vara and slippage of the proximal femoral epiphysis[2]. Consequently, the focus of effort in many countries over recent decades has been to foster prevention, early diagnosis and the early implementation of effective treatment. The results of many such studies highlight the improved results that follow such an effort confirming that for most children current treatments are effective as long as they are implemented in the early phases of the disease – before permanent damage is done to the joint[3-5].

This chapter will focus on changes that are having an impact on the prevention, etiology and management of septic arthritis.

Bacteriology

There has been a substantial change in the bacteriology of septic arthritis over the past decade or so although Staphlococcus aureus and Group B beta-hemolytic streptococcus continue to be common organisms. However, Haemophilus influenzae type B, which accounted for about 30% of published cases of septic arthritis, has been largely eliminated in countries with vaccination programs against this organism[6,7].

Vaccination against Streptococcus pneumoniae is also used in many countries and would be expected to similarly reduce infections due to this organism[8] . The widespread use of chickenpox vaccination may also have an impact in reducing the numbers of severe Group A beta-hemolytic streptococcal infections that are often associated with varicella infections[9] .

Many of the same countries that have shown gains from the latter immunization programs are experiencing increasing numbers of severe infections from community acquired multiple antibiotic resistant Staphlococcus aureus (CA-MRSA)[10] . This organism appears to be more virulent and less responsive to treatment than non-MRSAs[11]
A long standing problem in many published case series is that no bacteria are grown from the blood or joint fluid of at least half the cases of typical septic arthritis[12] . Recent studies have shown that the joint fluid from most of the latter cases contain DNA sequences for the fastidious Kingella kingae gram-negative bacillus[13] . DNA testing can detect Kingella kingae in joint fluid, but not in blood, for up to six days after the commencement of effective antibiotic treatment[13] . In many centres, Kingella kingae is the most common bacterium accounting for 50-60% of cases of septic arthritis[14] .

Diagnosis

There are several ongoing problems with the clinical diagnosis of septic arthritis which may result in late presentations and late onset of treatment. The first problem concerns failure to recognize that the child has septic arthritis – a problem that particularly applies to infections of the hip and shoulder. The second problem concerns failure to recognize that the acute arthritis may be due to a bacterial infection.

Careful clinical assessment remains the main way of diagnosing an acutely inflamed joint. It is relatively easy when the child has arthritis of readily visible joints such as the knee, ankle, wrist and elbow. It is less obvious when the child has arthritis of the hip and shoulder although the usual features of restricted painful movement and abnormal hip and shoulder postures are typical features.

Modern imaging technology has been very valuable in providing additional diagnostic information particularly for the hip and shoulder. Arthritis of the knee, ankle, elbow and wrist are usually easily diagnosed clinically. Plain radiographs are usually undertaken but are of little diagnostic value in early phases of the disease although they usually confirm the extent of the swelling. Additional imaging of the latter joints is usually not needed. However, additional imaging, particularly of the hip has become routine in many centres. Hip ultrasonography has been particularly valuable as it can be undertaken at all ages and it does not require sedation or anesthesia[15,16] . False negative ultrasounds are uncommon but care is needed to ensure that the scans of both hips are of high quality[17]. The pelvis and femur can also be scanned by ultrasound if there is no fluid within the hip or if there is diffuse swelling suggestive of osteomyelitis and subperiosteal abscess of the adjoining pelvis or femur[16] . Another major advantage of undertaking ultrasounds of the hip, particularly in the Emergency Department, is that the hip can be aspirated

under ultrasound guidance[18].

MRI and CT are also widely used in the investigation of children with suspected septic arthritis of the hip. MRI, in particular, has shown that some children with typical clinical features of septic arthritis may have no evidence of inflammation of the hip but have osteomyelitis of the pelvis or femur or myositis of periarticular muscles[19,20]. Because of the latter findings, current management of suspected septic arthritis of the hip needs to include imaging studies to confirm the site of the underlying pathology – ultrasound is the most readily available imaging method in most centres[16].

Differential diagnosis

The combination of clinical assessment and diagnostic imaging should enable a firm diagnosis of acute arthritis to be made. The next challenge, particularly in children presenting early, is to distinguish septic arthritis from other forms of acute arthritis. There are many other causes of acute arthritis including some that are specific to different geographical regions. They include transient synovitis of the hip, reactive arthritis, viral arthritis, juvenile idiopathic arthritis, rheumatic fever and mucocutaneous lymph node syndrome. In some regions acute tuberculous arthritis or Lyme disease also need to be considered.

Clinical practice guidelines have been produced to enable septic arthritis, particularly of the hip, to be distinguished from other types of acute arthritis, such as transient synovitis. In one practice guideline, fever, non-weight bearing, erythrocyte sedimentation rate (ESR) >40 mm/hr, white cell count >12,000 cells/ml and C-reactive protein (CRP) >2 mg/ml were used to make the distinction[21]. When all these variables were present there was a high likelihood that the child had septic arthritis. However, the value of such clinical predictive algorithms remains unclear as studies from a separate centre showed that when all five variables were positive that the predicted probability of septic arthritis was only about 60%[22].

Treatment

Although there are many unresolved treatment controversies, recent studies show that early diagnosis and treatment of septic arthritis is usually highly effective and usually achieves a clinically normal joint[1]. Consequently, it is essential that children with septic arthritis are urgently referred to treatment centres and it is essential that the latter centres commence treatment as soon as possible.

Intravenous antibiotic therapy can usually be commenced in the emergency department following the collection of blood and joint fluid for gram stain, cultures and cell counts. Peripheral joints can be easily aspirated while the hip can be aspirated under ultrasound guidance. Antibiotics need to be started immediately the samples are collected. Although gram stains are often used the results are of minimal value in the diagnosis of septic arthritis[23]. The white cell count is also of minimal diagnostic value in the early stages of septic arthritis. Culture results will not be available for some days and even under optimal conditions, about half of the joint fluid cultures will be negative. Consequently, the selection of antibiotics are determined by the patterns of local bacteria

and the immunization histories of the children.

The child is then admitted to the ward. The next issue concerns drainage of the inflamed joint. While most centres drain the joint routinely some centres are investigating whether it is necessary in children who present early and who respond rapidly to intravenous antibiotics[24] .

There are several choices for joint drainage. One alternative is open drainage which is often used for the hip but arthroscopic drainage can also be used for many joints, including the hip[25,26] . Information is not available concerning the relative risks and benefits of open versus arthroscopic drainage for children with septic arthritis. Another alternative is repeated aspiration of the joint including daily aspirations of the hip under ultrasound guidance[18] . While, repeated aspirations may be effective in early cases it may be more difficult for the child that having an open or arthroscopic drainage which are usually only undertaken once.

The timing of joint drainage is a further issue. Although the severity of septic arthritis varies, published information suggests that treatment, including joint drainage, needs to be commenced within four days of the onset of septic arthritis[2]. Consequently, delays in undertaking the joint drainage need to be minimized even though in many centres, antibiotic therapy is commenced in the emergency room, after collection of blood and joint aspirates, rather than in the operating room, after open or arthroscopic drainage of the joint.

Following surgical or arthroscopic drainage, the joint capsule is left open. A drain is usually not needed in early cases. Occasionally a soft tissue collection of purulent fluid may appear some days later. Such collections can usually be drained by aspiration.

For children presenting early, there is no need to use a hip spica or cast and there is usually no need to consider additional surgical treatment for dislocations and other complications that occur in late cases.

Careful ongoing clinical assessment is required to determine the response of the child to the treatment. Many children with early presentations are good responders with rapid systemic and local improvement in their symptoms and signs[3,27]. Accumulating evidence from case-series and from comparative studies show that intravenous therapy for less than a week followed by oral antibiotics for a further two weeks is as effective as more prolonged intravenous and oral courses of antibiotics[5] . However, children who are poor responders, for whatever reason, require more prolonged intravenous therapy and careful ongoing assessment. Such children may be poor responders because of late presentation, MRSA, multifocal osteoarticular disease, immune compromise, or associated complications such as bacterial endocarditis[11] .

The choice of antibiotics is reviewed once the culture results are available. In many centres, the empirical choice of antibiotics is continued if the cultures are negative. Recent studies have shown that many of the latter children have DNA evidence of Kingella kingae infection. Fortunately, the

latter bacterium is usually sensitive to cephalosporins which are often selected empirically for use in children with suspected septic arthritis[14,28] .

Joint movement can commence once the inflammation improves and normal joint function is allowed once the inflammation has resolved. The ongoing care is determined by the child's clinical status and the changing levels of the inflammatory markers. The ESR and CRP can both be used but the CRP is a more sensitive marker than the ESR[29] .

Summary

In many countries, immunization programs have substantially reduced the number of cases of septic arthritis due to Hemophilus influenzae type B and Streptococcus pneumoniae. At the same time, there has been an increase in the prevalence of severe community acquired MRSA infections.

Current evidence indicates that standard methods of treatment are usually effective in the early phases of septic arthritis. Consequently, a concerted effort is needed to ensure that effective treatment commences early. Antibiotics, chosen according to local patterns of bacteria, can usually be commenced in the emergency department after blood and joint fluid samples have been collected. Surgical joint drainage continues to be the standard of care in most centres. Careful ongoing clinical evaluations and serial measurements of inflammatory markers are used to determine the responsiveness of the child to the treatment. Most children who present in the early phase of septic arthritis are good responders and consequently can benefit from the move to short courses of antibiotics, short hospital admissions and can expect full recovery of joint function. The major problems that occur in children with septic arthritis are largely the result of late presentation and late treatment.

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CHAPTER 4

OSTEOMYELITIS AND SEPTIC ARTHRITIS IN NEONATES

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Before antibiotics were widely available, about 10% of cases of septicemia resulted in osteomyelitis[1]. Neonatal osteomyelitis is a rare condition with a reported incidence of from 1 in 5000 live births in the UK[2] to 1 in 15000 in the United States[3]. Certain organisms are more likely to cause osteomyelitis: during the epidemics of neonatal staphylococcus aureus infection in the 1950s and 1960s there was a higher incidence of neonatal osteomyelitis. Methicillin-resistant strains of S. aureus (MRSA) cause upto 30% of these infections[4]. Boys are affected more commonly than girls (sex ratio 1.6:1).

Preterm babies are at increased risk of developing osteomyelitis. In a study in the late 1970s, 9 of 39 babies (23%) with neonatal osteomyelitis weighed <2000g at birth[3] compared with 17 of 30 (57%) in the more recent study of Wong et al.[5] reflecting the increased survival of very premature babies.

Hematogenous spread

The hematogenous route is the most common mechanism for osteomyelitis; about 70% of blood cultures are positive[5,6] and multifocal osteomyelitis occurs in about 0% of cases[4]. Neonatal septicemia, however, is more common than neonatal osteomyelitis, so other factors also come into play. One of these, is the relative propensity of different organisms to seed to the bone.

In about one-half of all cases of neonatal osteomyelitis, there is a preceding bacterial infection such as skin sepsis, peri-umbilical sepsis, otitis media, pneumonia, conjunctivitis, or a deep abscess, suggesting

that the pathogenesis involves hematogenous spread to the bones. Bacterial osteomyelitis is also a rare complication of neonatal viral infections caused by varicella and herpes simplex viruses.

Umbilical catheters are associated with an increased risk of osteomyelitis[7]. This may be due to septic emboli from the catheter tip or direct inoculation of organisms from the umbilicus into the bloodstream at the time of catheter insertion. Cases of osteomyelitis have occurred following brief umbilical catheterization for exchange transfusion. Staphylococcus aureus is the commonest organism, but Gram-negative bacilli and fungi can also be responsible. The hip or knee joints are usually involved, generally on the same side as the catheter tip[7].

Hematogenous infection of the long bones usually starts in the most vascular part of the bone, the metaphysis, where there is a sluggish blood flow through the arteriolar loops[8]. From there, infection can spread to the adjacent growth plate (the physis), across the growth plate via transphyseal blood vessels to the epiphysis, or may rupture into the joint space, because the synovial membrane in the neonates extends down to the metaphysis. The transphyseal vessels which connect the metaphysis with the epiphysis disappear with increasing age and by 1 year of age are absent. In addition, the bone is very thin in neonates and the periosteum is loosely attached. Infection of neonatal bone almost always decompresses spontaneously with rupture into the joint, causing concomitant septic arthritis. Lifting of the periosteum occurs, often involving much of the length of the bone, and pus may track through the periosteum to form a subcutaneous abscess. It is because of ready decompression of pus in the bone into joint or subcutaneous tissues that neonatal osteomyelitis is relatively painless.

As the bone is very vascular, it heals rapidly. Sequestrum rarely forms; when is does, it is often resorbed. However, the rich blood supply also facilitates infection of the cartilaginous growth plate and epiphysis, and the resulting damage to the cartilage is generally irreparable. Neonatal osteomyelitis of the long bones often results in impaired growth of the bone [9,10].

Direct Inoculation

Heel-pricks should always be done in the fleshy side of the heel; the point of the heel overlies the os calcis, and calcaneal osteomyelitis or osteochondritis, commonly due to S. aureus or Proteus mirabilis, can complicate heel-pricks performed too near the midline.

Contiguous Spread

Scalp abscesses, usually caused by S. aureus, can spread to involve the underlying parietal or occipital bone. **Cephalo hematomas** may become infected, generally with S. aureus or Gram-negative bacilli (Escherichia coli, Pseudomonas) and extend to involve the parietal bone. **Paronychias** may occasionally spread to the bone of the underlying finger. Maxillary osteomyelitis may extend from maxillary antral **sinusitis,** although it can also occur in the absence of sinusitis, presumably due to hematogenous spread.

Transplacental Infection

This is the mode of infection in osteitis associated with congenital syphilis. It is an extremely rare cause of bacterial osteomyelitis occurring in association with early-onset sepsis.

Trauma

Although in many series of babies with neonatal osteomyelitis, there has been some association with obstetric trauma, such as forceps delivery, the proportion of babies with osteomyelitis experiencing such trauma has not generally exceeded that of normal babies.

Microbiology

As with older children, Staphylococcus aureus is the commonest cause of neonatal osteomyelitis, accounting for more than 80% of all cases up to the early 1970s, and continuing to be the major cause in most countries till date. However, in the USA there has been a shift to group B streptococcus (GBS) as an important and sometimes the major organism[11]. When MRSA is prevalent in the neonatal unit, this organism has been found to be an important cause of osteomyelitis. It is particularly likely to colonize and infect very preterm babies [4,12].

Although the organisms causing osteomyelitis might be expected to reflect the organisms causing sepsis, and in particular early-onset septicemia, certain organisms seem to have a tropism for bone and occur in the absence of overt septicemia. Most cases of GBS osteomyelitis occur in previously healthy babies who did not have clinical early-onset sepsis. In contrast, certain organisms that are fairly common causes of sepsis, such as Gram-negative bacilli, are relatively rare causes of osteomyelitis, although they were the commonest cause in a series from India[13]. Faecal streptococci, increasingly described as the cause of late-onset sepsis, has not been reported to cause neonatal osteomyelitis. Haemophilus influenzae is a very rare cause of neonatal and infantile osteomyelitis.

To summarise, it is clear that in many cases the organisms causing osteomyelitis seed bone at the time of acute septicemia, which may be of early or late onset. Some organisms virtually never cause osteomyelitis despite causing septicemia; other organisms, such as S. aureus, cause osteomyelitis disproportionately often. Thus, the tropism for bone of different organisms varies. In the case of some organisms, such as group B streptococcus, osteomyelitis appears often to result from an occult episode of bacteremia.

Clinical Presentation

The onset is either insidious or fulminant. In the **insidious form**, which is the commoner presentation, the baby is feeding and developing normally and often afebrile. In a recent series of babies with osteomyelitis, two-thirds were afebrile[5]. The initial presentation is with swelling of a limb or joint and reluctance to move the limb. Redness is rarely present and 'point tendeness' is absent or difficult to elicit. There may be irritability on handling, for example when changing the nappies. Sometimes the reluctance to move a limb is so severe as to cause a pseudoparalysis, which can be misdiagnosed as nerve palsy[14]. The classic example is a

mistaken diagnosis of Erb's palsy: the main distinction is that Erb's palsy is painless, whereas in osteomyelitis of the clavicle or humerus, movement of the arm is painful. Involvement of the femur can cause foot drop, and the resulting septic arthritis of the hip may cause the baby to hold the leg flexed, abducted and externally rotated. Pseudoparalysis of a limb may also be caused by the osteitis of congenital syphilis. Oedema may be a prominent feature.

In the newborn period, not only is the presentation often insidious, but multiple bones are involved in about 40% of cases. The infection commonly decompresses into the adjacent joint, and the initial presentation may be with an abscess or an unexplained swelling. In contrast, osteomyelitis in older children is acute, with fever; a single bone is most commonly involved, and exquisite local tenderness is the rule. It is, therefore, extremely important to examine assiduously all the joints and bones of a baby with possible osteomyelitis.

If the clinical diagnosis of osteomyelitis is not made early, the baby may develop a subcutaneuous abscess with more evident inflammation. Thus, retroperitoneal abscesses should suggest vertebral osteomyelitis, whereas an abscess in the thigh, buttock, groin or iliac fossa suggests femoral or pelvic osteomyelitis.

Maxillary osteomyelitis presents with fever, poor feeding, conjunctivitis, and erythema and oedema of the eyelid. Proptosis and chemosis are common. The cheek often becomes swollen and inflamed and an abscess may form which drains below the eye. There is often a unilateral purulent nasal discharge and swelling of the hard palate, which may become a draining abscess. The commonest error is to misdiagnose maxillary osteomyelitis as peri-orbital cellulitis.

In the **'fulminant' form of osteomyelitis**, signs of bone and joint involvement may occur at the time of, or some times after the signs of sepsis. The babies are lethargic, with or without fever, do not tolerate feeds, may have abdominal distension and jaundice. Multiple bones or joints may be involved. There is often evidence of abscess formation elsewhere, e.g. liver abscesses or pleural empyema, and babies are gravely ill. The commoner sites of neonatal osteomyelitis are femur (35%), humerus (17%) and tibia(14%).

Diagnosis

Clinical

The most important diagnostic test is clinical acumen. The possibility of neonatal osteomyelitis should be considered in any baby with soft tissue or joint swelling, subcutaneous abscess, cellulitis or immobility of a limb. Groin abscesses secondary to septic arthritis of the hip may be misdiagnosed as hernias or lymphadenopathy. Cellulitic lesions may be erroneously treated with 5-7 days of antibiotics without considering possible underlying osteomyelitis. Limb immobility may be misdiagnosed as due to nerve palsy.

Staphylococcus aureus septicemia -In a study by Wong and colleagues, 27 babies with S. aureus septicemia but no clinical signs of osteomyelitis or septic arthritis were investigated by bone scan[5]. Four (15%) had positive bone scans, suggesting S. aureus

septicemia alone may be an indication for bone scan.

Radiographs

Unlike older children, radiographic changes appear early in neonatal osteomyelitis. The thin periosteum ruptures easily, and osteolytic lesions. soft tissue swelling and periosteal elevation are often seen within 7 days of onset of infection.

Radiographs should be obtained in all newborns with suspected osteomyelitis and septic arthritis, and it is helpful to X-ray the opposite limb for comparison.

Ultrasonography

Although septic arthritis is primarily a clinical diagnosis, ultrasonography of the joint space can confirm joint effusion(s) in septic arthritis, and is particularly useful in doubtful cases and in babies with multiple joint involvements.

Bone Scan

It used to be thought that technetium-99m methylene diphosphonate (99m TC) bone scan was insensitive in neonatal osteomyelitis[15]. With improved resolution of scanners, bone scan is now both sensitive and specific: the sensitivity in a recent study was 84%, specificity 89%, positive predictive value 79% and negative predictive value 92% [5].

Technetium is taken up by active osteoblasts, so is of no value in septic arthritis unless there is concomitant osteomyelitis. In osteomyelitis, enhanced uptake of 99m TC is usual but occasionally vascular compromise results in 'cold spots' of reduced uptake.

Bone scans are often abnormal within 2-3 days of onset of symptoms, whereas radiographs are often not abnormal until symptoms have been present for 6-7 days

Gallium scan

Gallium-67-labeled citrate is taken up by iron-metabolizing cells, including neutrophils. It delivers five to six times the radiation dose of bone scan and is slower to be absorbed (48 hours), so is very much a second-line investigation. However, gallium scanning can be useful when bone scan is equivocal, or when osteomyelitis or septic arthritis is strongly suspected, but radiographs and bone scans are normal or inconclusive. In Wong's study, the use of gallium scans in addition to bone scans in selected patients gave improved sensitivity (90%), specificity (97%), positive (93%) and negative (95%) predictive values[5].

Hematological Investigations

The ESR is raised in only about half of all babies with osteomyelitis[5,16] and should not be used as a screening test for osteomyelitis. Other acute-phase reactants such as serum C-reactive protein (CRP) are similarly unreliable, and white cell counts, neutrophil ratios, platelet counts, etc. give non-specific information and may be normal in osteomyelitis [4].

Biopsy or Aspirate

A tissue diagnosis, by bone biopsy or joint

aspirate, improves the reliability of identifying an organism only marginally from 70% for blood culture alone, to about 80%[4]. An orthopaedic opinion should be sought on every baby with probable osteomyelitis or septic arthritis.

Septic Arthritis

Septic arthritis complicates about 50% of cases of neonatal osteomyelitis, particularly osteomyelitis of the long bones. Occasionally, septic arthritis occurs in the absence of demonstrable osteomyelitis, in which case the pathogenesis is either direct hematogenous seeding of the joint (primary septic arthritis) or secondary to occult osteomyelitis. Staphylococcus aureus is the commonest single cause of all cases of primary septic arthritis (about 45%) but Gram-negative bacilli (25%) cause proportionately more cases of osteomyelitis.

Clinically, septic arthritis usually presents with obvious swelling of one or more joints. The overlying skin is often not red, fever is usually absent, and, although the presence of pain on moving the joint and paucity of movement of a limb will differentiate septic arthritis from most other diagnoses, there may be surprisingly little discomfort or impairment of function.

The commonest joints involved are the hip and the shoulder, followed by the knee, elbow and ankle [4].

Septic arthritis, if untreated, will cause growth plate disturbances and subsequent shortening of an affected limb. Hence the need for urgent diagnosis and treatment.

Management

In view of the wide range of organisms that can cause neonatal osteomyelitis and septic arthritis, and the long duration of antibiotic treatment, it is particularly important to identify the organism responsible. Pus should, therefore, be aspirated by needle or open drainage from bone, joint or soft tissue abscesses. Blood should always be cultured. Up to 20% of joint aspirates are sterile in septic arthritis, possibly because joint fluid is bacteriostatic or because the organisms are limited to the synovium. Urine and CSF should also be cultured, as the likelihood of metastatic spread through bacteremia is high.

Surgical drainage is necessary for large soft-tissue abscesses, and open surgical drainage of the relevant joint is essential to prevent necrosis of the head of the femur or humerus. Smaller joints can usually be effectively treated by regular aspiration and rarely need open surgical drainage. Because there is spontaneous decompression due to infection of the shaft, it is not usually necessary to drill the cortex of the long bones[3] but pus in the bone under pressure should be drained surgically.

Antimicrobial therapy is guided by Gram stain on the aspirated pus. If no organisms are seen, or no pus is obtained, empirical therapy might comprise a penicillinase-resistant penicillin (flucloxacillin, oxacillin, vancomycin) to cover staphylococci and streptococci and an aminoglycoside or third-generation cephalosporin for Gram-negative bacilli.

Anaerobic infection will normally respond to this regimen, but, if this seems a likely

cause, either the addition of metronidazole (favoured in the UK) or the use of clindamycin (favoured in the USA) is advisable. Clindamycin is an excellent treatment for Gram positive cocci (except MRSA).

Data concerning older children are accumulating to the effect that treatment can be given orally after a few days. As oral absorption is uncertain in neonates, oral therapy is not advised. Oral therapy can only ever be countenanced if the baby is observed in hospital to monitor clinical progress and measure weekly serum bactericidal titres (titration of the patient's serum against the patient's organism or a laboratory strain of S. aureus[17]). Treatment of osteomyelitis for a period of 3 weeks or less results in at least a 15% failure rate, whereas treatment for a period of 4 weeks or more has a 5% or lower failure rate[18], therefore treatment should be for at least 4 weeks.

Early immobilization of the limb and joint is usually necessary, but as soon as there is no further pain physiotherapy should be started to mobilize affected joints.

SILENT OSTEOMYELITIS

The management of 'silent lesions' is controversial. If these are found by bone scan in addition to a clinically evident focus, the baby will obviously be treated for at least 4 weeks with antibiotics. More of a problem is the baby with S. aureus septicemia, who is found to have a positive bone scan, but no clinical signs, i.e. 'silent osteomyelitis' should be treated for 7-10 days as for septicemia, or for 4 weeks? The improved reliability argues for a full 4 weeks, but presumably, in pre-bone scan days, these babies rarely developed later overt osteomyelitis, so 7-10 days of treatment sufficed. There does not seem to be a clear-cut answer to which regimen is 'correct'.

PROGNOSIS

The prognosis is neonatal osteomyelitis and/or septic arthritis is much worse than for older children. Shortening of an affected limb is a common outcome, particularly in preterm babies, occurring in 30-50% of babies[10,16]. Early diagnosis and treatment is vital to limit long-term sequelae.

Prevention

Heel-pricks should never be done on the point of the heel. If staff see a baby with a sticking plaster overlying the os calcis, careful enquiry should be made to find who performed the heel-prick; -for educational, not punitive, reasons.

Invasive procedures should be kept to a minimum, and particular care should be taken when needles are introduced near bone or joint space.

Summary

- The neonatal periosteum is thin and the joint space large, so osteomyelitis and septic arthritis often coexist as pus ruptures from the bone into the joint.
- The presentation may be insidious or with fulminant sepsis.
- In the insidious form, there may be no fever, normal feeding and few signs.
- The possibility of osteomyelitis should be considered in any baby with soft tissue

or joint swelling, subcutaneous abscess, cellulitis or immobility of a limb.

- Radiographic changes appear early in neonatal osteomyelitis, usually within 1 week of symptoms, and radiographs should always be obtained of the affected area and the opposite side for comparison.
- Ultrasonography is useful in suspected septic arthritis.
- Bone scan is quick, has a low radiation dose and is sensitive and specific in neonatal osteomyelitis.
- Gallium scan is slow, has a high radiation dose, but is useful if bone scan is inconclusive.
- Clinical suspicion needs to be high, as early diagnosis and treatment improve the outcome of osteomyelitis.
- The prognosis of neonatal osteomyelitis is poor, with limb shortening a common complication in 30-50%.

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CHAPTER 5

Neonatal Septic arthritis

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Introduction

Modern perinatal care has considerably improved the morbidity associated with musculoskeletal infection in the neonates. However, early diagnosis and management continues to challenge the orthopaedic surgeons. The fetus is well protected inside the womb, against bacterial infections, by maternal immunity. Once the child is born it is largely the peri-natal factors which determine the susceptibility to infection. Over 95 % of neonates will have a normal transition to infancy, and will not suffer any bone or joint problems. The estimated incidence of infection is 1 -3/1000 admissions to the Neonatal Intensive Care Units (NICU)

Musculoskeletal infection in the neonates is seen in two distinct groups. One is the neonate, who is sick, premature and needs intensive care. Here the hospital environment, inherent immunity of the child, presence of pre-existing ailments (respiratory, GI and Skin), in-dwelling catheters all contribute to an increased risk of infection. The infection is usually due to bacteremia secondary to nosocomial infection.

The other group is a healthy neonate, who has been discharged from the hospital and then presents 2 -3 weeks later with bone and joint infection. In the second group, the cause is mainly the weak immunity of the neonate which has not adapted to the external environment.

Clinical Features

Clinical manifestations of infection can be quite confusing in a neonate. Both objective

and subjective signs and symptoms differ depending on the setting of infection: a NICU or communtiy presenter. Typical symptoms like high grade fever, and warmth or hot extremity may not be present in a sick child. Subtle signs like irritability, decreased active movements, pain with passive joint movement, skin cellulitis may be present to a varying degree. Many of these children are already on high grade antibiotics which suppress the normal inflammatory response and this coupled with multiple in-dwelling lines and poor immunity often contributes to a delay in diagnosis. As opposed to this a community presenter may manifest with fever, decreased movement of the extremity, poor feeding regime and local signs which may be useful in making a diagnosis of infection. However, a high index of suspicion is usually required in both groups of neonates to alert the examiner for further investigation.

Investigations

A routine haemogram (CBC) with ESR, CRP is usually required. Routine blood parameters to see for baseline Hb, CRP and ESR are helpful to diagnose and monitor the course of treatment. In the community setting, CRP is useful parameter and is highly sensitive for infection. In a immune compromised child it may not be very reliable. Rather than a single value, changing trend in a CRP is more informative. ESR is not very useful in neonates, but with chronicity of infection, a decreasing trend in ESR usually indicates subsidence of infection. Blood culture must be routinely performed and sometimes it can identify the pathogen. However, the blood sample must be promptly analyzed after collection and any contamination must be prevented.

Radiographs of the affected extremity are useful. Unlike children, infections in neonates can cause rapid bone destruction and subtle changes like erosion of the cortex, cavitation in the metaphysis or epiphysis appear by 2- 3 days. Ultrasonography is very useful to detect any joint effusion and sub – periosteal oedema. Although USG cannot clearly differentiate between pus and synovial fluid, in experienced hands USG guided aspiration may be very useful to confirm the diagnosis. USG is also helpful to diagnose a deep seated abscess which may mimic septic arthritis.

In select cases an MRI is the most sensitive; however it should not delay initiation of treatment in a suspected case of neonatal infection. A bone scan is rarely indicated in neonates except when the clinical picture and imaging studies are inconclusive.

Microbiology

The epidemiology of musculoskeletal infection is evolving and gram-postive organisms continue to dominate the list, especially with the emergence of MRSA. In the community setting, staphylococcus aureus still is the number one pathogen, followed by group B Streptococci and then the gram-negative organisms. In the sick neonate or a premature child with history of NICU admission, gram-negative orgnaism (Enterobacteriacae) are more likely to be the culprit. MRSA is also fast emerging as pathogen in neonates. With history of prolonged hospitalization, and previous long-term intravenous antibiotics administration one must also consider fungal species like Aspergillus and Candidia. The source of infection here is endogenous

following colonization of the babies in the NICU. About 10% of babies get colonized by 1 week and 64 % by 4 weeks. Multiple site involvement must raise the suspicion for fungal infection.

Rarely contamination of water in the neonatal unit can cause Coxsackie B4 septic arthritis. TB and syphilis must be considered in atypical case contexts.

Management

Treatment is directed towards obtaining a rapid cure as the sequalae of septic arthritis can be quite devastating. Any suspicion of infection in a neonate should initiate prompt investigation to identify the site and source of the infection. Ideally, a positive blood culture, joint or bone aspirate must be obtained before commencing anti-microbial therapy. But, often this is not the case, and many neonates are administered oral or iv antibiotics at the onset of symptoms making the diagnosis difficult.

The choice of antibiotic is usually based on the prevalence of infection in a particular community. In the absence of an identifiable pathogen, broad spectrum, 3rd generation cephalsporins are the drug of choice combined with Amikacin or Gentamicin to cover most common organisms. Linezolid, Vancomycin, Teicoplanin and Tobramycin are reserved until there is a positive report to support their use.

In any case, if there is no improvement in clinical parameters within 48-72 hours of anti-microbial administration, then surgical intervention is mandatory.

This may involve joint lavage, especially in a sick neonate to a classical arthrotomy. Knee, ankle, elbow are superficial joints which can be easily accessed by blind needle aspiration.

In neonates, any osteomyelitis is a potential septic arthritis. Hence, joint decompression is important besides bone debridement.

For the hip joint, Psoas and Pelvic area, either USG or IITV guided aspiration and lavage is required.

Surgical decompression of the infection results in rapid healing of bone and joint due to clearcane of tissue-destroying fluid and also due to decrease in the tamponade effect on the delicate circulation around the growth plate.

This is important of septic hip in a neonate. A negative exploration for the hip is far better than procrastination, as the joint destruction is permanent.

Pus or fluid obtained during surgery must be sent for Gram Staining and appropriate culture. Anti-microbial threapy can then be tailored for the individual child.

The duration of parenteral anti-microbial therapy is a matter of debate. While the final choice is dictated by the prevalent pathogen in the bacteriological and culture report, the duration of intra-venous treatment varies from 5 days to 5 weeks. Recent studies have shown that a shortened course of appropriate antibiotics for 5 days followed by oral antibiotics for 3 weeks is as efficacios as 6 weeks of parenteral therapy. The problems of prolonged intravenous cannulation can be

obviated by this shortened durtation of treatment.

Close monitoring of the clinical, blood and radiological parameters is required to ensure that the treatment is effective and the outcome satisfactory.

Antibiotics can usually be stopped by six weeks if the child has improved. Radiographs must be taken 6 monthly to see for any sequalae and usually by two years the child can be discharged from care.

Conclusion

Neonatal septic arthritis is unique for its presentation and management and poses a formidable challenge even to the most astute clinician. Prompt diagnosis and treatment of the native joint is not only rewarding but also saves the child from a lifelong disability.

CHAPTER 6

Understanding Musculoskeletal sepsis: A Pediatrician's Perspective

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Introduction

Musculoskeletal infections include osteomyelitis, septic arthritis, necrotizing fasciitis, and pyomyositis. They can occur in previously healthy children and lead to severe long-term morbidity if not recognized and treated promptly, thus, their early diagnosis is crucial. In addition to making a diagnosis, identification of the causative organism is imperative. Initial antibiotic management should cover the most common etiologic organisms, and consideration should be given to local incidence of community-acquired methicillin-resistant S. aureus (CA-MRSA).

Initial presentation of these conditions is often to the primary care pediatrician, which, sometimes, may lead to the inadvertent delay in identification and management of the disease. In this chapter, all the above four conditions are presented, describing their etiology, pathogenesis, clinical features and evidence based management, pertaining to the pediatric age group. Neonatal conditions are detailed in a separate section.

Osteomyelitis

Osteomyelitis is an infection of the bone and bone marrow usually of bacterial origin unless specified otherwise[1,4] and arthritis is infection of joint space.

Osteomyelitic lesions have been observed in Egyptian mummies dating as far back as four thousand years. In 1844 Nelaton coined the term Osteomyelitis[2].

This disease most commonly occurs in infants and children, however it may be seen at any age. Almost 50% cases are found in less than 5 years of age[1,3,5], and incidence is 2 to 4 times frequent in boys as compared to girls [1,3] presumably because trauma plays a critical role.

Patients with sickle cell disease have high incidence of this disease.

Osteomyelitis most commonly involves long bones, and femur, tibia and humerus together bears the 68% burden of disease, although any bone may be affected. In more than 90% cases single bone is involved and remaining have two or more areas affected [1].

Definition

Acute Hematogenous osteomyelitis (AHO), by definition, includes processes that have been operating for a week or less at the time of diagnosis.

It is assumed that osteomyelitis/septic arthritis is caused by bacteria, however, in many cases the offending organism can not be isolated. In such situation it is useful to have certain criteria.

Peltola and Vahvanen definition[6] :
Consider diagnosis firm when two of the following four are present:

1. Pus aspirated from the bone;
2. Positive bone or blood culture;
3. Classic symptoms of the localized pain, warmth, swelling and limited range of motion of the adjacent joint;

And, radiographic changes typical of osteomyelitis.

Etiology/Microbiology

Most of the diagnosed cases are pyogenic and most frequently isolated bacteria is *Staphylococcus aureus,* which is responsible for up to 61 to 89% of cases of AHO [7,8]. The second commonest organism is Group A b-hemolytic streptococci (GABHS), accounting for almost 10% cases.

Haemophilus influenzae, Streptococcus pneumoniae and Kingella kingae are another relatively common organisms in patients with AHO. Certain gram-negative bacteria are also known to cause AHO. Salmonella spp. are commonly identified in patients with sickle cell disease, and Pseudomonas aeruginosa is often identified in cases of osteochondritis after puncture wounds of the feet Mycobacteria, Brucella and fungi are rare causes of osteomyelitis[9]. Polymicrobial infection is rare and is seen most commonly in cases of puncture wounds or other trauma.

Although S. aureus is the most commonly reported organism in the neonatal age group, Group B streptococcus and enteric gram-negatives such as Escherichia coli are also common[10].

Recently, worldwide, Pediatric Intensive Care Units have seen dramatic increase in community associated methicillin resistant Staphylococcus aureus (CA-MRSA) [11]. The problem is of such magnitude that it has been termed as emerging epidemic [12]. It is difficult to treat and the mortality associated with this organism is unacceptably high, 50% as compared to 4% over all mortality due to severe sepsis [12].

Pathogenesis

Hematogenous spread is by far the commonest route of infection. Nonetheless, infection can occur through direct inoculation, and contiguous spread from a other local infection [13].

In children, most cases result from hematogenous deposition of organisms in bone after a transient episode of bacteremia. Approximately one third of patients report a history of blunt trauma [7]. Direct inoculation of bacteria into bone may occur during surgery or as a result of penetrating trauma, puncture wounds, or complex fractures.

The metaphysis is the region where osteomyelitis begins most often, and spread may occur from this point to involve any other location. Rarely, this process may begin in epiphysis. There is a specific reason for this preference of metaphyseal involvement.

In children, the blood supply of epiphysis is separate from that of the metaphysis[2] and metaphyseal vascular channels form loops near growth plate. Blood flow is rather slow, and the capillary basement membrane and reticuloendothelial system is deficient here. This creates an ideal medium for proliferation of pathologic bacteria. Experimental bacteremias have been shown to produce foci of infection *only* in these areas. Trauma likely plays more than circumstantial role.

Virulence factors of certain bacteria also favor the development of hematogenous osteomyelitis [13,14]. As the infection advances, cortical bone is destroyed and infection and inflammation may extend into the subperiosteal space. Necrotic cortical bone may separate and lead to the formation of a sequestrum, and new bone may form an incasing sheath around necrotic bone, known as an involucrum. By the process of sequestration and involucrum formation, noncollapsible cavities harboring bacteria, granulation tissue, and dead bone are produced with continuous or intermittent drainage of pus. This constitutes the chronic stage of osteomyelitis.

Clinical Manifestations

In case of bone and joint sepsis, pain is the leading symptom, but this is not always verbalized by children. Therefore it is extremely important for the pediatricians to appreciate the fact that pain may manifest in many other ways like limping, refusal to walk, refusal to bear weight or pseudoparalysis. Often, refusal to bear weight is the earliest symptom. Otherwise affected children may appear well or may have systemic involvement ranging from malaise to shock.

The very earliest sign is fever and local bone tenderness, followed later by a fluctuant mass if a subperiostial or soft tissue abscess has developed. Spread to adjacent joint (which is particularly common in neonates) should be ruled out by palpation and range of motion evaluation. Usually, passive motion of an extremity is not resisted unless a joint involvement or soft tissue abscess is present. Vertebral or pelvic osteomyelitis may present as abdominal pain and can resemble more common septic arthritis of hip.

Differential Diagnosis

The differential diagnosis for osteomyelitis includes cellulitis, septic arthritis, non displaced fracture, toxic synovitis, thrombophlebitis, trauma, fracture, rheumatologic diseases (eg. juvenile idiopathic arthritis), pain crisis in sickle cell disease, Ewing's sarcoma, osteosarcoma, and leukemia.

Laboratory Evaluation and Diagnosis

The diagnosis of acute osteomyelitis is often overlooked in the first few days because attention is generally paid to signs of sepsis and local findings are ignored or misinterpreted. Acute osteomyelitis should be suspected if there is pain and swelling of the limb with marked tenderness over the metaphyseal region of a long bone. One should not wait for radiological changes in the bone to appear before starting treatment. Otherwise it would be too late and chronic osteomyelitis is likely to follow. None of the blood tests are specific for osteomyelitis. Leukocytosis and elevated ESR and CRP may be seen, last two are used sometimes to monitor the progress and response to therapy.

Organism identification is extremely important for both, confirmation of the diagnosis and guiding antimicrobial selection. Needle aspiration is likely to grow an organism in almost 65% of cases[5,7] whereas blood cultures yield positive results in one third to little more than half of specimens [4,5].

The role of plain X-ray film in the diagnosis of early bone and joint sepsis is often undervalued. It is because, the most sought after change is osteopenia or bone lysis, which takes 7-10 days to develop. Actually, deep soft tissue swelling with obliteration of fat plane is the earliest radiographic evidence of osteomyelitis. This can easily be seen if contra lateral limb is also taken in X-Ray for comparison. This technique is less useful for axial skeleton, due to bulky overlapping muscles. The periosteal reaction is seen in 2nd and 3rd week [7,15].

Time line of appearance of radiologic features on X-Ray

In cross sectional imaging, Gadolinium enhanced MRI is the choice of imaging [15]. With sensitivity of 97% [16], it can differentiate between bone and soft tissue infection. MRI allows early diagnosis by reporting edema and exudate of the medullary space.

Days /weeks	Radiologic features of Osteomyelitis
1-7 days	Deep tissue swelling, loss of fat plane
7-14 days	Osteopenia/lytic bone lesion
10-21 days	Periosteal reaction

Bone scan or Nuclear scintigraphy is helpful when multiple sites are suspected, and in differentiating osteomyelitis from cellulitis. The technetium 99m methylene diphosphonate bone scan is the most commonly ordered nuclear imaging procedure [15].It is sensitive for the detection of early osteomyelitis[13] but is not specific for infection.

Advantages and disadvantages of various imaging modalities for osteomyelitis

Modality	Advantages	Disadvantages
Plain film	Inexpensive, quick, easy	Insensitive in early disease
CT	Improved sensitivity, relatively quick	Radiation exposure, may require sedation
MRI	Very sensitive, even in early disease, may reveal pus collections or extension into adjacent joint or soft tissue	Long study, often requires sedation,Expensive
Bone scan	Very sensitive, identifies multifocaldisease, may reveal unsuspected sites in preverbal children	Less specific, long study, often requires sedation, expensive, radiation exposure

Treatment

General supportive management

Children with AHO, at presentation, may be seriously ill. At least initially, the need to support patient's vital function takes precedence over establishing a precise diagnosis. The pediatrician must appreciate the importance of prompt resuscitation and stabilization. The sick children require rapid cardiopulmonary assessment and actions accordingly. This includes Airway, breathing and circulation; correction of hypoglycemia, if any; control of seizures and correction of arrhythmia.

Shock may require fluid boluses, inotropes or vasopressors; respiratory distress may necessitate oxygen therapy, and respiratory support in form of CPAP, non invasive or controlled mechanical ventilation.

Definitive management

Immediate inpatient treatment is imperative. Upon admission, a pediatric orthopedic surgeon should be consulted, especially if imaging reveals subperiosteal or soft-tissue abscesses, sequestra, or intramedullary purulence, because they require expertise which may not be commensurate with the best skills of the pediatrician.

In pediatric patients, empiric drug therapy should cover S. aureus and GABHS, as these two organisms constitute almost 70-90% of offending pathogens. Traditionally, a semi-synthetic penicillinase-resistant penicillin was recommended (eg, Cloxacillin, 150–200 mg/kg/d, divided in four doses)[1]. There are several reports which have indicated a sharp increase in the number of cases of community acquired methicillin-resistant S. aureus (CA-MRSA) infections[17]. When ever CA-MRSA is suspected, combination of vancomycin, clindamycin, sulfamethaxazole, rifampin, doxycycline, gentamycin and IVIG (2 gm/kg) may be required[11,12]. If vancomycin resistance is found, or improvement is not seen in clinical course and CRP levels, then linezolid or teicoplanin are the options[12].

If MRSA is not suspected then, in infants and children, a third-generation cephalosporin (eg, cefotaxime, ceftriaxone) provides coverage against many S. aureus (MSSA), most streptococci, H. influenze and K. kingae[1].

In patients with presumed pseudomonal infection (eg, puncture wound osteochondritis of the foot), one should consider an extended spectrum beta-lactam (eg, ceftazidime, cefepime, piperacillin/tazaobactam) plus an aminoglycoside for at least the first 2 weeks.

Once an organism has been identified, coverage can be narrowed based on results of susceptibility testing. The minimum recommended length of treatment is 3 weeks because of the increased likelihood of developing chronic osteomyelitis if the length of therapy is shortened[18].Most authors recommend treatment for 4 to 6 weeks[19]. If long-term intravenous antibiotics are administered, placement of a peripherally inserted central catheter should be considered for completion of the regimen as an outpatient. Several studies support switching to an oral antibiotic if there is a high likelihood of compliance, an organism has been identified, clinical improvement is noted, the patient is afebrile, and inflammatory markers have begun to normalize after the first week of parenteral therapy [4,5,20,21]. When changing to oral antibiotics, doses of two to three times those normally recommended are often used.

A surgeon's role includes performing diagnostic needle aspiration, decompression and drainage (when necessary), and long-term follow-up in complicated cases. Surgical intervention is reported to be required in approximately 50% of cases [4,7].

Chronic osteomyelitis

Up to 19% of patients with AHO who are inadequately treated may develop chronic osteomyelitis compared with 2% of patients who receive antibiotic therapy for longer than 3 weeks[7]. Chronic osteomyelitis is characterized by a chronic, suppurative course with intermittent acute exacerbations. This may occur after an open fracture or when subperiosteal or metaphyseal pus is not adequately drained. Treatment is often difficult and involves long-term antibiotics, sometimes up to 6 to 12 months, often in combination with one or more surgeries for debridement[18].

Brodie abscess

A Brodie abscess is a subacute form of osteomyelitis that results in a collection of necrotic bone and pus in a fibrous capsule, which is formed by surrounding granulation tissue[18]. Management involves surgical drainage followed by antibiotic therapy. Properly treated patients have a good prognosis.

Osteomyelitis in patients with sickle cell anemia

Osteomyelitis in patients with sickle cell disease may be difficult to differentiate from a vaso-occlusive crisis. Both can present with fever, bone pain, and tenderness.. In addition to S. aureus, Salmonella spp. are common etiologic agents [22], and empiric therapy (eg. a cephalosporin, possibly in combination with vancomycin) should be chosen accordingly.

Tubercular Osteomyelitis

The time lag between infection and

development of bone TB is around 1 year. The intial focus is usually an epiphysis or metaphysic, rarely the diaphysis. Tubercular Osteomyelitis is purely destructive or lytic with little or no bone reaction. Treatment is mostly medical, and consist of antitubercular chemotherapy for 9-12 months.

Fungal Osteomyelitis

These may be disseminated (sporotrichosis, candiasis) or direct (eumycetoma). Aggressive debridement is more important than that in bacterial osteomyelitis.

Septic Arthritis

Septic arthritis refers to bacterial invasion of the joint space and the subsequent inflammatory response. The peak incidence is in children younger than 3 years, and boys are affected approximately twice as often as girls [23]. The most commonly affected joints are those of the lower extremities, including knees, hips, and ankles, which account for up to 80% of cases [23-25].

Pathogenesis

Septic arthritis may occur as a result of hematogenous seeding of the synovium during a transient episode of bacteremia, from contiguous spread of an adjacent infection such as osteomyelitis, or by direct inoculation during surgery or as a result of penetrating trauma. Once the joint space is invaded by bacteria, endotoxins are released. This leads to destruction of the synovium and cartilage matrix. Although rarely fatal, destruction of the joint space leads to long-term sequelae in a significant percentage of patients[26].

Microbiology

S. aureus is the most common organism out side the neonatal period. GABHS and S. pneumoniae are also frequently found.

In the neonatal period, S. aureus remains a common organism, but group B streptococcus and gram-negative enteric bacilli are also frequently identified.

P. aeruginosa, H. influenzae type B, and K. kingae also has been reported as a causative agent. In addition to the usual organisms, patients with sickle cell disease are at risk for bone and joint infections by Salmonella spp. Neisseria meningitides is a rare cause of septic arthritis but is commonly associated with reactive arthritis.

Clinical presentation

Symptoms include edema, erythema, joint effusion, and tenderness. Patients tend to keep the affected joint in a position that maximizes intracapsular volume and comfort. Refusal to move an affected joint is referred to as pseudoparalysis, and even passive movement may be painful. Systemic symptoms such as fever, malaise, and poor appetite are also seen in most patients. In all age groups, approximately 75% to 80% of cases involve joints of the lower extremities, with the knees and the hips being most commonly affected [23, 24]. Other commonly affected joints include the ankles, wrists, elbows, and shoulders. Small, distal joints are less likely to be involved. Polyarticular

joint involvement occurs in less than 10% of patients but is seen in up to 50% of patients with infection caused by N. gonorrhoeae.[23,24, 26]

Differential diagnosis

It includes hemarthrosis, traumatic effusion, transient synovitis, reactive arthritis, Lyme arthritis, juvenile rheumatoid arthritis, arthritis of acute rheumatic fever, osteomyelitis, tumor, and slipped capital femoral epiphysis.

In cases of suspected septic arthritis, concomitant osteomyelitis of an adjacent bone should be suspected.

Diagnosis and evaluation

The clinical examination and, the evaluation of aspirated joint fluid are the two most important step. The fluid should be sent for gram stain, culture, and cell count with differential. Typical findings of aspirated synovial fluid are presented in table.

In approximately 60% of cases, an organism is isolated from culture of joint fluid[25], which allows for definitive diagnosis and narrowing of antibiotic coverage.

Plain films may demonstrate a widened joint space. Ultrasonography is useful in identifying and quantifying a joint effusion[27]. Bone scan and MRI are often used and may play a critical role in diagnosing concomitant osteomyelitis[27].

Management

Antibiotic therapy should be initiated immediately after blood and synovial fluid cultures have been obtained. The gram stain can help guide the initial antibiotic choice. If gram-

positive cocci are seen, empiric therapy with a semi-synthetic, penicillinase-resistant penicillin (eg, cloxacillin, 150-200 mg/kg/d, divided in four doses) is the traditional choice. Vancomycin or clindamycin should be considered in areas with high rates of community acquired methicillin-resistant S. aureus (see previous discussion). If Gram stain reveals gram-negative organisms or if no organisms are seen, one should consider a third-generation cephalosporin, such as cefotaxime or ceftriaxone, which covers most gram-positive organisms and K. kingae, Salmonella spp., and H. influenzae.

If a large amount of fibrin or debris is present,

	Septic arthritis	**Transient synovitis**	**Normal joint**
Color	Serosanguinous	Yellow	Yellow
Clarity	Turbid	Generally clear	Clear
White blood cells	>50,000 –100,000/mm3	5,000 –15,000/mm3	<200/mm3
%Polymorphonuclear Neutrophils	>75%	<25%	<25%
Culture Positive in	>60%	Nil	Nil
Glucose	<40 mg/dL	Equal to serum	Equal to serum

the infection is loculated, or there is a lack of improvement within 3 days, then surgical drainage is recommended.

Physiotherapy may be beneficial.

In uncomplicated cases, the total duration of therapy should be at least 3 weeks, preferably 4-6 weeks, with at least 1 week of antibiotics given intravenously. If a patient improves clinically after 1 week and inflammatory markers are normalizing, then the remaining antibiotics can be given orally. Despite appropriate management, approximately 40% of patients with hip involvement and 10% of patients with knee involvement suffer significant sequelae, such as growth plate damage and loss of function[26].

Pyomyositis

Pyomyositis is a bacterial infection of skeletal muscle with a predilection for large muscle groups, and it often results in localized abscess formation.

Pyomyositis is believed to occur when a transient bacteremia seeds a site of local muscle trauma or strain [28].Vigorous exercise, presumably a cause of muscle strain, also may be a causative factor . Other authors have suggested that an antecedent viral infection may be a predisposing factor in some cases[29].

S. aureus is the most commonly identified organism; it accounts for approximately 90% of cases of pyomyositis in tropical areas [29]. Clostridial infections can lead to a fulminant form of myonecrosis, which is often fatal [30].

The initial presentation of pyomyositis is often subacute, and initial symptoms may be vague like pain, fever, swelling and limp.

Pyomyositis occurs in three stages [31]. The invasive stage is characterized by low-grade fevers, general malaise, and dull, cramping pain. Abscess formation occurs during the suppurative stage. During the late stage of pyomyositis, patients develop high fevers, exhibit more local signs of infection, and complain of severe pain. Patients in the late stage of pyomyositis can develop systemic manifestations, including metastatic abscesses, arthritis, and renal failure. Septic shock and toxic shock may ensue if urgent management is not initiated. Although rare, death has been reported after this late stage of pyomyositis. Pyomyositis most commonly affects the quadriceps, gluteal, and iliopsoas muscles[29]. Other affected areas include the paraspinus, psoas, shoulder girdle, extremities (eg, gastrocnemius), chest wall, and abdominal wall[31].

Clostridial myonecrosis (gas gangrene) generally occurs 2 to 3 days after wound contamination with Clostridium perfingens and is characterized by myonecrosis, gas production, and sepsis. Subcutaneous emphysema and crepitus may be appreciated. Symptoms may progress rapidly with the appearance of hemorrhagic bullae and the development of cutaneous necrosis, acidosis, coagulopathy, and shock.

Differential diagnosis includes thrombophlebitis, malignancy, cellulitis, contusion, compartment syndrome, septic arthritis, acute appendicitis, and osteomyelitis.

Ultrasonography is a quick and inexpensive study that can detect muscle abscesses (32) and may be used to guide percutaneous drainage. Although, CT can provide good delineation of muscle structure and may demonstrate a fluid Collection, MRI with gadolinium is the most sensitive study for detecting early inflammatory changes. MRI may help identify patients with early disease who do not require surgery[32].

Laboratory studies tend to be nonspecific. A complete blood count generally demonstrates a leukocytosis with a left shift. The erythrocyte sedimentation rate is often elevated. Muscle enzymes, such as creatine kinase and aldolase, are generally normal. Fluid aspirated from the site of infection is more likely to yield an organism.

Management

Surgical incision and drainage are generally required, although certain patients who present with muscle inflammation but do not yet have abscess formation may be managed with antibiotic therapy alone. Because S. aureus accounts for most infections, a semi-synthetic penicillinaseresistant penicillin (eg, cloxacillin, 150-200 mg/kg/d, divided every 6 hours) is the traditional choice for empiric therapy. Combination therapy with vancomycin should be considered for empiric therapy in areas with a high incidence of community-acquired methicillin-resistant S. aureus (see discussion in the section on osteomyelitis). The optimal length of therapy is not known. In general, intravenous antibiotics should be continued until clinical improvement is evident. Based on sensitivities, appropriate oral antibiotics should be continued for a total of 2 to 6 weeks [29].

Necrotizing fasciitis

Necrotizing fasciitis is a rapidly progressive, deep-seated bacterial infection of the subcutaneous soft tissue that may involve any area of the body. It often follows a fulminant course and has a high mortality rate. Estimates of the mortality rate range from 25% to 75% [33,34]. Necrotizing fasciitis also occurs in young, previously healthy patients, including children. Seedling of bacteria and extension of the infection along fascial planes leads to necrosis of the superficial muscle fascia and the deeper layers of the dermis. Destruction and thrombosis of the small blood vessels in the area lead to necrosis of the surrounding tissues. The extensive tissue damage often leads to systemic symptoms, including multiorgan failure and shock. Predisposing factors include trauma, surgery, burns, and eczema [33]. In neonates necrotizing fasciitis may complicate omphalitis or circumcision. Less commonly associated factors include insect bites, perirectal abscesses, incarcerated hernias, and subcutaneous insulin injections. Necrotizing fasciitis has been reported in several cases as a complication of varicella infection [35]. Necrotizing fasciitis also may occur with a preceding GABHS pharyngitis or without any previous evidence of trauma or infection.
Necrotizing fasciitis is often polymicrobial in origin [34, 36] and involves gram-negative bacilli, enterococci, streptococci, S. aureus, GABHS and anaerobes such as Bacteroides spp, Peptostreptococcus spp, and Clostridium spp.

In children, necrotizing fasciitis often presents 1 to 4 days after trauma with soft-tissue swelling and pain near the infected area. Patients may appear well at initial presentation. Infants and toddlers may be fussy or irritable with refusal to bear weight. Induration and edema are generally apparent within the first 24 hours and are followed rapidly by blistering and bleb formation. Infection spreads in the plane between the subcutaneous tissue and the superficial muscle fascia. The skin takes on a dusky appearance, and a thick, foul-smelling fluid is produced. Pain and tenderness in the subcutaneous space is exquisite, but destruction of the nerves that innervate the skin may lead to anesthesia of the overlying skin. High fevers are common. The rapidly progressing infection can lead to toxic shock syndrome and severe systemic toxicities, including renal and hepatic failure, acute respiratory distress syndrome, and decreased myocardial contractility.

The differential diagnosis of necrotizing fasciitis includes other soft-tissue infections, such as cellulitis, pyomyositis, and gas gangrene.

Although white blood cell counts may be normal or elevated, there is often a pronounced polymorphonucleocytosis. Thrombocytopenia and evidence of coagulopathy also may be apparent. Attempts to identify causative organisms should be made through collection of anaerobic and aerobic blood cultures, although the results are frequently negative [34, 35].

Radiologic studies may support the diagnosis, but they should not delay surgical intervention. Plain films may show gas or soft-tissue edema but are otherwise nonspecific. Although CT may be useful, MRI is the preferred modality. MRI may reveal extension of inflammation along the fascial plains.

Management involves emergent, wide surgical debridement and may need to be repeated [33-35]. Delays in surgery are associated with increased mortality, and antibiotic therapy in the absence of surgical debridement is ineffective. In patients with polymicrobial infections, consider a beta-lactam/beta-lactamase inhibitor combination, such as ampicillin/sulbactam or piperacillin/tazobactam. Supportive therapy includes careful fluid management, pain control, and management of multisystemic organ failure, usually in an intensive care setting. Patients with a GABHS necrotizing fasciitis are at risk for toxic shock syndrome, and many experts recommend intravenous immunoglobulin in this situation[37]. Patients who survive may require amputation, skin grafting, and reconstructive surgery.

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CHAPTER 7

Role of Imaging : Are we using it Optimally ?

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Introduction

Modern imaging techniques have become an essential component in the management of bone and soft tissue infections.

Selection of the appropriate imaging technique is of paramount importance. Choice of imaging technique differs in different stages of the disease process and requires a thorough knowledge of the relative strength and weakness of each imaging modality. In recent years, growth in the use of Ultrasound (US), CT & MRI has added significantly to our knowledge.

Musculoskeletal (MSK) infections in children may involve bones, joints, muscles, tendons and supporting soft tissues.

Imaging helps to define, detect, diagnose and document the clinical abnormality better. It assists with surgical planning and assessment of the treatment response.

However, one must remember that the plain radiograph is always the first imaging study to be performed, followed by appropriate cross sectional imaging on the basis of clinical information.

Hip joint effusion

Transient synovitis is the most common cause of a painful hip & joint effusion in a child. It typically affects children between 5-10 years of age & is usually associated with a low-grade fever with only mild leucocytosis. The symptoms usually resolve within 24 to 48 hours with rest, without any complications.

Septic arthritis may arise as a hematogenous

infection as a result of sepsis; by direct implantation or by contiguous extension from a focus of osteomyelitis.

Radiography

Usually normal.

May show widening of joint spaces or displacement of fat planes.

Ultrasound (US)

It is the method of choice in evaluating hip joint effusion. Effusion distends the joint capsule anterior to the femoral neck. Normal distance between anterior surface of the neck of femur and the capsule is less than 3mm (Figure-1). Diagnostic US guided joint aspiration can be performed in the same sitting thus obviating the need for other invasive procedures.

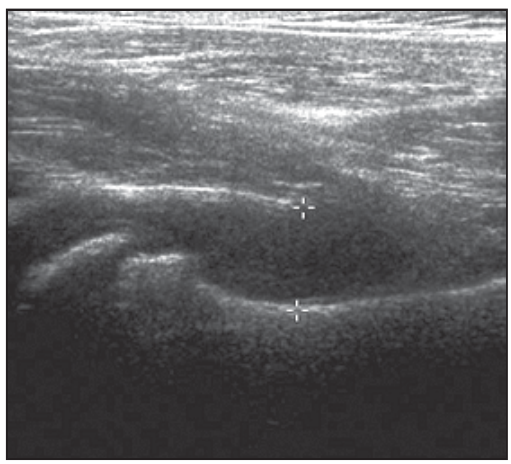


Figure 1 : Ultrasound showing the distended hip joint capsule due to intra-articular fluid.

No US features can distinguish transient synovitis from early septic arthritis. Color Doppler may show a high resistance index (RI) in the anterior cervical artery (mean RI – 0.92). However, the flow returns to normal in 4 to 8 weeks.

MRI

Joint effusion appears hypo-intense on T1 weighted images and hyper-intense on T2 weighted images.

MRI is generally not helpful in distinguishing between transient synovitis & early septic arthritis.

MRI features of septic arthritis:

Joint effusion can be seen in the involved joint. Post contrast (gadolinium) scan shows enhancement of the joint capsule, synovium and accumulation of the contrast within the joint cavity. (Figure-2)

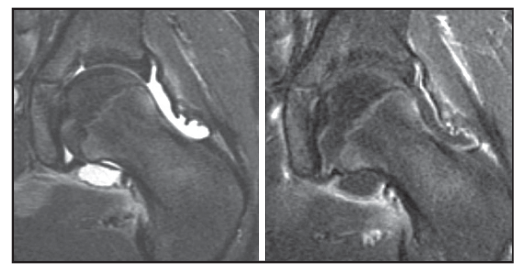


Figure 2 : STIR (left) & postcontrast (right) images show joint effusion and postcontrast enhancemen respectively, in a case of septic arthritis.

Abnormal signal within bone marrow bilaterally.

Synovial thickening with enhancement.

Low signal ossification centre on T1 images and flattened high signal epiphyses on STIR

(Short Tau Inversion Recovery) sequence.

CT

Although not as sensitive as US or MRI in detecting the joint effusion, CT is extremely useful demonstrating subtle bone erosions and epiphyseal osteopenia and irregularities.

Osteomyelitis (OM)

Acute infection in the bone results in marrow edema, cellular infiltration and vascular engorgement; and may progress to abscess formation. As the infection spreads within the intramedullary cavity, increased pressure causes extension to the cortex with subsequent spread to the subperiosteal space and through the periosteum into the adjacent soft tissues. Abscesses can develop in the intramedullary cavity, between the cortex and the periosteum; and in the soft tissues.Joint infections can occur and may result in subluxation, ischemia and necrosis.

Additional complications of osteomyelitis include fracture, slipped epiphyses, premature growth plate closure and chronic infection. In chronic osteomyelitis, necrotic devitalized bone fragment (sequestrum) is surrounded by granulation tissue. Periosteal new bone (involucrum) can develop around the sequestrum.

Acute hematogenous osteomyelitis

Imaging plays a crucial role in the diagnosis and management of children with osteomyelitis. Plain film radiography is usually the initial imaging study which may suggest the correct diagnosis, exclude other pathology and it can be correlated with other imaging findings. Radiographs however, do not show the bone changes of osteomyelitis until 7-10 days after the onset of disease. Initially, soft tissue swelling with blurring of tissue planes may be the only manifestation. Other findings include bone resorption and osteolysis, cortical erosion and periosteal elevation with new bone formation. Loss of approximately 30%-50% of bone mineralization is required for changes to be apparent on plain films.(Figure-3)

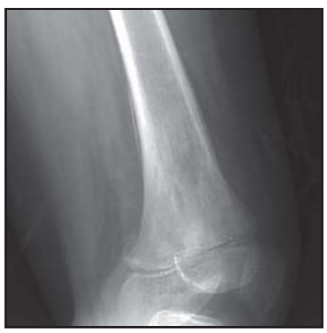


Figure 3 : Acute osteomyelitis showing periosteal reaction.

US has a limited role in the primary diagnosis of acute OM, but it can be used to identify fluid collections and guide aspirations. US findings of acute OM include subperiosteal fluid collection, periosteal reaction and cortical destruction. Subperiosteal abscesses

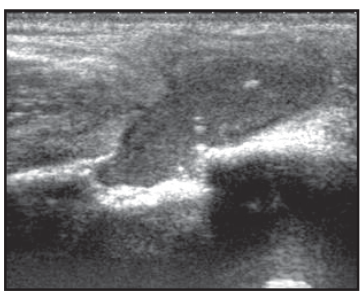


Figure 4 : Ultrasound image showing a subperiosteal abscess with bone fragments.

cause periosteal elevation with exudates and hemorrhage. Periosteal reaction appears as increased cortical thickening.(Figure-4)

CT provides detection of small foci of intraosseous gas, areas of cortical erosion or destruction, tiny foreign bodies serving as a nidus of infection, and involucrum and sequestrum formation.

MRI is an extremely valuable diagnostic tool in the evaluation of musculoskeletal infections. Affected marrow demonstrates low signal intensity on T1- weighted images and high signal intensity on T2 & STIR. In general osteomyelitis is higher in signal intensity than normal hematopoietic marrow on T2 & STIR images. MR imaging can distinguish between acute and chronic osteomyelitis.(Figure-5)

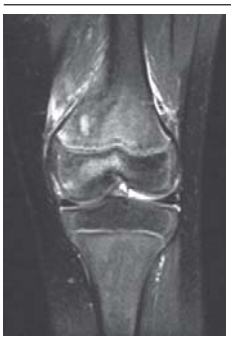
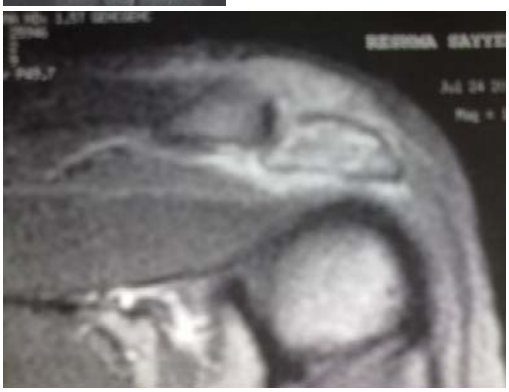


Figure 5 : Fat suppressed image showing osteomyelitis at the lower end of femur.



Chronic osteomyelitis

If untreated or only partially treated, acute and subacute osteomyelitis may become chronic. Cortical and trabecular bone sclerosis, cavities and sequestra are characteristic of chronic osteomyelitis. The affected bone is thickened and its outline may be wavy, with or without periosteal new bone. **Plain radiographs** suggest the diagnosis of chronic osteomyelitis and can be used for follow-up imaging. **CT** is extremely useful in detecting cortical metaphyseal tracts and channels, sequestra, bone destruction and identification of abscesses and cavities.

MRI helps in detecting any reactivation or persistence of infection by showing focal marrow changes and juxta-cortical soft tissue hyperemia and edema. The involved bone shows low signal intensity on T1 weighted images and high signal intensity on T2 weighted images. Sequestrum shows low signal intensity similar to the cortex on all pulse sequences. Post contrast scan shows enhancement of the involved bone marrow. The sequestrum does not show any enhancement.

US has a very limited role in the evaluation of chronic osteomyelitis. It may be used to diagnose soft tissue abscesses and sinus tracts.

Neonatal osteomyelitis

Neonatal osteomyelitis is characterized by a higher incidence of epiphyseal and joint involvement. Multifocal disease may portend a grave prognosis in the neonate. Common causes of neonatal osteomyelitis would

include sepsis, sickle cell disease and an immunocompromized status. **MRI** is a preferred modality in evaluating this condition due to the lack of ionizing radiation and higher sensitivity.

Brodies' abscess

It is formed when low virulence organism is contained by a strong partial host response. The initial purulent exudates is replaced by a granulation tissue. It is most commonly found in the metaphysic of the tibia. It is characterized **radiographically** by a variable zone of sclerosis with a central or eccentric round, oval or serpiginous radiolocency that tracks towards the adjacent growth plate. The cavity may contain a small, dense sequestrum that is visible on a plain radiograph or CT. **MRI** shows a layered appearance on T2 weighted images that show a hyperintense focus of granulation tissue surrounded by a hypointense rim of sclerotic bone, which in turn is surrounded by hyperintense zone of perilesional edema.

Soft tissue infections

Infectious cellulitis

Infetious cellulitis is characterized by diffuse inflammation of the skin and subcutaneous soft tissue. **Plain radiographs** often show only nonspecific soft tissue swelling.

US shows thickening and increased eschogenicity of the subcutaneous tissue with blurring of tissue planes. US may show a "Cobble-stone appearance" of subcutaneous edema (thin anechoic/ hypoechoic strands representing interlobular septal fluid between fatty lobules).

On **MRI**, cellulitis appears as ill-defined lines or dome-shaped areas of low signal intensity on T1 and high signal intensity on T2 images, with an intersperse network-like appearance in the hypodermal fat. Post contrast scan reveals mild enhancement in the involved tissue.

Soft tissue abscess

An abscess is a localized collection of necrotic tissue, neutrophils, inflammatory cells and bacteria. Abscesses have a thick irregular rim and surrounding soft tissue edema. Plain films may demonstrate nonspecific soft tissue swelling. Gas may be seen in the soft tissues, and in the absence of very recent penetration, this strongly suggests the presence of an abscess. **US** reveals a focal hypoechoic to isoechoic collection with debris and a hyperechoic wall. On **CT**, the findings of soft tissue abscess include distortion of soft tissue planes and a focal fluid collection. **MRI** shows a well defined round or spindle shaped focus containing fluid with low signal intensity on T1 and high signal intensity on T2 weighted images. The abscess shows surrounding rim

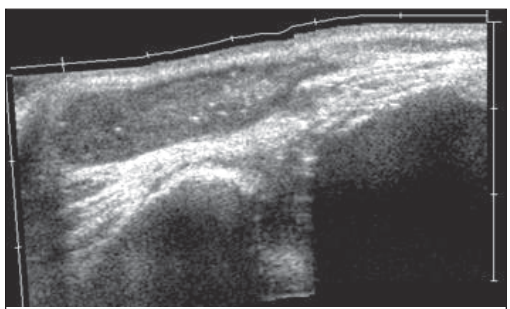


Figure 6 : Acromioclavicular joint septic arthritis resulting in a subcutaneous abscess (MRI & US)

enhancement following administration of gadolinium. (Figure-6)

Pyomyositis

Pyomyositis is aprimary muscle infection that is commonly associated with abscess formation. It is commonly seen in children with immune-compromised status and following local trauma.

US is helpful in localizing relatively superficial sites of pyomyositis. The stage of phlegmon formation is seen as that of an enlarged echogenic muscle with disorganized echotexture and ill-defined hypoechoic areas of breakdown. The stage of abscess formation appears as an intramuscular fluid collection with increased peripheral vascularity. (Figure-7)

MRI appearance of pyomyositis in the early stage may be that of diffuse heterogenous hyperintensity in the involved muscle and that of heterogenous postcontrast enhancement. In the later stages, it may resemble a soft tissue abscess.

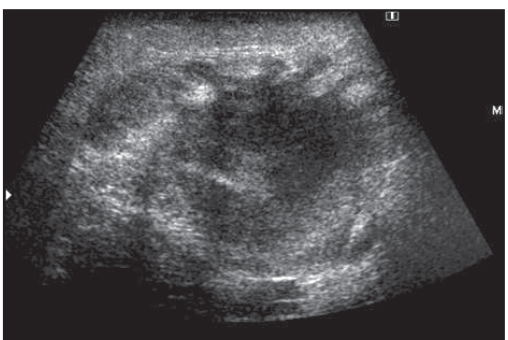


Figure 7 : Pyomyositis involving the serratus anterior muscle

Infectious tenosynovitis

Acute suppurative tenosynovitis is usually involves the tendon sheaths of the digital flexor muscles. It may occur due to the presence of a penetrating injury or the presence of a foreign body.

Plain radiography may aid in the detection of the radio-opaque foreign body.

US shows fluid within the enlarge tendon sheath. The tendon itself may be normal or enlarged if there is associated tendonitis. A foreign body may be visualized within or adjacent to the tendon sheath. (Figure-8)

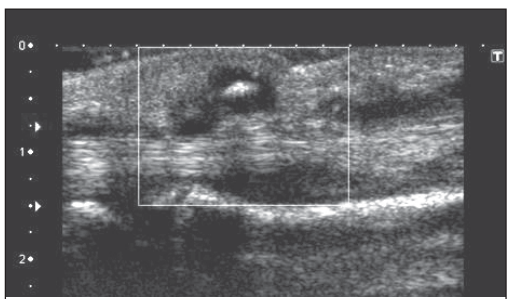


Figure 8 : Foreign body granuloma causing tenosynovitis

MRI reveals the thickened tendon sheath with postcontrast enhancement.

Septic bursitis

S.aureus is the most common organism causing septic bursitis. **US** demonstrates a fluid collection, which may contain debris or septa in the expected location of the bursa. The walls of the bursa may not be thickened. Color Doppler may show hyperemia at the periphery. Aspiration may be performed under US guidance. **MRI** is an excellent

modality to evaluate the local extent of the disease process.

Necrotizing fasciitis

Necrotizing fasciitis is a rare, but rapidly progressive and destructive infection. **CT** shows decreased attenuation of the superficial fascia compatible with necrosis and relative sparing of the underlying muscle. Gas may be seen dissecting along the fascial planes. Involvement of the subcutaneous tissue and the deep fascia is manifested by fascial thickening. The **MRI** appearance is similar to that of a soft tissue abscess.

Vertebral osteomyelitis and discitis

Discitis is an inflammatory process that arises in the intervertebral disc space. Plain radiographs of the spine can demonstrate paravertebral soft tissue swelling and. disc space narrowing . Frank erosion and destruction of the vertebral end plates and extension to the central portion of the vertebral body may be identified, with associated new bone formation. At this stage, vertebral compression and adjacent para-spinal mass representing abscess can be seen and these findings are more characteristic of osteomyelitis than discitis.

CT accurately demonstrates end plate erosions and para-vertebral masses. Enhancement of the intervertebral disc may be noted.

MRI has become the imaging modality of choice for the diagnosis of spinal infections. On T1 weighted images, the affected vertebral body and the disc demonstrate low signal intensity with blurring at the margins. On T2 weighted images, normal discs show differing signal between the centre and the periphery, whereas affected discs appear hypo-intense and flattened. The vertebral end-plate or entire vertebral body may appear hyper-intense and there may be an extension into the epidural and para-spinal spaces with abscess formation. On post contrast scans, abscess collections demonstrate abnormal rim enhancement, whereas areas of active inflammation in the vertebral body and disc show diffuse non-homogenous enhancement.

Summary

In evaluating a suspected case of musculoskeletal infection amongst the pediatric age group (or for that matter any age group), plain radiography is the most appropriate imaging modality to begin with. It serves as a valuable baseline investigation. Ultrasound is rapidly being accepted as the initial modality of choice in evaluating infectious pediatric hip disorders, infected superficial soft tissues and image guided therapeutic interventions. MRI scores over CT in the assessment of musculoskeletal infections due to the lack of ionizing radiation, multiplanar imaging capabilities, excellent soft tissue resolution and the ability to evaluate bone marrow changes.

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CHAPTER 8

Transient Synovitis or Septic Arthritis : Diagnostic Dilemma

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A couple of clinical scenarios are described where reaching to a definitive diagnosis was challenging in patients presented with acutely irritable hip.

Case-1:

A 7 year old male, presented with complain of pain in the right groin since the same day morning. It was associated with an episode of fever, which measured 101.2. Patient had a recent viral upper respiratory infection for which he received symptomatic treatment from Pediatrician. There was no previous history of any injury or similar episode. Patient was not able to bear weight on the right limb. He was irritable and was not allowing moving the limb. The blood investigations show total white blood cell count 11,800 /cmm with normal differential count. ESR measured 30 mm at 1 hour & 45 mm at 2 hours. C-reactive protein level was within normal range. X-ray of both hips did not show any abnormality. A hip ultrasound revealed moderate hip effusion (cortex to capsule distance on right side was 6mm compared to 3 mm on opposite side).

Findings which were guiding to a diagnosis of septic arthritis were inability to bear weight, Fever >101, elevated ESR and moderate hip effusion. Findings against it or in favour of transient synovitis were normal C-reactive protein levels and only marginal increase in white blood cell count.

Since there were no clear-cut features suggestive of septic arthritis, patient was prescribed oral anti-inflammatory medication (Tablet Ibuprofen 40 mg/Kg /day in 3 divided doses) and bilateral skin traction at home for 1 week. Parents were asked to

report of any episode of fever or worsening symptoms in the interim.

At one week follow up, the child came walking to the clinic. He had full range of motion at the hip joint and he could comfortably bear weight on the extremity. There was no episode of fever during previous week. Follow up blood investigations resumed to the normalcy. He remained asymptomatic by the time the second follow up visit.

Case-2:

A 3 year old boy presented to the outpatient department with complains of limp while walking for the last 5 days. He had pain in the right groin which was more pronounced in morning. He had an episode of viral infection and fever before 10 days. There was no history of pain in other joints or any similar episode in past. The child was afebrile. On clinical examination, he had mild tenderness on deep palpation at the base of scarpa's triangle. Limb was lying in external rotation. Hip abduction was 30 degrees & further restricted & painful on the affected side, compared to 60 degrees on the unaffected side. Hip flexion-extension & rotations were within normal range. X-ray of the hip did not reveal any abnormality. Ultrasound demonstrated mild hip effusion. Blood investigations showed total white blood cell count 11,900 /cmm with lymphocyte predominance, ESR measured 40 mm at 2 hours and C reactive protein was marginally elevated measuring 8mg / L (normal range up to 6 mg/L).

Based on his ability to bear weight, course of illness and blood investigations, conservative treatment was considered. Patient was prescribed oral anti-inflammatory medication & skin traction.

Patient presented again after 4 days with complains of more pronounced pain and inability to bear weight. He had two episode of fever >101 despite of regular oral Ibuprofen medication. He was irritable & any attempted range of hip motion was painful. Repeat blood investigation revealed total count 14,000 and C-reactive protein 40 mg/L. Hip ultrasound showed moderate to severe effusion which was increased as compared to previous study. Under general anesthesia hip joint was aspirated. It retrieved about 1.5 ml of sero-purulent material. Hip arthrotomy was performed & joint was irrigated. Empirical antibiotics were started intravenously. Joint fluid culture was positive for Staphylococcus aureus sensitive to Cloxacillin. Patient improved clinically & started weight bearing from day four after surgery. Further course of recovery was uneventful.

These two cases reflect the diagnostic dilemma of a treating physician on the first day of presentation of a patient with acutely irritable hip. The chapter will look in to the current diagnostic algorithms described in the literature, their limitations and treatment guide-lines.

Introduction

An acutely irritable hip in a child presents a unique diagnostic challenge. The common possibilities which draw our attention are Transient Synovitis, Septic arthritis, Inflammatory arthritis, Perthe's disease and

Diagnostic Criteria				
	Culture of Hip Aspirate(Not Contaminants)	**Bacteria on GramStaining of Hip Aspirate**	**Blood Culture**	**White Blood-Cell Countin Hip Aspirate *(× 109/L)***
Confirmed Septic Arthritis	+	Any	Any	Any
	-	Any	Any	Any
	-	-	Any	>50
Presumed Septic Arthritis	-	-	-	>50
Transient Synovitis	-	-	-	<50

Tumours. Frequently, transient synovitis and septic arthritis are left as the two most probable diagnoses. As in the early phase, these two conditions share similar clinical findings, laboratory parameters and radiological picture; it occasionally becomes difficult to stamp the final diagnosis. A prompt diagnosis is essential as the treatment of the two entities is entirely different. Whereas transient synovitis is a self-limited disorder that is managed nonoperatively, septic arthritis requires early intervention to avoid an unfavorable outcome. In the absence of a single, easily performed test that clearly distinguishes between septic arthritis and transient synovitis, clinical prediction algorithms have been proposed using combinations of different variables.

In a retrospective study, Kocher et. al. made diagnoses of true septic arthritis, presumed septic arthritis and transient synovitis based on the White cell count in the joint fluid, results of fluid and blood culture and the clinical course[1].

A probability algorithm for differentiation between transient synovitis and septic arthritis

	Independent Predictors
1	History of Fever (Oral temp. > 38.5° C / 101 ° F)
2	Non weight- bearing
3	WBC count > 12,000 /cmm
4	ESR >40 mm at 1 hour

was constructed on the basis of independent multivariate predictors. They found the following four independent predictors for this differentiation: History of fever (Oral temp. >38.5 C / 101 F), non weight-bearing, serum white cell count of more than 12,000 per cubic mm and erythrocyte sedimentation rate of more than 40 mm per hour.

Based on the univariate analysis and logistic regression analysis, Kocher et.al. found predicted probability of Septic Arthritis as follows:

No. of factors present	**Predicted Probability of Septic Arthrities (%)**
0	0.2
1	3
2	40
3	93.1
4	99.6

Kocher et.al. prospectively applied these clinical prediction rule in their patient population and found diminished performance of the algorithm[2]. The same algorithm has been applied retrospectively[3] as well as prospectively[4] at other centres. Both these studies did not find this algorithm valid for their patient population.

Caird et. al. prospectively collected data of the patients who underwent hip aspiration for the suspicion of septic arthritis. They recorded C-reactive protein levels besides the fore-mentioned independent predictors. They found a C-reactive protein level of >2.0 mg/dL as a strong independent risk factor in predicting septic arthritis.

Although different studies have shown conflicting outcomes, with the general awareness about the four prediction criteria, process of care and efficiency of care certainly can get better[5]. The information about the fore-mentioned criterions can increase the co-ordination between orthopedic surgeons & referring Pediatricians and keep them on a same page.

Radiographs of patients with an irritable hip are mostly inconclusive. It may show increased joint space and soft tissue shadow coinciding with moderate to severe effusion. Ultrasound can detect the severity of hip effusion. But in the early stage, it can not differentiate between septic arthritis and transient synovitis. Few authors tried to delineate the diagnostic significance of Magnetic Resonance Imaging (MRI) in children with hip pain[6]. Authors concluded that MR imaging can detect the joint effusion as well as early changes in the bone and soft tissues with marked sensitivity. However, they did not recommend its routine use in every patient with hip pain. MRI is the investigation of choice in patients with prolonged and recurrent symptoms where diagnosis is in doubt.

Treatment guidelines:

1. Patients with acutely irritable hip joint with normal white blood cell count & ESR (1 & 2 hours) are clearly indicative of transient synovitis of hip. A period of skin traction at home and oral anti-inflammaroty till the child becomes asymptomatic will be of help. Most of the children improve within two weeks' time.

2. Patients with acutely irritable hip joint with marginally elevated white blood cell count & ESR pose a dilemma. A C-reactive protein level should be carried out. Patient's weight bearing ability should be taken in to consideration. A normal C-reactive protein level and relatively bengin clinical examination directs the diagnosis towards transient synovitis. These patients should be followed every weekly. Parents should be advised to inform of any worsening of symptoms in the interim. On the other hand, an elevated C-reactive protein and an alarming clinical examination can be attributed to an early septic process or a proximal femoral osteomyelitis. In a doubtful case, it is worth to start empirical injectable antibiotics & observe the clinical response and trend in blood parameters.

3. Looking at the consequences of a delayed diagnosis of septic arthritis, acquiring an aggressive approach & performing an

arthrotomy in doubtful case is not irrational.

Summary

Diagnosis of the etiology of an acutely irritable hip is a challenging issue. In the early phase, there are no definitive clinical signs or laboratory parameters to confirm either diagnoses of transient synovitis or septic arthritis. Using a clinical predictor algorithm for septic arthritis, process of care can be made more uniform. As there is an overlap of diagnostic areas, each case should be individualized and management should be based on clinical judgment. In cases where the diagnosis in doubt, acquiring an aggressive approach & considering arthrotomy of hip, atleast saves patient from non-forgiving consequences of septic arthritis.

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CHAPTER 9

Management of septic arthritis in children

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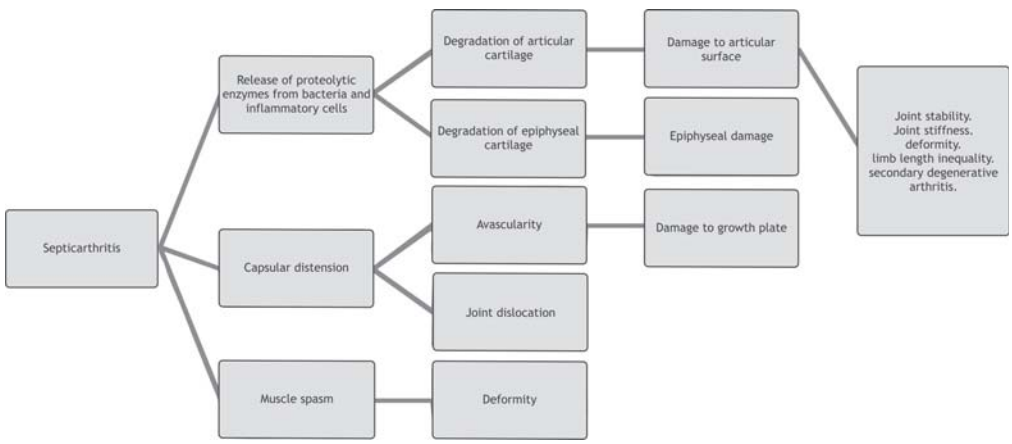
The Facts and Figures

The knowledge of these general facts regarding pattern of involvement may be invaluable in diagnosis of the condition.

1. Septic arthritis is more common than osteomyelitis in infancy and childhood.
2. Most common joints-the hip and knee – 60 % cases.
3. Polyarticular in about 5 percent.
4. Age group 75 percent occur in children below 5 years.



Pathophysiology

The following flowchart demonstrates the sequence of events leading to sequelae of septic arthritis.

The organisms

It has been a traditional teaching that the most common organisms are gram-positive aerobes (80%) and approximately 20% of cases are caused by gram-negative anaerobes with *Staphylococcus aureus* the most common among the gram positive with less commonly implicated bacteria include group A and group B streptococci, *Streptococcus pneumoniae* and *Haemophilus influenza.* Neonates are more susceptible to group B streptococcal infection.

Over recent years, the microbes isolated in bone and joint infections have changed. In the 1970s and 1980s. The introduction of the Haemophilus influenzae type B vaccine has resulted in a vast reduction in cases secondary to hemophilus, but a number of new organisms have appeared. Recent publications would suggest that perhaps only 40% of infections are the result of S. aureus. We have noticed a recent upsurge of septic arthritis caused by methicillin-resistant strains of *Staphylococcus aureus* (MRSA). Although these infections were once thought to be predominantly hospital acquired, but of late, several cases of community-acquired MRSA also have been identified

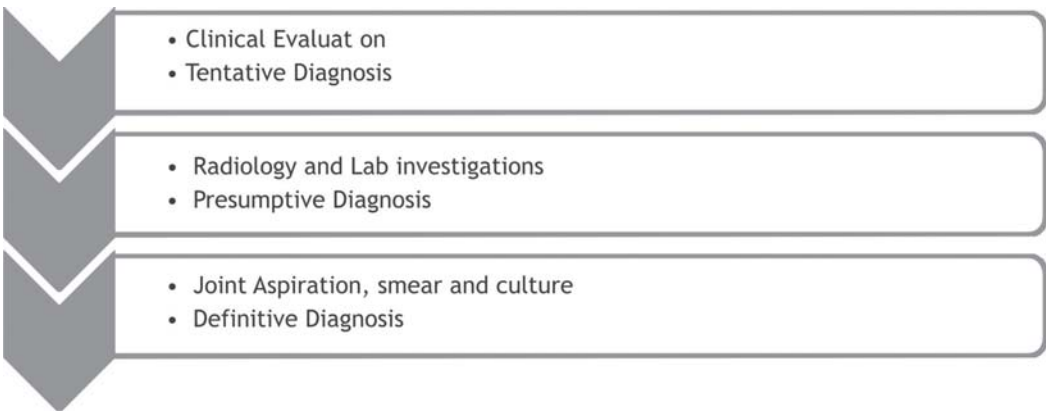
Diagnosis

Need for an early diagnosis

The damage to the cartilage, growth plate and bone due to avasularity and enzymatic distruction sets in early.The cartilage destruction starts as early as 8 hours following the onset.The avascularity sets in within 24-48 hours of the temponade. The biggest challenge is therefore to control the infection and drain the joint before the damage takes place

The challenges of diagnosis septic arthritis

- No single test can be relied upon
- Inflamatory markers may be normal or only slightly elevated early in the disease
- The xrays may be normal early in the



disaease

- *The imaging modalities* such as xrays, ultrasound, bone scan or MRI suggest a process of inflammation and effusion but can not diagnose septic arthritis
- *The laboratory investigations* such as blood counts, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) may help in suggesting that there is an infective process going on but cannot definitely confirm the diagnosis of septic arthritis.
- The only way the joint infection can be conclusively diagnosed is by demonstrating bacteria in the fluid removed from the joint. However, an organism may only be cultured in approximately 60 percent of cases of true septic arthritis.
- Knee jerk antibiotics may blunt clinical preasentation
- Realizing the limitations of investigations in confirming the diagnosis of septic arthritis, it is imperative that treatment is commenced on the basis of a high index of suspicion. Definitive treatment should not be withheld for want of confirmatory laboratory tests.

On the basis of a careful clinical examination, a tentative diagnosis of septic arthritis needs to be made. If joint aspiration does not yield fluid with bacteria demonstrable either in a Gram-stained smear or on culture, a presumptive diagnosis may be made with the help of the results of other laboratory tests in conjunction with clinical findings.

Kocher's criteria

Kocher et al identified clinical and laboratory predictors of septic arthritis:

1. history of fever
2. inability to bear weight on the limb
3. ESR >40 mm/hour
4. White blood cell (WBC) count > 12 000/ mL.

The predicted probability of septic arthritis was 0.2 if none of these predictors was present. This means if none of the factors were present there was only 2 % chance of the condition being septic arthritis. The probability of a diagnosis of septic arthritis was 40, 93.1 and 99.6 percent if two, three or four of these predictors, respectively, were present.

Although Kocher noted these four risk factors and validated these risk factors in a subsequent report, other centers have found that these four factors may not have as high a predictive value in determining a septic hip as was originally thought. In a recent report from Melbourne it was noted that a significant number of patients had normal parameters and suggested that clinical acumen still plays a crucial role in the management.

Radiology

X-ray findings are often normal. Look for soft tissue swelling around the joint, widening of the joint space, and displacement of tissue planes.

Ultrasound is very sensitive in detecting joint effusions generated by septic arthritis. It also can be used to define the extent of septic arthritis and help guide treatment. Sometimes Ultrasound helps to differentiate septic arthritis from other conditions (eg, soft tissue

abscesses, tenosynovitis) in which treatment may differ.

MRI can show changes of marrow edema and help to differentiate between transient synovitis, inflammatory arthritis and septic arthritis by virtue of changes in marrow edema and synovial lining. It can also diagnose additional osteomyelitis. In a recent study markers of SA on MRI included bone marrow oedema and absence of T1-weighted and T2-weighted low signal intensity synovial tissue. Furthermore, soft-tissue oedema and reduced contrast enhancement in the epiphyses were more frequent in children with SA.

Differential diagnosis

Conditions that Mimic infection

- Transient synovitis: May be difficult to differentiate early on. The laboratory reports, presence of mixed echogenesity on US and severity of symptoms and signs point to infective process. When in doubt a joint aspiration should be performed
- Inflamatory arthritis: Fluid out of proportion to symptoms
- Other conditions to keep in mind
  - Malignancies: Leukemia, Ewing's sarcoma, Metastasis
  - Langerhans cell histiocytosis
  - Sickle cell disease and bone infarct
  - Storage disorders: Gaucher disease

Management

Antibiotic therapy

Aim

To control and eradicate the infective process

Which antibiotic

The antibiotic selected should be effective against the organism responsible for the infection. Since Gram-positive organisms are most frequently responsible for the infection, an antibiotic that is effective against these organisms should be started empirically. In hospital acquired infection a combination broad spectrum antibiotic is started to be effective against gram positive and gram negative organisms

How long?

In the past it was recommended that treatment with antibiotics should be continued for six weeks.

However, recent studies suggest that the duration of medication may be reduced to four weeks or less without adverse outcome in the long term To start with an IV route is preferred Once the clinical signs improve and CRP levels touch baseline the antibiotic may be given orally.

Monitoring the treatment

1. *Clinical parameters: Fever, heart rate, Pain, range of movements,Weight bearing status*
2. *Lab parameters: ESR, TC/DC, CRP Among this CRP is the best indicator of response to therapy.*
3. *USG to look for reduction in joint effusion*
4. *Xrays to look for lytic areas and joint position*

Failure of CRP to fall by 1 week

1. Recollection

2. Missed multifocal septic arthritis
3. Systemic infection- pneumonitis, pleuritis, pyelonephritis, peritonitis
4. Wrong antibiotic, resistant organism
5. Associated osteomyelitis

Shortened antibiotic course

A recent paper from Melbourne suggests a shortened antibiotic regimen of 3 days Intravenous antibiotic with 3 week oral antibiotics in patients with childhood septic arthritis and osteomyelitis. After 3 full days of intravenous antibiotics the patients were assessed with regard to converting to oral therapy. An improvement in symptoms (pain, movement), normalization of temperature, and stabilizing CRP were defined as prerequisites for conversion. Persistent pain, fever, and rising inflammatory markers dictated that therapy should continue and that surgical exploration could be indicated. All patients were kept in hospital for 1 day after conversion to oral therapy to ensure tolerance. Oral antibiotics were continued for 3 weeks, usually at half the intravenous dose if tolerated. They found that a temperature of greater than 38.4 on admission and CRP greater than 100 were the best predictor of needing antibiotics for more than 3 days The addition of ESR, WCC, or both did not help in determining which patients will require prolonged therapy. They could successfully convert 59% of patients by day 3 and 86% by day 5 resulting in only 14% of patients requiring intravenous therapy for 6 days or more.

Surgical Intervention

Aim

1. Joint decompression: To reduce temonade, relieve pain and spasm, and obtain sample for smear and culture
2. Joint lavage: To washout the enzymes and debris harmful to joint cartilage

Methods

1. Aspiration and lavage: Minimally invasive. Repeated joint aspirations are not a good option for hip joint as it does not decompress joint adequately, prolongs antibiotic therapy and hospital stay
2. Arthrotomy: Allows joint inspection and complete joint clearance. Septic hips in young children are drained anteriorly to avoid disrupting the posterior blood supply to the femoral epiphysis. It is critical to do a definitive capsulotomy. Be sure that the joint is aggressively irrigated and that there is no purulent collection left behind. Some have recommended decompression of the femoral neck if there is associated osteomyelitis that has not decompressed itself into the joint
3. Arthroscopy: All advantages of arthrotomy being minimally invasive

Immobilization of the joint

Aim

To relieve spasm, prevent deformity and instability

Methods

With brace, plaster or traction

Prognosis

Depends on the following factors

- Duration of disease
- Type of organism

- Age of child
- The joint involved
- Intervention
- Associated systemic disorders and immune status

Summary

We recommend high index of suspicion while diagnosing septic arthritis in children and an aggressive treatment approach. Initial investigations include blood cultures, and hematologic markers (WCC, CRP, and ESR) followed by appropriate imaging. Ultrasound should be used to confirm SA and MRI can be used in selected cases. Empirical antibiotics (Amoxycillin Clav combination with amikacin) should be commenced after prompt drainage of joint collections. Further choice of antibiotics will depend on culture report and clinical course. Short antibiotic treatment guided by improvement in clinical parameters and CRP is effective in most cases.

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CHAPTER 10

Acute Osteomyelitis in Children

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Introduction:

Acute Haematogenous Osteomyelitis (AHO) is primarily a disease of bone and bone marrow. It is common in the first decade of life and there is a slightly higher incidence in boys compared to girls.

AHO can involve any bone and at any age after birth due to a variety of causes. Neonatal osteomyelitis is commonly associated with septic arthritis due to the peculiar vascularity of the physis and epiphysis. Once the growth plate forms, it acts as a barrier and in toddlers and children the infection is usually confined to the metaphysis.

Pathophysiology of AHO:

Infection starts in the metaphysis of the long bones (femur 27%, Tibia 22%, Humerus 12%) due to certain anatomical and biological factors: the hair-pin bend of the blood vessels renders the circulation in this part of the bone sluggish. Paucity of cells of the reticuloendothelial system further decreases the resistance of host environment to destroy pathogens. With trivial trauma, the haematoma which forms in the metaphysis acts as a perfect soil for bacteria to seed and take control. As the organism proliferate the inflammatory exudates causes destruction and compression of the already tenuous blood flow and thus relentless spread of infection. As the spongy metaphyseal bone gives away, this exudates under tension causes elevation of the periosteum and sets the stage for acute spread of infection.

Microbiology

Common organisms include staphylococcus aureus (70%), H. Influenzae (less after widespread use to HiB vaccine), Group B

Streptococci, Klebsilla and Enterococcus. Type of environment and host immunity may influence the bacteriology. Community – Acquired MRSA is also emerging as a potent cause of infection in children in many parts of the world. The PVL strain of MRSA should be suspected when there is multifocal infection, very high ESR (> 80mm), thrombocytopenia or coagulopathy.

Sometimes bone infection follows a bout of pneumonia and skin infection like pyoderma or a foot puncture wound (pseudomonas). In Sickle cell disease, salmonella osteomyelitis and in children with chicken-pox, Group B Streptococcus infection is common.

Clinical Features:

AHO can occur in three different age group: neonates (< 2months), Infantile (18 months to 2 years) and Early Childhood (3 – 12 years).

AHO may follow after trivial trauma and the history is usually of rapid onset of pain in the affected limb not relieved with analgesics, swelling in soft tissues if the bone is superficial, and decreased use of the extremity. Fever is present in 60 – 70% of the cases.

Some children may present with cellulitis and occasionally a suppurative lesion.

In small children the pain may be poorly localized, resulting in limp and reluctance to weight bear. Differential diagnosis may include fracture, toxic synovitis, JRA, tumour and leukaemia.

Basic laboratory tests include CBC, ESR, CRP and Blood cultures.

Radiology:

In suspected cases, radiographs may not reveal early changes. Bone lysis, osteopenia, necrosis and periosteal elevation occur after 10 days. Sonography is very sensitive and can diagnose subtle signs like sub-periosteal edema, soft tissue swelling within 2 -3 days of onset of infection.

Sometimes USG guided aspiration can be attempted to determine presence of infection. Aspiration has found to yield positive results in 67 % – 80 % of cases.

If deep seated infection is suspected in the pelvis and spine, then MRI scan is most useful.

Bone Scintigraphy is useful when infection is suspected but difficult to ascertain clinically in a particular case.

Management:

Treatment involves control of infection, prevention of tissue destruction, relief from pain and restoration of function. Antibiotics can achieve the first two, if started with in 48 – 72 hours of onset of infection. After 3 days, surgical decompression / debridement is required to prevent further tissue destruction.

Pain relief is achieved with splinting and early physiotherapy is commenced to prevent muscle dystrophy.

Antibiotic Treatment: Parenteral antibiotic

therapy is the mainstay in the management of AHO. Ideally antibiotics should be started after sending blood for culture and routine test, but this is seldom the case. Many children have received oral antibiotics 2 – 3 days prior and this decreases the chance of obtaining a positive culture.

First or Second generation cephalosporins (Cefazolin or Cefuroxime) are usually commenced in higher doses to combat the infection. In children allergic to penicillin, clindamycin or Lincomycin can be given after consultation with the Infectious Disease Personnel. Linezolid and Vancomycin should only be used once suspectibility is proven either on blood or aspirate culture or if the child is seriously ill. Vancomycin is active against group A Streptococci, Streptococcus pneumonia and Staph. Aureus.

Intravenous antibiotic duration varies from 10 days to 3 weeks. Appropriate antibiotic response should include clinical and haematological improvement. A decreasing CRP and WBC count with absent of local signs and symptoms should initiate conversion to oral antibiotics for total of 6 weeks. The end-point is difficult to define but antibiotics can be stopped once the ESR and CRP are normal.

Surgery

Surgical treatment is almost always required if the child present with an abscess, failure of medical treatment and a progressive infection despite medical therapy. A visible osteolytic lesion, subperiosteal abscess should also warrant surgery especially if it involves the proximal femur, humerus and distal tibia. Here the metaphysis is intra-articular and the infection can rapidly spread into the joint.

Surgery must include not only drainage of sub-periosteal abscess but also decompression of intra-medullary cavity and complete removal off all necrotic tissue. The affected extremity must be splinted to prevent muscle spasm and pathological fractures.

Antibiotics have a greater tissue penetrance after bone deridement.

Conclusion:

AHO must be suspected in any child with bone pain not improving after 2 -3 days of medical therapy. In a child any abscess or cellulitis around a joint should initiate investigations to rule out underlying bone involvement. If antibiotics fail to alleviate the symptoms then prompt surgical debridement is required to prevent a chronic osteomyelits.

CHAPTER 11

Chronic Osteomyelitis in Children

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Overview

Chronic osteomyelitis requires judgement in balancing the surgical and medical treatment. The anatomic changes the surgeon makes are often necessary to heal the condition, but can fail if they are done without understanding and management of the medical aspects of the disease. Surgeons should preserve periosteum assiduously during debridement, it is from this tissue that the healing potential arises.

Etiology

Chronic osteomyelitis is persistence within bone of a bacterial infection which initially arrived there by either hematogenous spread or direct inoculation. If hematogenous, it is likely to be a single microbe. If by direct inoculation, it is common to have polymicrobial infections. In either case the encapsulated gram positive organisms, particularly staphylococcus, are common pathogens.

Pathogenesis

Osteomyelitis can occur in the diaphysis, metaphysis, and more rarely the epiphysis of the bone. Epiphyseal osteomyelitis is often associated with septic arthritis of the nearby joint. Metaphyseal osteomyelitis, in the juxtaphyseal position, is typically from deposition of circulating bacteria in the end capillary network near the growth plate. Diaphyseal osteomyelitis can result after open trauma to a long bone – typically a tibia.

Haematogenous osteomyelitis and/or septic arthritis occur in otherwise healthy children, as does open trauma. Prompt medical treatment with appropriate antibiotics alone leads to full resolution and no recurrence in the majority of cases where osteomyelitis is diagnosed early.

Established infection can disrupt the intraosseous blood supply leaving a varying amount of dead bone, known as a sequestrum. New bone will form within the healing tissue at the margins of the sequestrum, this new healing bone is known as the involucrum and generally arises from the circumferential periosteum. If the periosteum has been destroyed by trauma, infection, or surgical intervention then a complete and strong involucrum cannot form.

Once osteomyelitis is established it tends to be a localized phenomenom, without systemic fevers and signs of sepsis that are common in the acute phase. The infection is to an extent 'walled off' in bone. Despite this, local exacerbations can occur, and the infection can seed to other bones and joints or to other sites in the body.

The body continues to attempt to heal the chronic osteomyelitis by absorbing or expelling the sequestrum, and growing the involucrum to give the limb stability. A sinus tract may form and remain unhealed while small quantities of pus and occasionally bone fragments are expelled from the sequestrum – a process which can take years. The ongoing infection draws on the nutritional and physiologic reserve of the patient and makes him unwell, in a child the overall growth may be slowed by the chronic disease.

The affected limb may be painful, weak, and atrophic with reduced muscle mass and reduced range of motion of nearby joints. In the presence of chronic infection a traumatic fracture may not heal, and a pathological fracture can occur in intact bone with chronic osteomyelitis, so in either case there may develop a painful pseudarthosis. This can so compromise the overall function of the limb that the patient effectively ceases to use it.

Natural History and Prognosis

Many patients with chronic osteomyelitis neither die from it nor recover from it, but coexist with the infection in the limb for years with varying loss of function depending on the site.

Among children with open growth plates, it is likely that a chronic metaphyseal or epiphyeal infection will cause part of the growth plate to close. This will cause an angular deformity due to ongoing growth, usually followed by early closure of the entire growth plate and consequently a short limb as well as a deformed limb. Shortening and deformity may not be of functional consequence in the upper limb but may cause considerable problems in the lower limb.

Diagnosis

On history the initial infectious episode with

fever, pain, local swelling and loss of function will have occurred either spontaneously (for hematogenous osteomyelitis) or after an open or occasionally a closed fracture. The limb generally has not recovered complete function even months after the intial episode. Children are generally healthy but a history of chronic conditions including immune deficiencies or sickle cell disease should be sought.

A specific history can give clues to the likely microbiological diagnosis, for example a penetrating injury from a nail passing through a sports shoe is likely to inoculate the bones of the foot with pseudomonas.

On physical examination the affected limb will likely be atrophic with reduced function, and reduced range of motion and strength at the joints above and below the affected bone. The affected area is likely to be relatively swollen or thickened and it may or may not be tender, it may or may not be warm to the touch. The presence of a sinus calls for careful examination of the limb segment below as the sinus tract may be long and tortuous and the outlet may be remote from the sequestrum and affected bone. There may be a pseudarthrosis which can vary from stiff to very mobile and unstable.

Radiographs of the affected limb may show permeative destruction of the bone with ill-defined borders but more typically a geographical pattern of destruction is present. The body's response to the infection is often evident as sclerosis around the involved area as well as new, thick subperiosteal bone. A pseudarthrosis is usually readily evident radiographically if present, some stiff pseudarthroses may have complex serpiginous shapes. In children, the status of the growth plates should be carefully evaluated. Bony bars may be present, and converging Harris growth lines may indicate present or incipient angular deformity.

Routine laboratory investigations will reveal a modestly elevated ESR and CRP in the majority of cases. The white cell count may or may not be elevated depending on how active and extensive the infection is. Cultures of peripheral blood are usually negative in chronic osteomyelitis but are often sent because they may be informative if positive.

One of the most valuable tests is culture of material from the infected bone. Provided the patient is not on any antibiotics, cultures should be positive about 70% of the time. Needle aspiration may be sufficient to make a microbiological diagnosis. If it is not, then pus, bone, and tissue obtained at the time of biopsy or debridement should be sent for tissue cultures. Longstanding infections may involve multiple organisms or unusual organisms, especially in the case of open fractures or open sinuses. Correct identification of the organism is often an important step in selecting the appropriate antibiotic treatment and resolving the case, sometimes the biggest contribution the surgeon makes is a biopsy allowing accurate microbiological diagnosis.

Sinugram

Injecting radioopaque dye into the sinus can help in identification of the track and the

sequestrum it arises from. Injection of methylene blue into the sinus helps with identification and excision of the track during surgical debridement.

CT and MRI

CT scans are useful in evaluating bony features in three dimensions. These include looking for the extent and anatomy of the sequestrum and the involucrum, and for looking for bony bars across growth plates. CT with contrast is useful for showing larger abscesses in soft tissue, and sometimes for distinguishing where the vascular and healing bone begins.

MRI can be useful in showing the exent of the infection in the entire bone, although it can be difficult to distinguish between involved tissue and surrounding edema. Cartilage sequences are a good way to look at the health and anatomy of the growth plate, and MRI is an excellent modality for showing abscesses and soft tissue involvement. MRI is less good at bony details, it is difficult to guess at the strength or even the structure of a piece of cortical bone by looking at its absence on an MRI.

Biopsy

In some cases a biopsy of tissue will be sent to the pathologist to distinguish between a chronic infection and a bone tumor. Bone tumors involving infiltration of bone by hematological elements are most likely to mimic infections – eosinophilic granulomas, lymphomas, ewings tumors, and neuroblastomas in the young.

Medical Treatment

Children with chronic osteomyelitis need nutritional evaluation and support. Many were nutritionally deplete prior to the illness and most are during its course. Adequate dietary calories, protein, and trace elements should be assured to maximize the effectiveness of antibiotic and surgical treatment. Most of the time this can be done by improving the regular diet per os. Invasive nutritional support is only needed in the most depleted of orthopaedic patients, and then is much better given parenterally than by vein.

Antibiotic therapy is the mainstay of treatment of chronic osteomyelitis. Antibiotics need to be continued until the dead infected bone is gone and is replaced by healthy healing tissue. This may mean many weeks or months of treatment for some children. Intravenous antibiotics are used for initial treatment and are often used around the times of surgical interventions, but in many cases the prolonged treatment can be by the oral route. It cannot be overstressed that repeated cultures may be needed to ensure that the correct antibiotics are being given. Clinical response to therapy can be judged by resolution of local signs and by radiographic progression towards healing. Lack of response is more likely to mean the wrong antibiotic than the wrong route, but higher blood levels and better tolerance are sometimes achieved with intravenous treatment. Intravenous antibiotics can be administered for many weeks or months in the ambulatory setting through a central line or a PICC line but each of theses access

routes has its own needs for care and potential for complications so oral treatment is preferred if available.

Surgical Treatment

Some cases of chronic osteomyelitis may heal completely with appropriate antibiotic treatment alone, but many will need surgical treatment as an adjunct. The surgeon must decide what the specific purpose of the surgery is, and whether it is the right time to do it.

Surgery can be used for diagnosis, debridement, stabilization, or reconstruction. Sometimes most or all of these functions can be accomplished at the first operation, but sometimes nature requires a respectful and patient approach.

Diagnosis includes precise knowledge of the infecting organism(s) in order to get the antibiotics right and cure the patient. Very often deep tissue biopsies will be needed to maximize the chances of culturing the involved organism.

Debridement is the job of the macrophage and of the surgeon. The surgeon works on a gross anatomical scale and wants to remove all clearly dead and devitalized tissue, while at the same time leaving strong stable bleeding bone that can heal. If these goals cannot be met at the first surgery it may not be the best time for an extensive debridement. It is important not to remove periosteum. It is important not to strip periosteum excessively and create more devitalized bone.

Treating the patient medically while a sequestrum becomes well defined and the involucrum becomes mature and strong may allow for a successful and curative debridement later.

If the involucrum is not strong enough and does not mature, or if the sequestrum involves the entire diameter of the bone and the periosteum has been destroyed, then the surgeon may have to do a debridement that destabilizes the bone. A debridement that destabilizes the bone should be avoided if possible – by waiting if the antibiotics are working and there is sufficient bone and blood supply remaining – but in some cases it will not be possible to complete the debridement without destabilizing the bone. In other cases the bone will be destabilized by a traumatic pr pathological fracture, and stability will help both the fracture and the infection to heal.

External fixation is an excellent way of attaining mechanical stability in the presence of infection because it does not require a permanent metal implant placed when infection is active. Shortening the bone acutely can be a useful strategy for attaining stability and union.

During external fixator treatment it is important to keep the joints mobile and the limb as functional as possible. Joint contractures and muscle atrophy can be minimized by a proactive approach to physical therapy.

Soft tissue coverage may be a problem in chronic cases. Flaps and skin grafts will fail

without adequate debridement of infected tissue beneath. Local muscle flaps or myocutaneous free flaps have the advantage of bringing a rich blood supply to help with the healing but again require health tissue beneath, although they can be placed directly onto healthy bone.

Reconstruction

External fixators can be used for bone lengthening and angular deformity correction during the reconstructive phase once the infection has healed and the bone has united. Many reconstructive problems exist depending on the site and extent of involvement. Osteotomies, lenghtenings, and arthrodesis may all have a role to play depending on the precise clinical circumstance.

Summary

Chronic osteomyelitis is a complex disease and will present many challenging variants. The overall plan is to make a good microbiological diagnosis, often through a biopsy and preliminary debridement. Medical treatment with correct antibiotics and nutritional support are necessary for cure. At the appropriate time, a debridement or debridements to remove devitalized bone is undertaken. If necessary, stability can often be achieved with external fixation. Periosteum must be preserved and respected because ultimately it is the source of much of the bony healing. Soft tissue coverage may be required in some cases, and some patients may benefit from delayed reconstruction of an angular deformity, a short limb segment, or a badly destroyed joint. Surgeons treating chronic osteomyelitis must have the mindset of gardeners, not of carpenters. Our interventions must respect and support nature's ability and time scale to grow new healed bone.

CHAPTER 12

Differential diagnosis of Pediatric bone & joint infections

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Introduction

In the areas where bone & joint infections are frequently encountered, physicians are conditioned to diagnose them promptly. It is likely that the common pathologies, which clinically & radiologicaly resemble the bone & joint infection may get overlooked. Knowledge about these entities is essential not only to prevent the patients from having antibiotics administered unnecessarily but also to promptly manage the clinical mimickers.

Broadly the differential diagnosis of Pediatric bone and joint infection can be divided in to four subgroups as in the Table 1.

Inflammatory Conditions

Transient synovitis presents as the most common condition mimicking septic arthritis in the early stage. Its prompt differentiation is required as the treatment of both the conditions is entirely different and the outcome if remain untreated are extremely devastating[1]. This has been described in details in Chapter-7.

Juvenile idiopathic arthritis (JIA) especially the monoarticular affection can mimic septic arthritis initially. Hip joint is not the first joint to be affected in JIA while it is the most common joint involved in septic arthritis. The symptoms usually are of gradual onset in JIA. Typically, the joint affected by JIA looks worse than it functions. Most patients may report a previous episode of joint pain resolved after short course of anti-inflammatory in JIA. White blood cell count in joint fluid is usually less than 100, 000 per mL whereas in septic arthritis it is usually higher.

Table-1 Differential diagnosis of Pediatric bone & joint infections

A. Inflammatory conditions: • Transient synovitis • Juvenile idiopathic arthritis
B. Infectious conditions*: • Rheumatic fever • Post streptococcal reactive arthritis (PSRA) • Osteomyelitis associated with Sickle cell anaemia • Tuberculous Osteomyelitis • Osteomyelitis associated with thrombophlebitis * *conditions where the treatment of co existing condition is crucial*
C. Tumorous conditions: • Leukemia • Ewing's sarcoma • Lymphoma
D. Non-tumourous, non-infectious conditions: • Caffey's disease • Scurvy • Charcot's joint

Infectious Conditions

Patients with rheumatic fever typically have a history of upper respiratory tract infection before two weeks, although septic arthritis can also have a similar history. A joint affected by rheumatic fever has exquisite pain which is out of proportion to the clinical joint examination. Its migratory nature and multiple joint affections also differentiate it from septic arthritis. Diagnosis of rheumatic fever is based on the Jones criteria. Major criteria include carditis, arthritis, chorea, subcutaneous nodules, and erythema marginatum. The minor criteria are arthralgia, elevated ESR or CRP, heart block on electrocardiogram (ECG), and a history of previous rheumatic fever. The diagnosis is made when a patient has two major criteria, or one major and two minor criteria.

For patients who have a documented history of recent group A Streptococcus exposure, those who do not meet the Jones criteria, but have significant arthralgia without other identifiable cause, the diagnosis of poststreptococcal reactive arthritis (PSRA) has been used[2]. A recent streptococcal infection may be documented by the presence of an antibody response to group A Streptococcus or positive throat culture. Patients with acute rheumatic fever are treated with long-term prophylactic antibiotics to prevent recurrent rheumatic fever and associated carditis. The risk of carditis to children with PSRA is unclear, and the role of long-term prophylactic antibiotics following PSRA is controversial.

Osteomyelitis is a frequent occurrence in patients with Sickle cell anemia. It is important to find the source of bone pain, whether it is due to bone infection or infarction. An ongoing Sickle cell crisis should be adequately treated[3]. Unlike in acute osteomyelitis, a long intravenous antibiotics course is required before consideration of operative treatment. This is due to the fact that drug delivery to bone is relatively less due to multiple bone infarcts. A detail of this entity has been described in Chapter-18.

Patients of osteomyelitis or septic arthritis with history of pulmonary septic emboli should be investigated for septic

thromboembolism[4]. Typically, these patients show the affected area extensively swollen like a tight compartment underneath. They are very irritable and extensively tender to touch. A Doppler study is required to confirm the diagnosis. A reduced platelet count can be attributed to ongoing septicemia as well as the thromboembolism. Low molecular weight heparin in prophylactic dosage with platelet rich plasma should be administered before considering arthrotomy. Unless diagnosed promptly, this condition can become fatal.

Focal erosion and infiltrative type of Tuberculous osteomyelitis can mimic bacterial osteomyelitis[5]. A long course of disease and poor response to conventional antibiotics should arouse suspicion about the possibility of Tuberculosis. A detailed description of this entity is presented in Chapter-16.

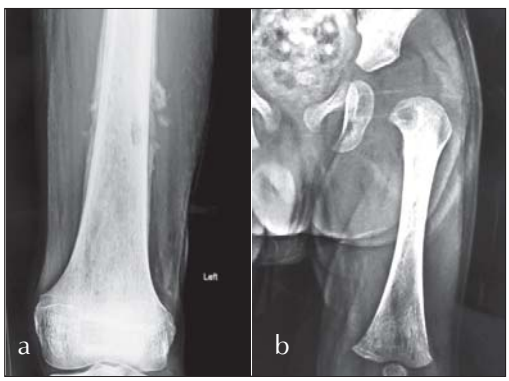

Fig.1 a. Infiltrative type Tuberculous osteomyelitis b. Focal erosion type affection of femoral neck.

Tumorous Conditions

About 30% children have bone pains as the presenting complaint in Leukemia. Almost 60% of patients have high white blood cell count & ESR[6]. Bleeding tendency, bone pain at multiple sites and easy bruising should arouse suspicion about leukemia. X-ray pictures in leukemia may show varying degrees of lysis, sclerosis or subperiosteal new bone formation. Patients should be subjected to peripheral smear examination to find abnormal forms of white blood cells to diagnose the condition.

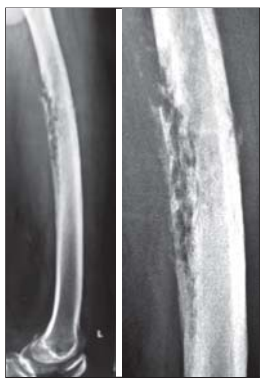

Fig. 2 A patient with leukemic infiltrates in the midshaft femur was initially diagnosed as osteomyelitis with sequestrum formation.

Ewing's sarcoma and lymphoma primarily originating from bone are the other tumors which should be kept in mind. The dictum remains right: "Biopsy all infections & Culture all tumors."

Non-infectious non-tumorous Conditions

Caffey's disease (Infantile cortical hyperostosis) is a self-limiting benign condition. As the name suggests, it is usually seen in early infancy. It is difficult to differentiate Caffey's disease from osteomyelitis, especially in the early phase of disease. Pain and fever may take few

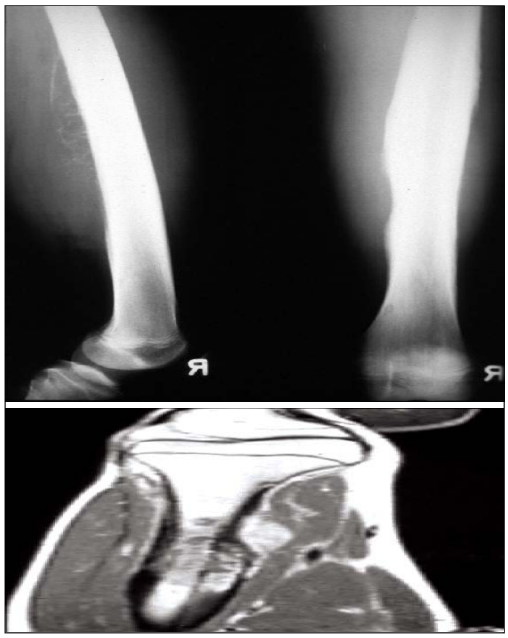

Fig.3 A patient diagnosed to have osteomyelitis initially, found to have an infiltrating lesion on MRI. Biopsy revealed the diagnosis of Ewing's sarcoma.

months to subside in Caffey's disease. The laboratory parameters remain elevated and do not help in differentiation. Multiple bone involvement is a cardinal sign to diagnose infantile cortical hyperostosis. Ulna is the most common bone to get involved followed by clavicle, scapula and long bones of leg. Mandibles can be affected and show hyperostosis. In a suspected case, a full body x-ray can be of help. MRI shows normal architect of the native bone in Caffey's disease, while marrow changes are associated with osteomyelitis. Treatment remains palliative in this condition and the role of immunoglobulins or steroids is questionable. The disease is usually self-limiting and may recur episodically, but

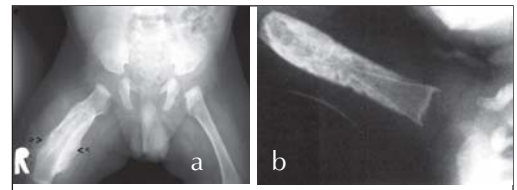

Fig:4 a. A 5 month old infant diagnosed to have hematogenous osteomyelitis of right femur. b. Caffey's disease was diagnosed 2 weeks later when the right humerus was also involved. Patient improved with oral anti-inflammatory medications.

typically resolves by the age of 2 years[7].

Patients affected from Scurvy remain irritable, avoid weight bearing & show pseudo paralysis of the affected limb. These symptoms are also seen in patients with acute osteomyelitis and can lead to a wrong diagnosis. Laboratory markers may remain

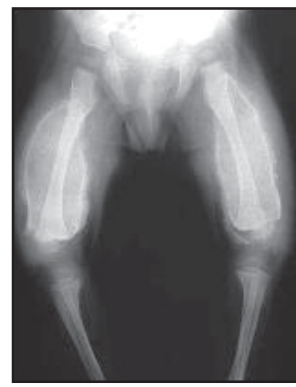

Fig: 5 A full blown case of Scurvy with characteristic organized subperiosteal haemrrahage in both femora.

within normal range in Scurvy. Serum or blood levels of Vitamin C can be of help. In the early phase, x-rays show typical changes in epiphysis & metaphysis. In a treated case, subperiosteal hemorrhage gets organized and shows a diffuse periosteal reaction. Patients respond dramatically to oral Vitamin C supplementation.

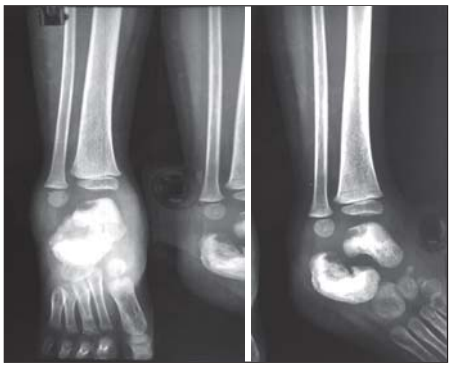

Fig. 6 A 2.5 year old girl which was initially diagnosed as septic arthritis of ankle & subtalar joints, later found to have Charcot joint secondary to congential indifference to pain. The diagnosis was confirmed by Histamin Skin flare test.

Radiological picture of Charcot joint may resemble with that of an advanced septic arthritis. The history & clinical examination will reveal the existence of a myelomeningocele or rarely patient may be affected from congenital insensitivity to pain. A Histamine skin flare test is diagnostic for congenital indifference to pain. Radiological picture looks worse and out of proportion to that of clinical function. A prolonged protection in splint is required to prevent significant cartilage damage.

Summary

Bone and joint infections are common encounters in the developing world. Although the conditions which mimic osteoarticular infections are confronted infrequently, knowledge about their existence can help clinicians at many instances. As most of the times, laboratory findings & radiological picture are equivocal, clinical course & physical examination remain the mainstay of diagnosis in confusing cases.

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CHAPTER 13

Antimicrobials in Pediatrics

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Antibiotics are the therapeutic agents used most frequently in clinical practice.In many of these cases, however, antimicrobials are inappropriately prescribed.Despite their widespread use in pediatrics, few antibiotics have been studied adequately to be considered safe and effective for use in children. When using antibiotics in children, many factors that are different from those for adults should be considered, which includes not only pharmacokinetics, pharmacodynamics and adverse effect profile but also issues like taste, smell and ease of administration.

In this section we present antimicrobials' doses, the route of administration, empiric antibiotic therapy for musculoskeletal infections and lastly, comparative palatability and bioavailability of oral preparations.

Commonly used Antimicrobials in Pediatrics

Medication (Generic name)	Dose/day	Route	Frequency	Preparations available & Remarks
Amikacin	Preterm Neonate: 15mg/kg Term Neonate: 15mg/kg Children: 15-25mg/kg	IM or IV infusion over 30 min	Once a day ispreferred	Inj: 50mg/ml, 125mg/ml, 250mg/ml
Amoxicillin	Children: 20-100mg/kg	Oral, IM, IV	q8h	Syp: 125mg/5ml Tab: 125,250,500mg Inj: 125,250, 500mg,1gm

Medication (Generic name)	Dose/day	Route	Frequency	Preparations available & Remarks
Amoxicillin-Clavulanate	(Calculate as per amoxicillin content) Preterm Neonate: 30mg/kg Term Neonate: 30mg/kg Children: 20-100mg/kg	Oral, IV	q8-12h	Syp: 228.5mg/5ml, 457mg/5mlTab: 228.5, 457,600mg Inj: 150,300, 600mg, 1.2gm
Ampicillin	Preterm Neonate: 50-100mg/kg Term Neonate: 100mg/kg Children: 100-200mg/kg	IM, IV	q12h q6h q6h	Syp: 125mg/5ml Tab: 125,250,500mg Inj: 125,250,500mg, 1gm
Ampicillin-Sulbactum	Children: 100-200mg/kg of Ampicillin	IM, IV	Q6h	Inj: 750mg, 1.5gm
Azithromycin	Children: 10mg/kg on day 1 than, 5mg/kg on day 2-5.	IM, IV Infusion	Q24h	Syp: 100 & 200mg/5ml, Tab: 100,250,500mg, 1gmInj: 500mg/100ml
Cefaclor (2^{nd} gen)	Children: 20-40mg/kg	Oral	q8-12h	Syp: 125/5ml Tab: 125,250,500mg
Cefadroxil (1^{st} gen)	Children: 30mg/kg	Oral	q12h	Syp: 125,250/5ml Tab: 125,250,500mg
Cefazolin (1^{st} gen)	Neonate: 40-60mg/kg Children: 50-100mg/kg	IM, IV IM, IV	q8hq8h	Inj: 250,500mg
Cefdinir (3rd gen)	Children: 14mg/kg	Oral	q12-24h	125mg/5ml
Cefepime (4^{th} gen)	Neonate: 60-100mg/kg Children: 100-150mg/kg	IM, IV	q8-12h	250,500mg,1gm
Cefixime (3rd gen)	Children: 8mg/kg	Oral	q12h	Syp: 50,100mg/5ml Tab: 50,100,200mg
Cefoparazone-sulbactum (3rd gen)	Neonate: 100mg/kg Children: 100-150mg/kg	IM, IV	q12hq8-12h	Inj: 1,2 gm Cefoparazone: 250,500mg
Cefotaxime (3rd gen)	Preterm Neonate: 100-150mg/kg Term Neonate: 150-200mg/kg Children: 100-200mg/kg	IM, IV	q12h q8-12h q6-8h	Inj: 250,500mg, 1gm
Cefpodoxime (3rd gen)	Children: 10mg/kg	Oral	q12h	Syp: 50,100mg/5ml Tab: 50,100,200mg

Medication (Generic name)	**Dose/day**	**Route**	**Frequency**	**Preparations available & Remarks**
Ceftazidime (3rd gen)	Preterm Neonate: 100-150mg/kg Term Neonate: 150-200mg/kg Children: 100-150mg/kg	IM, IV	q12 hq8-12h q8-12h	Inj: 250,500mg, 1gm
Ceftriaxone (3rd gen)	Neonate: 50-75mg/kg Children: 50-100mg/kg	IM, IV	q12-24h q12-24h	Inj: 250,500mg, 1gm
Cefuroxime (2^{nd} gen)	Neonate: 40-100mg/kg Children: 200-240mg/kg Children: 20-30mg/kg	IM, IV IM, IV Oral	q12h q8h q8h	Syp: 125mg/5ml Tab: 125,250,500mg Inj: 125,250,500mg
Cephalexin (1^{st} gen)	Children: 25-100mg/kg	Oral	q6-8h	Syp: 125,250mg/5ml Tab: 125,250,500mg
Chloramphenicol	Neonate: 25mg/kg Children: 50-100mg/kg	IV IV, oral	q24h q6-8h	Syp: 125mg/5ml Cap: 500mg Inj: 1gm
Ciprofloxacin	Neonate: 20mg/kg Children: 15-30mg/kg	IV, oral	q12h q12h	Syp: 100,200mg/5ml Tab: 100,250,500, 750mg; Inj: 200mg/100ml
Clindamycin	Neonate: 10-15mg/kg Children: 30-40mg/kg	IM, IV IM, IV, oral	q8-12h q6-8h	Cap: 300mg Inj: 150mg/ml
Cloxacillin	Children: 100-200mg/kg	IM, IV, oral	q6h	Syp: 125mg/5ml Tab: 125,250mg Inj: 250,500mg
Co-trimoxazole (TMP-SMZ)	Children: 6-20mg TMP/kg	Oral	q12h	Syp: SMZ 200mg+ TMP 40mg/5ml Tab: SMZ 400mg+ TMP 80mg Tab DS: SMZ 800mg+ TMP 160mg
Doxycycline	Children: 2-5mg/kg	Oral	q12-24h	Tab: 100,200mg
Gentamycin	Neonate:5-7.5mg/kg Children: 5-7.5mg/kg	IM or IV infusion over 30 min	Once a day is preferred	Inj: 40mg/ml
Imipenem-cilastatin	Neonate:20-60mg/kg Children: 60-100mg/kg	IM, IV	q8-24h q6-8h	

Medication (Generic name)	Dose/day	Route	Frequency	Preparations available & Remarks
Linezolid	Neonate:20-30mg/kg Children: 20-30mg/kg	IV, oral	q8-12h q8-12h	Syp: 100mg/5ml Tab: 100,300,600 mg Inj: 200mg/100ml, 600mg/300ml
Meropenem	Neonate:40-60mg/kg Children: 60mg/kg	IV	q8-12h q8h	Inj: 125,250, 500mg, 1gm
Metronidazole	Neonate:7.5-30mg/kg Children: 30mg/kg	IV, oral	q12-24h q6-8h	Syp: 200mg/5ml Tab: 500mg Inj: 500mg/100ml
Ofloxacin	Children: 15mg/kg	IV, oral	q12h	Syp: 100,200mg/5ml Tab: 100,200,400mg Inj: 200mg/100ml
Penicillin G	Neonate:500000-100000 units/kg Children: 100000-250000 units/kg	IM, IV	q6-12h q4-6h	Inj: 500000 units
Piperacillin-tazobactum	Neonate:150-300mg/kg Children: 300-400mg/kg	IM, IV	q8-12h q6-8h	Inj: 1.125, 2.25, 4.5gm

Antifungals

Medication (Generic name)	Dose/day	Route	Frequency	Preparations available & Remarks
Amphoterecin B(conventional)	Neonate: 1-1.5mg/kg Children: 1-15.mg/kg	IV infusion over 4-6 h	q24h	Inj; 50mg. Reconstitute and dilute with D5.
Amphoterecin B(liposomal)	Neonate: 5-7mg/kg Children: 2.5-10mg/kg	IV infusion over 2 h	q24h	Inj; 10,50mg. Reconstitute and dilute with D5.
Fluconazole	Neonate: 6-12mg/kg Children: 6-12mg/kg	IV infusion over 30 min	q24h	Inj: 200mg/100ml
Flucytosine	Neonate: 50-100mg/kg Children: 100-150mg/kg	Oral	q6-12h q6-8h	Tab: 250,500 mg

Details about anti-tuberculous medicines are given in Chapter-16.

Empiric therapy for Musculoskeletal infections

Subset	Likely pathogen	First line therapy	Alternative therapy	IV to oral switch
Neonate	S. aureus, GBS, gram negative bacilli	Cloxacillin (150-200mg/kg) +Cefotaxime (150-200mg/kg)	Cefotaxime may be replaced with an Aminoglycoside.	
Acute Hemato-genous Osteomyelitis (AHO) in <5 yr	S. aureus (MSSA), GABHS, H. influenzae, Streptococcus pneumoniae	Cefotaxime (150-200mg/kg) or Cefuroxime (200-300mg/kg) +/- Cloxacillin (150-200mg/kg)	Meropenem (60mg/kg)	Coamoxyclav (100mg/kg) or Clindamycin + Quinolone
AHO in > 5 yr	S. aureus (MSSA) S. aureus (MRSA)	Cloxacillin (150-200mg/kg) Vancomycin (60mg/kg) or Clindamycin (30mg/kg) or Linezolid (30mg/kg)	Cefotaxime (150-200mg/kg) or Cefuroxime (200-300mg/kg)	Coamoxyclav (100mg/kg) or Clindamycin Linezolid (30 mg/kg) or Clindamycin (30mg/kg)
Any age	S. aureus (CA-MRSA)	Vancomycin (60mg/kg) + Clindamycin (30mg/kg) + Gentamycin (5mg/kg) + Rifampicin (10mg/kg) + SMX-TMP (5mg/kg) +/- IVIG	Vancomycin may be replaced by Linezolid	Linezolid + clindamy-cin + Rifampicin + SMX-TMP

To sum up, upto 5 years, Cefotaxime+Cloxacillin and beyond 5 years Cloxacillin makes a sensible choice, till the culture report comes.

Comparative palatability of selected antimicrobials suspensions used in pediatrics

Pleasant Taste	Inconsistent Taste	Unpleasant Taste
Amoxicillin	Amoxicillin/clavulanic	Cefpodoxime
Cefdinir	Azithromycin	Cefuroxime
Cefixime	Ciprofloxacin	Clarithromycin
Cephalexin	Erythromycin	Clindamycin
Rifampin	Trimethoprim/sulfamethoxazole	Linezolid

Bioavailability of oral antibiotics

Bioavailability	Antimicrobials
Excellent	Amoxicillin, Quinolones Clindamycin, Rifampin, TMP-SMX, Doxycycline, Chloremphenicol, Metronidazole
Good	Most beta-lactams, Most oral cephalosporins,Macrolides, Acyclovir
Poor	Vancomycin

Excellent: Oral administration result in equivalent blood/tissue levels as the same dose given IV

Good: Oral administration result in lower blood/tissue levels than the same dose given IV

Poor: Oral administration result in inadequate blood/tissue levels

Tips for successful antibiotic therapy

1. Develop culture of taking cultures.
2. Choose antibiotic as per the likely causative organism, its expected resistance pattern and flora of your hospital.
3. Deescalate as soon as indicated.
4. Use narrow spectrum drugs and monotherapy where ever possible.
5. Remember, combinations are not always synergistic.
6. Do not use two beta lactamase inhibitor simultaneously, for eg. Piperacillin/Tazobactum + Cefoparazone/Salbactum. It is irrational.
7. Never be in hastle of changing antibiotic. Wait for at least 24-48 hours before declaring it as “not working”.

CHAPTER 14

Joint aspiration techniques

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Analysis of the synovial fluid through arthrocentesis remains the key diagnostic test in a suspected case of Septic arthritis.[1] The important message for the physician is to be aggressive in looking for infectious arthritis. The speed of diagnosis is the most important determinant of the outcome.

- **Indications for aspiration**
  - Diagnostic indications
    - Unexplained arthritis with synovial effusion
    - Suggestion of an infected joint
    - Suspicion of crystal-induced arthritis
    - Evaluation of therapeutic response in septic arthritis
  - Therapeutic indications
    - Drainage of a septic joint
    - Relief of elevated intra-articular pressure
    - Injection of medications
    - Evacuation of a painful hemarthrosis
- **Contraindications to aspiration**
  - Severe coagulopathy
  - Severe thrombocytopenia
  - Overlying cellulitis
- **Potential complications of aspiration**
  - Iatrogenic infection: The risk of inducing joint infection is low when sterile technique is used.
  - Tendon injury, rupture, nerve and blood vessel injury, which can result from improper needle insertion
- **Equipment needed for aspiration**
  - Alcohol sponges
  - Iodinated solution and surgical soap
  - Gauze
  - Hemostat
  - Sterile gloves and drapes
  - 18-gauge needle

- Sterile 20-mL syringes
- Blood collection tubes
- Anaerobic transport media
- local anesthetic agent(lignocaine)

- **Skin preparation for aspiration**

We recommend proper cleansing of the skin by swabbing with alcohol to remove natural oils and debris, followed by an iodine-based antiseptic and then by swabbing with alcohol.

Synovial fluid should be evaluated in gross terms for the color, clarity, viscosity, and mucin clot formation.

Microscopic evaluation includes leukocyte count differential, wet smear inspection by polarized light, and phase contrast microscopy. Cultures should be performed for bacteria, fungi, viruses, or tubercle bacilli if indicated.

Various joints aspiration techniques:

HIP ASPIRATION:

The anterior, lateral, or medial approach may be used to aspirate the hip joint. As the hip joint is deep, aspiration under fluoroscopic guidance helps to assist with intracapsular needle placement. In addition, this technique allows for contrast arthrography to confirm joint penetration in difficult cases. Ultrasound-guided aspiration is a useful technique that is more accessible and avoids radiation exposure in infants and toddlers. In these young patients, sedation may be necessary to perform a useful arthrocentesis.[2]

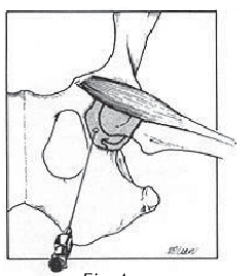


Fig-A.
Medial approach

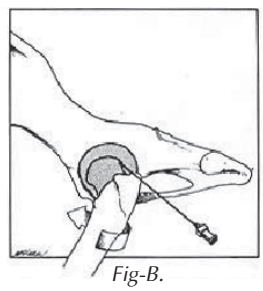


Fig-B.
Lateral approach

With the patient in the supine position, insert an 18-gauge spinal needle approximately 2 cm distal and 2 cm lateral to the intersection of the femoral artery and the inguinal ligament. Direct the needle posteromedially at an angle of 60 until bone is reached. Confirm the position of the needle using image intensification or ultrasound.

A lateral approach also may be used, inserting the needle just anterior and inferior to the tip of the greater trochanter. With the hip internally rotated, advance the needle in a proximal and medial direction toward the femoral neck.

In young children, the hip may be aspirated using the adductor, or medial, approach. The hip is flexed and abducted and the needle is placed inferior to the proximal adductor longus tendon, aiming toward the femoral head.

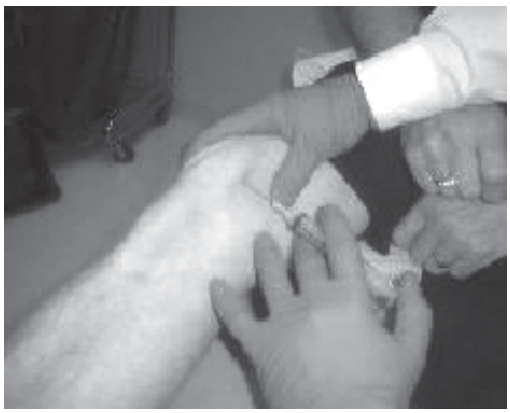
Practical message:
In all techniques, small volumes of dilute radio-opaque dye may be used to confirm intracapsular needle placement.

KNEE ASPIRATION:

Positioning:
Place a rolled towel below the patient's knee.

Technique:

- While stretching the skin over the insertion site, insert the needle briskly into the joint space while gently aspirating until synovial fluid enters the syringe (usually 1-2 cm in an adult of average size). See image below.



Left knee aspiration using the medial parapatellar approach.

If a bone is encountered, pull the needle back, verify the anatomical landmarks, and advance the needle in a corrected direction.

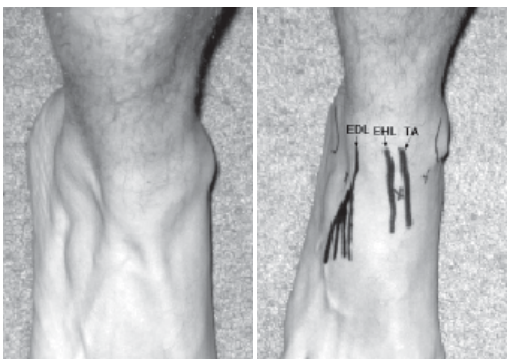
- If removal of more fluid is desired, a hemostat can be used to secure the needle in place while the syringe is replaced with a new one.
- Remove the needle and apply a bandage.
- Parapatellar approach (preferred)[3,4]
  - Identify the midpoint of either the medial or lateral borders of the patella.
  - Insert an 18-ga needle 3-4 mm below the midpoint of either the medial or lateral borders of the patella.
  - Direct the needle perpendicular to the long axis of the femur and toward the intercondylar notch of the femur.

Practical message:

- If fluid stops flowing into the syringe, attempt to "milk" the suprapatellar region by applying gentle pressure to the region.
- Relaxation of the quadriceps muscle facilitates insertion of the needle.
- Placement of a towel under the popliteal region to flex the knee to 15-20 degrees may facilitate entry by opening up the joint space.

ANKLE JOINT ASPIRATION

Anatomical landmark:

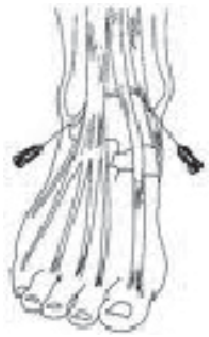


Positioning:

- The patient should be placed either sitting or supine on a stretcher, with the knee flexed at 90º and the leg either hanging from the side of the stretcher or bent with the heel resting against the stretcher.
- Plantar flexion of the ankle against minimal ankle dorsiflexion force by the patient helps define the anatomy in older children.

Technique:

The most common and safest means to aspirate the ankle joint is an anterolateral approach.



The insertion point of the needle should be 2.5 cm proximal and 1.3 cm anterior to the tip of the lateral malleolus, just lateral to the peroneus tertius tendon.

- This is the preferred approach for ankle joint aspiration because it avoids potential injury to the dorsalis pedis vessels or the deep peroneal nerve, which course through the medial aspect of the foot.
- Identify the ankle joint line, the lateral malleolus, and the lateral border of the extensor digitorum longus.
- Extension of the foot against the patient's resistance or active flexion/extension movement by the patient helps the practitioner identify the space between the base of the lateral malleolus and the lateral border of the extensor digitorum longus.
- Insert a needle (18-20 gauge) at the joint line midway between the base of the lateral malleolus and the lateral border of the extensor digitorum longus, advancing the needle perpendicular to the fibular shaft.

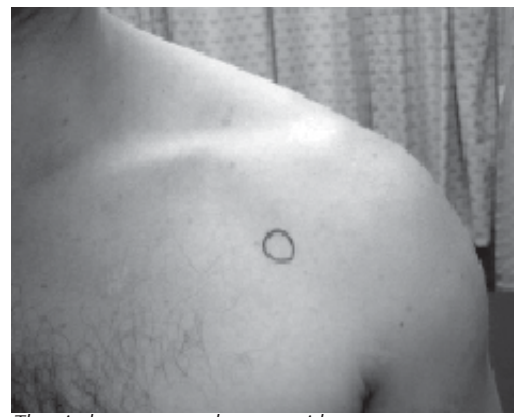
SHOULDER JOINT ASPIRATION

Positioning:

- The patient should be seated in a comfortable position.
- For the anterior approach, rest the patient's hand on his or her lap so the shoulder is internally rotated.
- For the posterior approach, place the patient's hand on the contralateral shoulder.

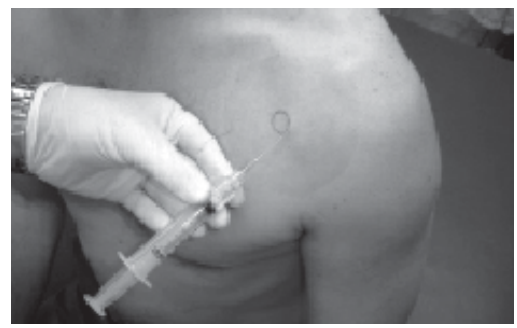
Anterior approach:

Palpate the coracoid process and the humeral head. As the arm is internally rotated, the joint space can be felt as a groove lateral to the coracoid process (see image below).[5]



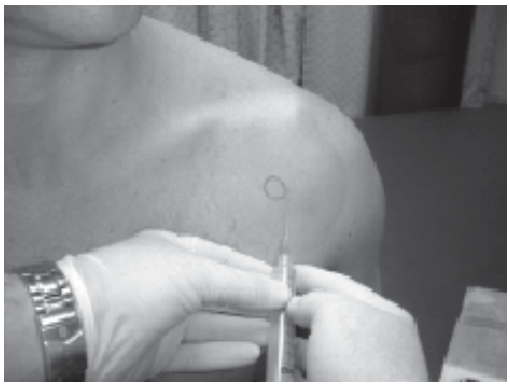
The circle represents the coracoid process

Insert the needle medial to the head of the humerus and just below the tip of the coracoid process (see image below)



Insert the needle medial to head of humerus and just below tip of coracoid process.

Direct the needle slightly laterally and superiorly into scapulohumeral joint space (see image below).[6]



Direct the needle slightly laterally and superiorly.

Posterior approach

- Insert the needle 1-2 cm inferior and medial to the posterior tip of the acromion.
- Direct the needle anteriorly and medially toward the coracoid.[7]

Practical message:

Take care not to direct the needle medially into the axillary neurovascular structures.

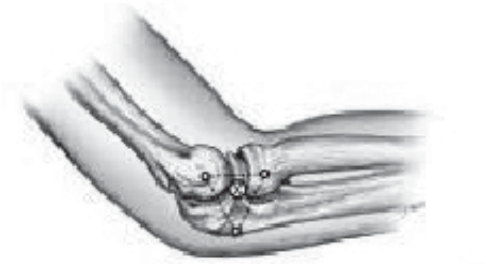
ELBOW JOINT ASPIRATION

Positioning:

- Place the patient sitting upright on a stretcher.
- Bend the patient's elbow to 90 degrees.
- Pronate the patient's forearm and rest it with the palm down on a side table set at the appropriate height for comfort.

Technique:

- Identify the olecranon process, lateral epicondyle, and radial head, and find the depression (or bulge, if the effusion is large) found in the soft triangle. This site is used for all approaches.[8] See image below.



Triangle formed between olecranon, lateral epicondyle, and radial head as site for needle placement.

- Identify the site of entry, and mark the site with a plastic needle sheath or sterile marker.
- Prepare the skin with a cleansing agent and drape with towels.
- Anesthetize the area by injecting 1-2 mL of lidocaine 1% and forming a skin wheal.
- Insert an 18-gauge needle into the depression perpendicular to both the skin and radial head from the lateral side. This is the lateral approach, which is preferred.
- Alternatively, the posterolateral approach can be used. An increased risk of injury to the radial nerve and triceps tendon exists, but this approach is useful if the bulge of an effusion is palpated inferior to the lateral epicondyle.
- In the posterolateral approach, insert the needle perpendicular to the skin but parallel to the radial shaft.
- Ultrasonography may aid detection of even a small effusion in the olecranon fossa.[9]
- Advance the needle slowly while aspirating the syringe until synovial fluid is obtained.

Practical message:

- The landmarks may be easier to find if the arm is first extended to locate the depression and then flexed and pronated for the procedure.

WRIST JOINT ASPIRATION

Positioning:

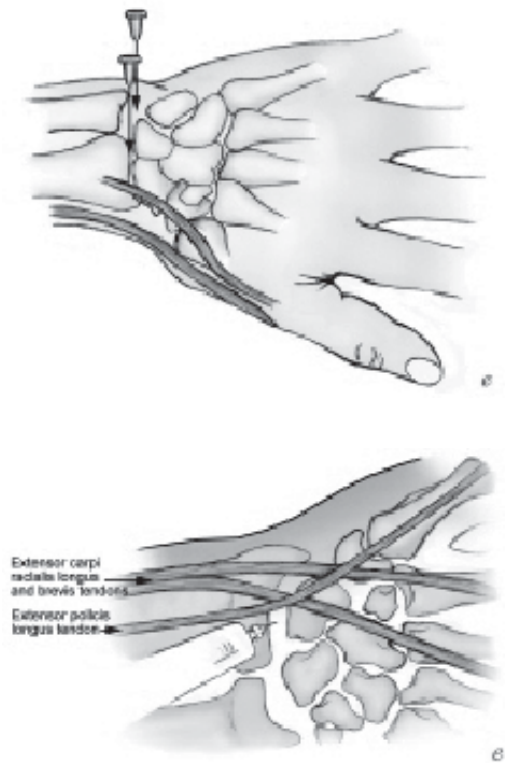
- The patient should be placed in a comfortable supine or recumbent position.
- The wrist should be slightly palmar flexed to facilitate the procedure.

Technique:

The most common site of aspiration is between the first and the second extensor compartments at the radiocarpal level. The procedure includes the following steps:

- The wrist should be slightly palmarflexed.
- Rest the wrist on the table and pronate the forearm.
- Identify the Lister tubercle (a bone prominence in the dorsal distal radius where the extensor pollicis longus bends radially to reach the thumb).
- Insert the needle just distal to the Lister tubercle and ulnar to the extensor pollicis longus tendon.

The less common approach is between the third and fourth or between the fourth and the fifth extensor compartments.



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CHAPTER 15

Non tuberculous Infectious Spondylodiscitis in Children

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Introduction

Prompt diagnosis remains the greatest problem in non tuberculous infectious spondylitis. It must be considered whenever a child has symptoms of even mild infection combined with functional disorders of the trunk or lower limbs or even gastrointestinal disorders. The diagnosis is easier to make as the child becomes older. With modern imaging techniques the distinction between infection of the disc space and vertebral osteomyelitis has blurred. The persistent belief in alternative etiologies for what has been termed "discitis" in children is very puzzling, when one considers that the insidious onset, disc space narrowing, magnetic resonance imaging appearance, and difficulty isolating the organism observed in pediatric spondylitis are almost similar to the situation encountered in adults. In many cases, the infection resolves without specific antibiotic therapy. Still, the treatment should combine a systemic antibiotic regimen and immobilization until the clinical and biologic parameters return to normal. Monitoring includes clinical examinations, radiographs, and MRI either for early diagnosis or to check the extent of perispinal abscess. The functional outcome is generally very good if treatment is adequate.

Etio-Patho-physiology

The anatomy of the disc in the young differs from adults, in the presence of arterioles in

the cartilage canals of the developing vertebral endplate[1]. The vertebral blood supply undergoes involution from richly anastomotic intraosseous arteries communicating with the disc in the fetus, infant and preschool child, to the end arteries seen in the adolescent and adult [1,2,3,4,5,6,7,8]. This copious blood supply could predispose to an infective agent settling in the disc and could also explain the usual good recovery and lack of long-term damage .

Vascular anatomy is considered less important with the scenario of modern imaging modalities demonstrating early involvement of the intervertebral disc in infections at all ages[2,9,10,11,12,13,14]. In discitis, the inflammation is restricted to the disc, whereas in spondylodiscitis, both the disc and the adjacent bone are affected [13,15].

Current pathophysiologic theories propose that, in both children and adults, hematogenous bacterial emboli lodge and progress to involve the disc, facilitated by bacterial or inflammatory enzymes or perforations in the vertebral end plate[16,17]. Some support the idea of a traumatic[18] or inflammatory[19] cause as well. Spinal epidural abscess can also occur. In children it usually has more posterior epidural location and greater spinal column extension. The epidural space is wider in the lower thoracolumbar region. Children have more posterior and less segmented epidural fat than adults[20].

Bacteriology

Large number of cases of spondylitis have been treated successfully without antibiotics, tempting many authors to propose that the disc narrowing and adjacent reactive bony changes are a result of some other developmental or reactive process[21,22,23,24]. Most authors have cited the large percentage of negative cultures as further support for a nonbacterial etiology. The organism has most often been identified from blood cultures and less often from boipsy . Such difficulty with organism isolation is typical of other pyogenic musculoskeletal infections also[25,26]. Therefore, alternative, nonbacterial, etiologies such as viral infection, trauma, or a nonspecific inflammatory disorder are unlikely [21,24,27,28,29,30,31,32].

The predominant pathogen in spinal infection is S. aureus[33]. The emergence of methicillin resistance (MRSA) is increasingly important [34]. Community-acquired MRSA has been recognized in the pediatric population [35,36,37]. A high rate of K. kingae, a gram-negative coccobacillus related to the Neisseria family usually found in the oropharynx is also increasingly reported[38]. The immunocompromised states in sickle cell anemia and leukemia and their associated organisms, are well described in the literature [39,40,41].An association between the disease and previous infections (ear-nose-throat, gastrointestinal tract, urogenital tract) has been reported.[42,43]. Pneumococci and salmonella[44] are also common, whereas anaerobic bacteria [45]and fungal organisms[42] are infrequently detected. Knowledge of the local epidemiology and prior exposure might suggest the aetiology[46].

Clinical Presentation

In contrast to adult-onset spondylodiscitis, the incidence of which is increasing, childhood spondylodiscitis is an extremely rare disease, the exact incidence of which is

unclear[44]. It is essentially different from the adult onset form with regard to its course and degree of severity and frequently presents with uncharacteristic mild signs and symptoms, making it difficult to diagnose.

Discitis in childhood has been separated into three age groups with different presentations, namely the neonate, the toddler and the older child [47,48]. Two peak ages of onset (0 to 2 years and 10 years), is seen [15,46,49,50,51].

The clinical manifestations can be very discrete. Nonspecific complaints like rapid fatigability, loss of appetite, lack of energy, weight loss, loss of desire to play, refusal to sit or walk, and fever are common[52]. Absence of fever is noted frequently in toddlers[21,48]. Guri described the infantile form as the hip syndrome as early as 1946[53].Frequently, hip syndrome [50] can be a presentation. A tender, stiff spine, a child who refuses to stay seated, and a child with unilateral sciatica or psoas spasm are all tell-tale signs. Neurological deficit is rare[52]. Abdominal pain may mask discitis. It is suggested that this type of pain is due to retroperitoneal irritation resulting from psoas abscess[54].Some reports relate upto 30% of abdominal pain syndromes being caused by spondylodiscitis. [21,55]. There could be evidences of primary site of infection like ear-nose-throat, gastrointestinal tract or urogenital tract on examination[42,43]. Keim,[56] and Rocco and Eyring[49] have described the use of classification systems to describe the clinical features.

These vague or even misleading clinical signs and symptoms make the diagnosis difficult. This is confirmed by the long delay in diagnosis by many reported series [48,57,58,59,60].

Imaging

The appearance on standard radiographs rarely progresses beyond disc space narrowing with erosion or sclerosis of the adjacent vertebral end plates[2].A 99mTc bone scan, which can be positive within one week of the onset of symptoms,[61] has been shown to be a safe method for diagnosing infection of the disc space[15]. Because of the possibility of distant bone disease, to rule out other joints hip/sacroiliac and anatomic field limitations of MRI, bone scans can be useful for screening[62]. Though sensitive, it lacks specificity.

The radiology literature on pyogenic infectious spondylitis affirms the feasibility and usefulness of CT scan and MRI in discitis. They can be more sensitive and specific than bone scan for diagnosing infectious spondylitis[10,21,55,63]. The first reported use of MRI in a child with discitis was in 1986[64]. Over the last decade, the availability of MRI has increased substantially. MRI at presentation is diagnostic in all and helps to differentiate between discitis, vertebral osteomyelitis and pathology of the hip or spinal cord. T1-weighted MRI with gadolinium contrast can demonstrate abnormal enhancement of the disc and the adjacent parts of the vertebral bodies and can differentiate between a paravertebral inflammatory mass and an abscess . T2-weighted MRI shows a loss of disc height, an abnormal disc signal and irregular vertebral endplates[10,55,62]. The early use of MRI reduced the delay between presentation and diagnosis[48].

It is difficult to distinguish between the imaging appearance of pyogenic infectious

spondylitis in children and adults[65].As a result, the concept of a noninfectious inflammatory disc space narrowing in children has become less appealing. Young children may require sedation or general anesthesia to obtain an optimum evaluation of CT and MRI studies.

Diagnostic Tests

The laboratory manifestations (complete blood count, CRP and ESR) are nonspecific and taken alone, they rarely suffice for a diagnosis[52]. Like CRP, platelets play key roles in host defenses against infection and may account for the thrombocytosis [66].

It is important to draw blood cultures because they may isolate the causative organism[2,52].Most of the times it gives negative results. Nevertheless, blood cultures before therapy and in cases of increasing fever should be done in order to obtain all kind of information relevant for therapy[52]. Furthermore, it is known that identification of organisms in children with spondylodiscitis is difficult and rarely successful[21].The reasons for failure to culture a pathogen may be either a brisk host-defense response to a low-grade pathogen which significantly reduces the number of bacteria in the disc tissue, an artefact from inadequate sampling, or improper collection of the specimens. It has negligible influence on the choice of antibiotic regime and the long-term effects of the procedure are unknown[48]. The literature reports variable rates of culture for disc biopsies in children of all ages with discitis, with a positive rate of culture between 0% and 67%[15, 21,29,51,67].

A direct biopsy is probably not necessary on a routine basis because most of the organisms known to cause pyogenic infectious spondylitis in children are sensitive to first-generation cephalosporins[2].Biopsy should be reserved for patients not responding to intravenous antibiotic therapy in whom tuberculosis, fungal or other infections are suspected, and in those who are immunocompromised[48].

Complications like difficulty in inserting the needle due to narrow disc space, aortic injury, persistent motor deficit after nerve root damage in the lumbar region, pneumothorax after thoracic disc needle puncture and pneumothorax complicated by Escherichia coli lung infection after thoracic biopsy are reported[52].

Differential Diagnosis

Although classic pyogenic infectious spondylitis has a relatively distinct clinical and radiographic pattern, other disorders to consider include Scheuermann kyphosis, tuberculosis, kyphosis, Langerhans cell granulomatosis and rarely a malignant disease (primary vertebral body malignancy, metastatic disease, or leukemia with vertebral involvement)[2,17,68].

Treatment

In contrast to the adult form, paediatric spondylodiscitis is often a self-limiting condition[15,21,28,44]. Because of this and the known fact that the potential for bone destruction is very low, conservative treatment consisting of antibiotics and immobilization is normally sufficient[17,28]. An empiric course of intravenous antibiotics that covers S. aureus (a first-generation

cephalosporin) is begun. Parenteral antibiotics are continued until the symptoms are largely relieved and the laboratory values(CRP and ESR) approach normal. Parental antibiotic therapy is followed by a 4- to 6-week course of oral antibiotics[2,60]. Recommendations regarding the duration of treatment vary[2,44,47,57]. Some authors question the need for antimicrobial therapy altogether[51,69]. Compliance is also always an issue especially with oral antibiotic[2].The presence of a paravertebral mass suggested more advanced inflammation necessitating to treat these patients more aggressively with a longer duration of oral antibiotic therapy[48].

Generally, termination of antibiotic is considered justified when the patient was free from pain, passive spinal mobility is unrestricted, and normalization of the ESR has been achieved. Spine CRP levels respond faster to therapeutic interventions than ESR[70,71].

Many consider spinal immobilization to be the decisive therapeutic measure [29,52]. Immobilization allows the infection to heal and additionally maintains the spine in a normal position to prevent even worse deformities from occurring[52].Other authors[15,50] do not advise immobilization but offer bed rest and a brace only if the patient has severe functional impairment. In juveniles and adolescents, back pain may be more prolonged and a corset or back brace may be required for several weeks[2].

Fulminant cases requiring surgical intervention have been described[2,57,72]. Patients who do not respond to antibiotics may require acute surgical drainage[2,29,61,72,73]. The natural outcome is inevitably fibrous or bony ankylosis. Late MRI shows the loss of hydrous characteristics of disc[75]. Many authors have noted spontaneous vertebral fusion[15,22,74,75]. The rate of ankylosis was lowest in the younger children due to rich vascular supply[48,52]. The literature for children of all ages contains few descriptions of the rates of fusion, which vary widely from 14% to 44% [15,24,74,75].

Conclusion

The evaluation and treatment of paediatric non-tuberculous infectious spondylodiscitis has greatly improved with the ability to make an early diagnosis by an increased awareness of the disorder ,the use of the bone scan and MRI. The MRI is now the most specific noninvasive diagnostic tool for evaluating childhood spinal infection; however, bone scan remains the best screening study when the presentation and symptoms are not specific. The rapid response of severely symptomatic spondylitis patients to intravenous antibiotics provides convincing evidence that the condition is bacterial in most cases. Favourable functional outcome is a rule.

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CHAPTER 16

Pediatric Spinal Tuberculosis

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Introduction

According to WHO, November 2010, one third of the world's population is infected with the TB bacillus. The incidence of new TB cases in 2009, was 9.4 million with 14 million prevalent cases, most of which occurred in the South-East Asia region. An estimated 1.7 million (20 per lac) people died from TB in 2009, most from Africa[1]. The overall occurrence of extra-pulmonary tuberculosis in children is unknown, however, it is quoted to be between 5% to10% in children younger than 5 years, of which half of them occur in the spine[2]. Skeletal involvement is usually secondary, with the primary lesion occurring in the chest or genitourinary system. Skeletal manifestations of tuberculosis occur commonly in the spine[3] .

Pathogenesis

The tubercle bacilli tend to lodge in highly vascular areas such as the spine, coupled with the scarcity of phagocytic cells in this area; making it a favourite destination for them[4]. Although uncommon at one point, pediatric spinal tuberculosis is seen frequently in out-patient pediatric & spinal clinics. The infection reaches the skeletal system through vascular channels, generally the arteries, as a result of bacillemia, or rarely in the axial skeleton through Batson's plexus of veins. Simultaneous involvement of the paradiscal part of two contiguous vertebrae

in a typical tuberculous lesion of the spine lends support to the insemination of bacilli through a common blood supply to this region. However, the commoner modes of presentation include:

1. The "central type" of vertebral body disease and "skipped lesions" in the vertebral column is usually due to the spread of infection along Batson's plexus of veins.

2. Typical "paradiscal "lesions are considered to be caused by the spread of disease via the arteries

3. The "anterior type" of involvement of the vertebral bodies seems to be due to the extension of an abscess beneath the anterior longitudinal ligament and the periosteum, stripping the periosteum from the front and sides of the vertebral bodies. This results in the loss of the periosteal blood supply and destruction of the anterolateral surface of many contiguous vertebral bodies[5].

Two types of bone and joint tuberculosis are recognized: the "caseous exudative" type, which is characterized by more destruction, exudation, and abscess formation, and the "granular" type, which is less destructive, having dry lesions and abscess formation is rare. In clinical practice both types coexist, one predominating the other. Lesions in children are generally of the "caseous exudative type"[5].

Clinical Presentation

The most common mode of presentation in a child less than 2 years is development of a gibbus, which usually draws the attention of the parents towards a spinal problem. Many a time, the constant crying of the baby is regarded and treated as"colic". Many a child may present with inability to sit & preference for lying down, something which is usually unheard of in an active child. The usual symptoms of anorexia or fever may or may not be always prevalent. Most would typically present to a pediatrcian first, and then to the pediatric orthopedic or spinal consultant.

Under the age of four, backache is children should be regarded as pathological unless & until proved otherwise. Although non-specific musculoskeletal pain is considered as the most frequent cause, any back pain in a child needs to be assessed & investigated. One of the earliest signs of spinal vertebral infection is backache. Most patients usually have a mechanical component to their back pain, and find sitting for prolonged periods quite painful, and are relieved on lying down. They may not have developed a gibbus as yet, but routine radiographs may show early signs of vertebral infection. In countries where tuberculosis is rampant, more than 80% of patients with spinal involvement have some sort of detectable kyphosis at the time of presentation[6].

Some patients who have taken treatment for spinal tuberculosis in childhood, may present with deformed spines in their adolescence. The major problem of pediatric spinal tuberculosis is the development of deformity. Tuberculosis causes vertebral body destruction and tends to involve the cartilaginous end-plates. The affliction of the growth plate along with destruction of the anterior portion of the pediatric spine leads to a kyphosis. This deformity is further complicated by an imbalance in the growth

patterns, with the posterior growth centres continuing to grow, and the anterior centres not registering any growth.

Predicting Spinal Deformity in Childhood Spinal Tuberculosis

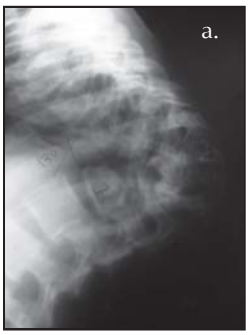
Rajasekaran observed continued progression of the deformity during the quiescent phase until the growth was complete in 40% of his patients, while 43% had spontaneous improvement and 17% showed no change[7,8]. The progression of deformity was either of an angular kyphosis or by a buckling collapse[8].

The status of the posterior column and the type of stabilisation undertaken were the main factors determining deformity. The vertebrae can restabilise when there is a large contact area on the distal vertebrae (type-A restabilisation), usually seen when the vertebral body is partially destroyed or in the lumbar region.

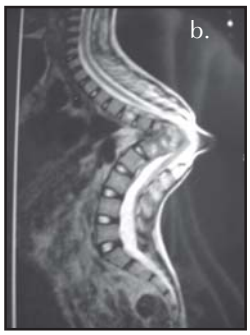
When vertebral destruction is severe, with marked loss of vertebral height, and the patient already has a moderate kyphosis, one or both facets may subluxate or dislocate, with the proximal vertebra stabilising with point contact on the distal (type-B restabilisation). The compressive force produces suppression of growth resulting in a deformity of between 40 and 60. The remaining part of the vertebral body may grow as a wedge.

Type-C restabilisation occurs when there is severe destruction of the anterior column. The dislocation of both facets leads to a buckling collapse. The proximal vertebral body may rotate through 90 with its anterior border resting on the distal vertebra. The horizontal vertebrae are spared gravitational forces and hence grow longer, adding to the kyphosis. Buckling collapse is likely to occur in children younger than seven years of age with three or more vertebral bodies affected in the dorsal or dorsolumbar spine[7,8,9].

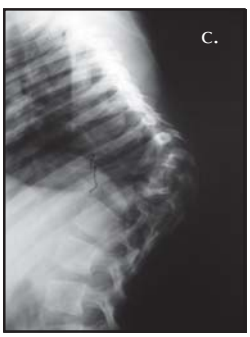
Figures for patient 1, along with legend.



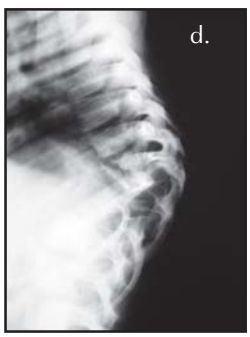
a. 10 yr old child with D10,11 Koch's spine, treated conservatively.



b. Healed disease with increase in kyphosis to 45 at 18 months.



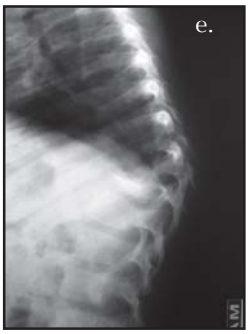
c. At 36 months, deformity has reached 70.



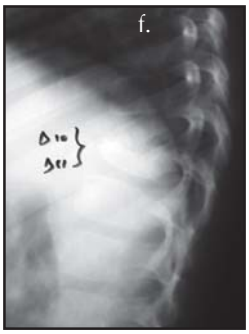
d. At 4 yrs, deformity increased to 100

According to Rajasekaran children at risk of late progressive deformity can be identified early by the presence of "spine-at risk" radiologic signs[9].

Fig 1A–D. The four radiographic signs for

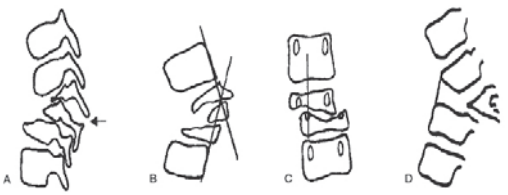


e. At 7 yrs, deformity reached 130, when child was 17 years in age.



f. MRI reveals the stretched out cord over the internal gibbus.

spine-at-risk are shown. (A) The facet joint separates at the apex of the curve, causing instability and loss of alignment. (B) The posterior retropulsion of the diseased vertebral segment is identified by drawing



two lines along the posterior surfaces of the first upper and lower normal vertebra. (C) Lateral translation is confirmed when the line drawn through the middle of the pedicle of the lower vertebra does not touch the pedicle of the superior vertebra. (D) In the initial stages of collapse, the line drawn along the anterior surface of the lower normal vertebra intersects the inferior surface of the upper normal vertebra. Tilt or toppling has occurred when the line intersects above the middle of the anterior surface of the upper vertebra. (Reprinted with permission from Rajasekaran S: The natural history of post-tubercular kyphosis in children: Radiological signs when predict late increase in deformity. J Bone Joint Surg 83A:954–962, 2001.)

Prognosis also depends upon location of the lesion: Those with dorsal lesions have maximal deformity at the time of presentation, partly due to the additive effect of the normal thoracic kyphosis. However, the rib cage offers protection against additional collapse[7]. Patients with dorsolumbar lesions have the worst prognosis as they tend to collapse more during the active phase of the disease and even more during the growth period[7].Those with lumbar lesions have the best prognosis with the least deformity at presentation, a lesser increase during the active phase, and also a tendency for substantial decrease during the growth period[7].

Investigations

HEMATOLOGICAL - The erythrocyte sedimentation rate is usually elevated but is neither specific nor reliable in the diagnosis of spinal tuberculosis. Usually a generalized lymphocytosis tilts the balance in favour of a tuberculous diagnosis. The enzyme-linked immunosorbent assay (ELISA) has a reported sensitivity of 74% with extrapulmonary tuberculosis and a very high sensitivity of 96%, against the mycobacterial antigen A60[10].Stroebel et al have reported a sensitivity of 94 per cent and a specificity of 100 per cent for osteoarticular tuberculosis by ELISA using antibody to mycobacterial antigen6[11].The polymerase chain reaction is being tested for the diagnosis but is currently not available in all clinical settings. A brucella complement fixation test may be useful in endemic areas as brucella can

clinically mimic tuberculosis.

SKIN TESTS - A positive Mantoux test can be observed, one to 3 months after infection. A previously vaccinated child may show positivity with the Mantoux test for upto 5 years[12]. The test may be negative in almost 20 per cent patients with active disease if the disease is disseminated, or if the patient is immunocompromised or suffering from exanthematous fevers . Co-existent infection by human immunodeficiency virus may also give a false negative skin test[12].

Imaging

Radiographs are difficult to interpret owing to the small size of the vertebral body in the very young patient, however, in the juvenile & adolescents, sufficient bony destruction must have happened to be visible on the X-ray. Also, the deformity if it has developed, needs to be measured and documented for future reference.

However, in today's world, the diagnosis of spinal tuberculosis is just an MRI away. Although the MRI cannot differentiate between pyogenic or tuberculous infection [13], certain characteristics are quite unique; and in conjunction with a high index of suspicion, in an endemic country like India, an MRI diagnosis of "most likely tuberculous in origin", can be made safely.

The MRI characteristics of vertebral body tuberculosis have been extensively reported. The thoracic spine is most commonly affected; the radiological features include bone marrow oedema and enhancement, posterior element involvement, canal stenosis, and spinal cord or nerve root compression[14]. Inter-vertebral disc enhancement, vertebral collapse and kyphosis deformity are particularly suggestive of tuberculosis[15]. Vertebral intra-osseous abscess, disc abscess, abnormal para-spinal signal intensity, and involvement of multiple vertebral bodies are common in tuberculosis but rare in pyogenic bacterial disease[16,17]. Brucellar spondylitis cannot be distinguished radiologically from tuberculosis [18].

Management

The management usually depends upon the time of presentation of the child. It may present in the acute situation or may present late with healed kyphotic deformity.

Active uncomplicated Kochs Spine

If the child presents with the active lesion, early enough, it may be manageable with only chemotherapy and brace or cast. Standard four drug anti-tuberculous therapy is usually administered, with isoniazid, rifampicin, ethambutol & pyrazinamide.

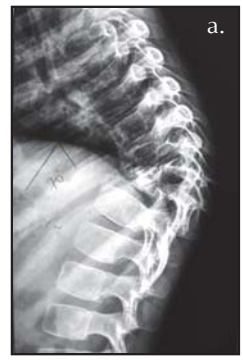
Non-compressive lesions with paradiscal involvement without significant collapse may be amenable to casting or bracing in conjunction with chemotherapy. Some degree of kyphosis is bound to occur with this method, as healing usually occurs following bone to bone contact and fusion between the adjacent vertebral end-plates. A whole body cast including the thoracic and lumbar spine, extending upto the pelvis is usually provided. The adolescent may be fitted with a removable plastic thoracic brace, for a variable period ranging from 3-9 months. If the cervical spine is afflicted, a

Minerva cast or halo-jacket apparatus may be needed. The use of flimsy four post collars & SOMI brace is mentioned only to be condemned, as they do not produce adequate immobilisation, and provide a false sense of security to the patient and physician alike.

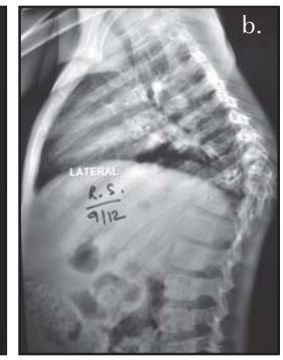
Active Disease with Abscess or Neurological Compromise

Sometimes the child may present with a huge epidural or anterior abscess with destruction of the vertebral body, with associated kyphosis. In this situation, decision may be needed to undertake a radical debridement along with reconstruction of the vertebral column. Whenever it can be predicted with reasonable certainty that further growth in the pediatric patient will result in a kyphotic deformity owing to the destruction of one or more vertebral bodies, surgery is indicated [19]. In such situations the four signs of "spine at risk" by Rajasekaran may also be utilised to arrive at a surgical decision[9]. The major problem of undertaking radical debridement in children is reconstruction of the large defect with bone graft. Overall, in most cases, owing to the greater length & strength of bone graft required, fibula is chosen over iliac crest or rib. Instances have been reported when the entire thoracic spine was involved and the spinal reconstruction had to be done from T2 to T12 with a fibular graft[20]. Despite adequate positioning of the fibular graft into the slot in to a normal healthy vertebral body, graft slippage rate is high, especially when more than two vertebral bodies need to be spanned.

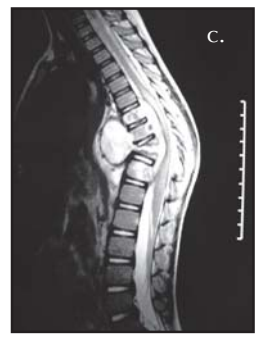
Figures for patient 2, along with legend.



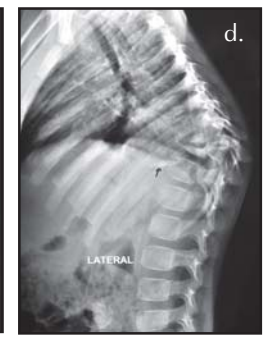
a. 4 yr old child presented with tuberculosis of D10,11 with kyphosis of 70 with paraplegia.



b. MRI revealed huge epidural as well as anterior abscess with involvement of D8 to D12 vertebral bodies.



c. Corpectomy of D10, 11 done and fibular grafting done. At 6 months, patient showed good graft consolidation with residual deformity of 57.



d. Healed disease, 2 yrs post surgery, deformity has increased to 70, necessitating posterior surgery.

Most authors agree that posterior spinal fusion is indicated to prevent late development of kyphotic deformity. Controversy exists regarding the timing of posterior fusion in these patients. One group of authors recommend undertaking posterior

surgery within 3 months of the anterior surgery to assist anterior fibular graft during its weakest phase[20]. However, another group of authors prefers to wait and observe the child periodically over time and if, there is evidence of increasing kyphotic deformity, a posterior spinal fusion is undertaken. However, this may be too late and predictive recommendations as observed by Rajasekaran need to be considered in pediatric spinal tuberculosis patients. According to him, children younger than seven years of age, with three or more affected vertebral bodies in the dorsal or dorsolumbar spine and two or more 'at-risk signs', are likely to have progression of the kyphosis with growth and should undergo correction [7,8,9].

Use of Instrumentation in Spinal Tuberculosis

The additional use of instrumentation in the pediatric spine, over and above a fusion merits a discussion as well. Although traditional teaching was against the use of metal in presence of infection, the advent of newer anti-tuberculous drugs allows the safe use of instrumentation in the spine. The indications for instrumented stabilisation include i) panvertebral disease or ii) long segment disease, requiring a bone graft length greater than two vertebral bodies[21] or iii) when kyphosis correction is contemplated[22,23].

One of the earliest instrumentation systems to be used for Koch's spine included the Hartshill rectangle. This was followed by the use of more sophisticated equipment like the pedicle screw system in patients with tuberculosis of the spine. The major problem of pedicle screw systems is the non-availability of low profile systems, in a smaller diameter range, which tends to lead to skin breakdown issues in the pediatric patient population. However, it does provide the benefit of early ambulation and rehabilitation of the patient, in addition to the safety of the graft.

Surgery in Healed Post-Tubercular Kyphotic Deformity

Almost 40% of children with tuberculosis of the spine tend to progress and eventually develop a kyphotic deformity[7].Depending upon the extent of the disease, the vertebral stabilisation occurs and kyphosis of varying degrees tends to develop. An internal gibbus also develops which tends to cause late onset paraplegia if kyphosis is allowed to progress. Surgery in healed tuberculosis with kyphotic deformity usually involves spinal osteotomy with corpectomy along with anterior and posterior reconstruction being performed in two stages[24]. However, single stage, only posterior surgeries, wherein a pedicle subtraction osteotomy or spondylectomy is carried out have been developed recently and are quite challenging[25,26]. The basic concept is to shorten the posterior column so as to correct the deformity and achieve bone to bone contact for fusion. Single stage closing opening wedge osteotomy has been described by Rajasekaran for the simultaneous correction of the deformed spine of high magnitude(118 degrees of kyphosis)[27]. Such extensive surgeries require a lot of meticulous planning and experience for appropriate execution, and should not be attempted by the average ORTHOPEDIC surgeon.

Conclusion

Pediatric spinal tuberculosis is a problem, wherein the sinister varieties need to be identified and monitored and appropriate action needs to be taken early so as to prevent a catastrophic deformity. If treated appropriately, grotesque deformities can be prevented from occurring, and those unfortunate children may be managed with low risk surgeries. Management of pediatric spinal tuberculosis should be a team effort between the pediatrician, the pediatric orthopedic surgeon as well as the spine surgeon, as the case may be, to achieve the most optimum result.

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CHAPTER 17

Osteoarticular tuberculosis

Dr. S. M. Tuli

Epidemiology, Prevalence, and regional distribution

At present there are nearly 30 million people suffering from tuberculosis worldwide, and of these 1% - 3% have involvement of the skeletal system. Tuberculosis will exist for as long as there are pockets of malnutrition, poor sanitation, overcrowding and immune compromised populations.

Vertebral tuberculosis is the most common form of skeletal tuberculosis, accounting for 50% of all cases in reported series. Approximate distribution in The major areas of predilection are Approximate distribution in spine (50%), hip (20%), knee (10%), ankle and foot (5%), hand and wrist (3%), elbow (2%), shoulder (1%), bursal sheaths and other bones (8%).

Pathology and Pathogenesis

An osteo-articular tubercular lesion results from hematogenous dissemination from a primarily infected focus that may be active or quiescent, and in the lungs, lymph glands, or other viscera. The infection reaches the skeleton through vascular channels, generally the arteries, as a result of bacteremia or, rarely, in the axial skeleton though Batson's plexus of veins. If whole body screening could be done in all patients, 40% of them will show an additional active, clinical or subclinical, lesion in viscera, lymph nodes or other parts of skeletal system.

Development of clinical tuberculosis of the skeletal system is a reflection of weakened immune status, of the host.

Osteoarticular disease:

Tubercular bacilli reach the joint space via the blood stream through subsynovial vessels, or indirectly from epiphyseal lesions that erode into the joint space. Destruction of the articular cartilage begins peripherally. Since the weight bearing surfaces are preserved for a few months, there is potential for good functional recovery with effective treatment.

The disease may start in bone or in the synovial membrane, but the one rapidly infects the other. The initial focus starts in the metaphysis in childhood or at the end of the bone in adults. The osseous areas of predilection for hip disease are shown in the figure. (Figure -1)

Radiologically, there is marked local demineralization and destruction. In bones with superficial cortical surfaces (such as metacarpals, metatarsals, phalanges, tibia, and ulna), the lesions may produce reactive subperiosteal new bone formation surrounding lytic area, giving rise to a spindle shaped swelling.

Cartilaginous tissue is resistant to tuberculous destruction. However, penetration of the epiphyseal cartilage plate occurs predominantly in tuberculous disease, rather than in pyogenic infection. Metaphyseal tuberculous lesions may infect the neighboring joint through the subperiosteal space, through the capsule, or through destruction of the epiphyseal plate. Once the tuberculous process has reached the subchondral region, the articular cartilage loses its nutrition and attachment to the bone and may lie free in the joint cavity. Damage to the physis in childhood may result in shortening or angulation of the limb.

When infection starts as tuberculous synovitis, the course is usually slow. The synovial membrane becomes swollen and congested, and an effusion develops. The granulation tissue from the synovium extends over the bone at the synovial reflections, producing erosions. At the periphery of the articular cartilage, granulation tissue forms a pannus that erodes the margins and surface of the joint. Flakes or loose sheets of necrotic articular cartilage and accumulations of fibrinous material in the synovial fluid may produce the rice bodies found in synovial joints, tendon sheaths, and bursae. Where articular surfaces are in contact, the cartilage is preserved for a long time because the spread of pannus is retarded. Necrosis of subchondral bone by the ingrowth of tuberculous granulation tissue produces kissing lesions or sequestra on either side of the joint.

Cold abscess

A marked, exudative reaction is common in tuberculous infection of the skeletal system. A cold abscess is formed by the products of liquefaction and the reactive exudation. It is composed of serum, leucocytes, caseous material, bone debris, and tubercle bacilli. The abscess penetrates the periosteum and ligaments, and migrates or gravitates in various directions, following fascial planes and the sheaths of vessels and nerves. The cold abscess feels warm, although the

temperature is not increased to the same extent as in acute pyogenic infections. A superficial abscess may burst to form a sinus or an ulcer lined with tuberculous granulation tissue. On aspiration, the contents of the cold abscess range from serous fluid to thick, purulent pus.

Osseous changes and tubercular sequestra:

Following the infection, marked hyperemia and severe osteoporosis take place. The softened bone easily yields under the effect of gravity and muscle action, leading to compression, collapse, or deformation. Necrosis may also be caused by ischemic infarction of segments of bone. Sequestration gives the appearance of coarse sand and rarely produces a radiologically visible sequestrum. Because of loss of nutrition, the adjacent articular cartilage may become separated as sequestra. Some of the radiologically visible sequestra in tuberculous cavities may result from calcification of the caseous matter.

The future course of the tubercle

Before the availability of anti-tubercular drugs, the 5 year follow-up mortality of patients with osteo-articular tuberculosis was about 30%. Presently available antitubercular drugs have changed the outlook, the mortality is very low now. Depending upon the sensitivity pattern, the host immunity and the stage of the lesion at the inception of treatment, the tuberculous lesion may resolve completely, heal with residual deformity and loss of function, be completely walled off and the caseous tissue may calcify, persist as a low-grade chronic fibromatous granulating and caseating lesion or may spread locally by contiguity and systematically by blood stream.

Diagnosis and investigations:

Skeletal tuberculosis mostly occurs during the first three decades of life. The characteristics are insidious onset, mono-articular or single bone involvement, and the constitutional symptoms of low-grade fever, lassitude (especially in the afternoon), anorexia, loss of weight, night sweats, tachycardia, and anemia. Local symptoms and signs are pain, night cries, painful limitation of movements, muscle wasting, and regional lymph-node enlargement. In the acute stage, protective muscle spasm is severe. During sleep, the muscle spasm relaxes and permits movement between the inflamed surfaces, resulting in pain and the typical night cries.

Despite the list of symptoms and signs it is not uncommon for the patient to present only with local joint symptomatology. Children can look physically well except for the involved joint.

Diagnosis:

In developing countries the diagnosis of tuberculosis of bones and joints can be made reliably on clinical and radiological examination. It is ideal to have positive proof of the disease by semi-invasive or invasive investigations. Skeletal tuberculosis must be included in the differential diagnosis of chronic or subacute mono-articular arthritis, chronic abscess, a draining sinus or chronic osteomyelitis. It is important to remember that tuberculosis can mimic any disease, and nay pathology can mimic tuberculosis on

clinical features and on imaging modalities.

Confirming the diagnosis:

Biopsy is the only certain method which can be used to confirm the diagnosis. Any pathological material obtained from joint, bone, or lymph nodes, must be submitted for histology, microbiology and for PCR for tuberculosis. However even on histology the changes may be non-specific: in some studies the results of biopsy reveal chronic, non-specific inflammation in 50% of cases. All attempts however must be made to confirm the diagnosis before putting the patient empirically on antitubercular drugs.

Localized osteoporosis is the first radiological sign of active disease. The articular margins and bony cortices become hazy and there may be areas of trabecular destruction and osteolysis. The synovial fluid, thickened synovium, capsule, and pericapsular tissues produce soft-tissue swelling, and the joint space narrows. As the destructive process advances, bone architecture collapse and joints deform or displace. The epiphyseal growth plate may be destroyed, producing altered growth, angulation, or premature fusion. With healing of the disease process there is remineralization, reappearance of bone trabecula, and sharpening of cortical and articular margins.

In the center of a tuberculous cavity there may be a sequestrum of cancellous bone or calcification of the caseous tissue giving the appearance of an irregular, feathery nidus in a cavity.

If secondary infection supervenes, subperiosteal new bone formation can be seen along the involved bones. Plaques of irregular (dystrophic) calcification in the wall of a chronic abscess or sinus are almost diagnostic of long-standing tuberculous infection.

Computed axial tomography (CT) and magnetic resonance imagining (MRI) demonstrate the localization and extent of bone and soft-tissue lesions, and improve suspicion of the disease at a very early stage (3-6 weeks).

MRI scanning in the earliest stages reveals inflammation and not infection, just as radiosotope scintigraphy may show a hot area during the active stage of the disease. However these are neither specific, nor does it differentiate between the osseous and soft-tissue pathology. The feathery tubercular sequestra and dystrophic calcification are discernible on CT scans, but cannot be seen on MRI.

Blood:

A relative lymphocytosis, low hemoglobin, and increased erythrocyte sedimentation rate (ESR) are typically found in the active stage of disease. A raised ESR, however, is not necessarily proof of activity of the infection. Its repeated estimation at monthly intervals gives a valuable index of the activity of the disease. In counties where tuberculosis is endemic the serological test which has been found to be useful is polymerase chain reaction for tuberculosis (PCR). A positive PCR confirms the diagnosis of tuberculosis if the tested material was obtained from a clinically inflammed area. A negative PCR however does not exclude tuberculosis.

Biopsy:

Whenever there is doubt (particularly in the early stages), it is mandatory to prove the diagnosis of tuberculosis by biopsy of the diseased tissue (granulations, synovium, bone, lymph nodes, of the margins of tuberculous ulcers or sinuses). Microscopic examination of material from the aspirate, core biopsy, needle biopsy, or open biopsy will reveal typical tubercles in untreated cases. The presence of epithelioid cells surrounded by lymphocytes, even without central necrosis or peripheral foreign-body giant cells, is adequate histological evidence of tuberculous pathology in a patient who is suspected to be suffering from the disease. At the time of open biopsy of a joint or bone, the orthopedic surgeon should perform therapeutic synovectomy or curettage. The infections of bone and joint that present as granulomatous lesions are, in order of frequency: tuberculosis, mycotic infection, brucellosis, sarcoidosis, and tuberculoid leprosy. Guinea pig inoculation is perhaps the most reliable proof of tuberculous pathology, however it is no longer considered cost-effective.

Management of osteoarticular tuberculosis

General principles:

With the use of modern drugs, the indications for surgery have become universally more selective and directed towards the prevention and correction of deformities and the improvement in function of the diseased joints. At the stage of tuberculous arthritis, if the disease remains closed, the natural outcome is generally a fibrous ankylosis. If an abscess discharges and sinuses develop, the outcome may be a bony ankylosis. The prognosis in articular tuberculous depends upon the stage of the disease when the specific treatment is started (Table-1).

Concomitant disease must be treated. Associated pulmonary involvement is important to recognize. Admission to hospital is necessary only for complications or for those requiring traction under supervision to correct deformities.

The functional treatment of articular tuberculosis: (Rest, mobilization, and bracing)

In the active stage of disease, the joints are rested in the position of function by means of removable splints. Prolonged immobilization may lead to spontaneous ankylosis, especially when large joints are destroyed. Patients with early disease are allowed one-hourly intermittent guarded active and assisted exercises under anti-tubercular drug cover, with the aim of retaining a useful range of movement in the functional arc of the involved joint. Traction helps to correct deformity and to rest the diseased part. Gradual mobilization is encouraged, with the help of suitable braces, approximately 3 months after the start of treatment, while the healing is progressing. As the disease heals and pain subsides, weight-bearing and activity in encouraged. If symptoms and signs of activity increase the patient goes back a stage. If there is steady progress, activity is increased within the limits of discomfort. Bracing is gradually discarded after about 2 years although in most cases this period is much shorter.

Aspiration is the method of choice for large

collections. Open drainage of an abscess is indicated if the collection is significant and aspiration fails. It is customary to instill streptomycin + isoniazed after aspiration; however it is not essential because antitubercular drugs easily penetrate the tuberculous lesions after systemic therapy.

The large majority of ulcers and sinuses heal within 6-12 weeks under the influence of systemic anti-tuberculous drugs. The full course of treatment is still necessary. Fewer than 1% of sinuses require longer treatment and excision of the tract, with or without debridement. Sinus ramification is always greater than can be appreciated, and complete surgical excision is therefore impracticable.

Final end Result: The expected outcome depends upon he stage at which the ereatment was started (Table-1). For many patients with advanced disease on diagnosis the ultimate outcome will be an ankylosed joint in the position of function.

The commonly used drugs and dosages have been summarized in table. 2 The doses and drugs are worked out on the bases of age and weight of patients and any drug reaction. The duration of thereby must last for 12 to 18 months.

Anti-tubercular drugs are the most important therapeutic measure in osteo-articular tuberculosis, speeding recovery and minimizing the incidence of complications, recrudescence, and death. Patients with early disease, sensitive organisms, and a favorable pathological lesion (absence of large cavitations, pathological dislocation, ischemic tissue, and infracted bone) achieve full clinical healing without recourse to surgery. Osseous tubercular lesions are slower to heal than synovial lesions.

After prolonged antitubercular therapy the histological appearance ceases to be characteristic. The epithelioid cells become less compact and the tubercle is unrecognizable, because both the epithelioid cells and lymphocytes are widely scattered. Central caseation may disappear, but fibrosis remains a significant feature in advanced tuberculous disease.

Surgery in Tuberculosis of Bones and Joints

No surgery is a substitute for a correct course of anti-tubercular drugs. A trial of conservative treatment is usually adequate in pure synovial tuberculosis, lowgrade or early arthritis of any joint, and even advanced (Table 1—.2 stage III or IV) arthritis, especially in the upper extremity.

Surgery should be considered only when the general condition of the patient has been stabilized by drug treatment, before the development of drug resistance. In general, a minimum of 1-4 weeks of drug therapy is advisable before any major surgical intervention.

Extent and type of surgery

Fusion of a major joint (except in the spine) is seldome indicated as primary treatment during childhood. Juxta-articular osteotomy, soft-tissue release, synovectomy, and debridement should produce mobile, stable joints. If a juxtaa-rticular osseous focus is threatening the joint despite adequate anti-tubercular drugs, excisional surgery of the

focus should be performed. Non-responsive cases of tubercular synovitis and early arthritis respond to subtotal synovectomy and synovectomy combined with joint debridement, respectively. At any stage of the disease, if a lesions is proving resistant or the diagnosis is in doubt, operation is mandatory. Debridement should be limited to infected synovium, sequestra, cavitites of pus, and sinuses. Repetitive active and assisted movements of the joint should preserve a functional arc of movement after the operation.

In advanced arthritis (Of hip, knee, ankle, wrist and elbow) with pathological dislocation the best position of function is achieved by traction periodic corrective plaster ar by operative repositioning of the joint. Once the best position of function is achieved the joint is splinted for 3 to 6 months with intermittent active exercises.

In advanced arthritis of the knee, ankle, wrist, hip: and elbow, the position of function is achieved by operative debridement followed by splintage for 3-6 months. If the disease has healed leaving a painless range of movement (20àà* or more) in an unacceptable position, a juxta-articular osteotomy may be performed to yield the best functional arc. Osteotomy may also be indicated to correct varus or valgus deformity particularly in the hip or knee. If the growth plates of the involved joint are open, surgical arthodesis should be deferred until the child is older than 12 years.

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Note: Most of this write-up is adapted form author's earlier publications in Children's Orthopaedics and Fractures Pub.by Churchil Livingstone, and in Clinical Orthopaedics and Related Research.

CHAPTER 18

Utility of different laboratory tests in Pediatric Osteoarticular Tuberculosis

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Tuberculosis (TB) is a major health problem in the Indian subcontinent. India accounts for nearly 20% of the total TB burden. Of these, nearly 1-5% of cases have skeletal TB[1] . As TB is endemic in India, most orthopedic surgeons diagnose osteoarticular TB based on clinical and imaging findings only and initiate empirical anti-TB treatment. There has been a growing body of new and exciting methods in mycobacteriology, but there is still no single test that is diagnostic in all the situations. Over all fact is that only the laboratory investigations can give ultimate solution of diagnosis and management provided a few proper methodologies are selected according to clinical situations and stage of disease. The following laboratory methods for diagnosis are available,

A. Methods providing direct evidence of presence of Mycobacteria

1. Demonstration of Acid Fast bacilli:
   a. Z N stain
   b. Fluorescent microscopy – Auramine phenol stain
2. Culture Examination:
   a. L J medium – Conventional solid culture medium
   b. Automated methods with culture in Liquid media: BACTEC MGIT 960, BacT Alert 3D
3. Nucleic acid detection: Polymerase chain reaction, DNA probe, TMA and NASBA for RNA etc.
4. Fast Plaque assay

B. Methods providing indirect evidence of infection:

1. Histopathology & Cytology
2. Tuberculin test
3. Detection of sensitized lymphocytes: Interferon – ^{3} assay; QuantiFERON – TB

4. ELISA: Detection of IgM antibody
5. Adenosine deaminase assay

The above mentioned methods are variably helpful for diagnosis of tuberculosis. They all have their own merits and demerits.

The prevalence of MOTT (Mycobacteria other than Tuberculosis) and MDR / XDR Tuberculosis are increasing day by day. So, only diagnosis may not be sufficient and mycobacterial identification and its antituberculous drug susceptibility may be warranted for proper management of patient. These can be possible when culture is done and we have the growth of mycobacteria in vitro. Few Nucleic acid techniques may detect resistance gene in bacteria present in the specimen.

Demonstration of Acid Fast Bacilli:

It is a most widely available, cheap, rapid and highly specific method. If the AFB are detected by ZN staining, it is the most important evidence of Mycobacterial infection. But the sensitivity of this test is very low. At least 5,000 to 10,000 bacilli per ml of clinical material are required for its detection by Z N stain. The sensitivity of microscopic examination may be improved by fluorescent stain with Auramine phenol; but, this requires sophisticated fluorescent microscope and expert personnel for interpretation & as it is a subjective assay, sensitivity and specificity is center dependent.

Culture Examination:

Culture is a still gold standard even in an era of molecular technology. When the focus of the lesion is traceable, specimens (fluid/ tissue) from suspected site should always be sent for culture examination. There are many reasons, why the culture is essential investigation in osteoarticular infections,

i. It has highest specificity[2] (98%) and positive predictive value.
ii. As low as 10 bacilli / ml of material can be detected.[2] Arthrocentesis with mycobacterial cultures of synovial fluid yields positive results in up to 80 percent of patients with tuberculous arthritis.[3]
iii. Growth of the organisms is necessary for precise species identification and drug susceptibility testing.

The conventional culture method with use of LJ medium is widely available in our area. The only drawback is it needs average 5 to 6 weeks to be positive and may needed to wait for 10 – 12 weeks to stamp for negative. Broth based automated system had brought evolution in last decade. BACTEC 460 based on radiometric method was a popular method indicating growth as early as 5 days. But, nowadays BACTEC MGIT and BacT / ALERT 3D have largely replaced radiometric system to overcome the issue of radioactive biohazards. Both the system MGIT and BacT / ALERT 3D has turnaround time of about 8 days in smear positive sample; Which is about 14 to 16 days in smear negative samples with sensitivity of 80 % in case of osteoarticular tuberculosis. These two systems also provide sufficient biomass of bacteria at time of positive indication of growth, which directly can be processed for identification and sensitivity.[4]

Molecular techniques:

At present various molecular methods are in practice including Polymerase chain reaction

(PCR), Nucleic Acid Sequenced based amplification (NASBA), Transcription mediated amplification (TMA), LCR, SDA etc. PCR technology detects a DNA sequence specific of Mycobacteria from the speciemens; here prior to detection the specific sequence of bacilli is multiplied several fold which increase the sensitivity of the test. The chance of false negative is more in the samples like urine and pus which likely contains PCR inhibitors.[4] NASBA and TMA technologies detect rRNA, concentration of which is abundant in sample as compare to DNA so these are a little more sensitive methods. PCR technology can detect live as well as dead bacilli[2] while the methods targeting RNA will detect only live bacteria in the sample.

The most advantage of PCR based techniques is the rapid turnaround time because all of them are a single day procedures. They also have very high sensitivity as compare to smear examination. Hence, these tests can greatly increase confidence in the clinical diagnosis pending culture results. However, with consideration of false positive and false negative results, nucleic acid amplification methods do not replace the need for culture, and especially when drug susceptibility tests are to be performed. Moreover, PCR can detect nucleic acids from dead as well as live M. tuberculosis and, therefore, can remain positive for long periods in patients on therapy. Thus, this method should be used only for initial diagnosis and not follow-up evaluations of patients who are receiving anti mycobacterial drugs.[2]

Fast Plaque TB:

A novel technology, based on ability of mycobacteriophage – a kind of virus which can only infect mycobacteria. The multiplication and survival of this virus which present in test kit can only be possible if live bacteria are present in sample. It is a rapid – assay, results available within 24 hours of sample preparation, no instrumentation required, safe - no culturing of pathogen required, assay sensitivity is 100 - 300 bacilli/ml as per manufacturer's specification. This technology can be extended for antibiotic susceptibility testing

Histopathology and cytology:

A positive histopathological finding provide a very high positive predictive value in endemic area like India. The proper site of biopsy important in obtaining results, unless the biopsy is taken from a granulomatous area where a cyst is apparent on the radiograph, or from its immediately adjacent synovium, the histological results are likely to be equivocal.[5] According to a study, in the samples of fine needle aspiration biopsy, granulomatous reaction, with or without caseation necrosis, was found in 73%; Acid-fast bacilli were found in 64%, and the M. tuberculosis cultures were positive in 83% of all cases.[6]

Tuberculin test: (Mantoux test – MT)

The test is demonstrating cell mediated hypersensitivity (type IV) reaction against tuberculous antigens in vivo. Positive test suggests, prior sensitization of the host with tuberculous antigen i.e. exposure to M.tuberculosis. However, it can not differentiate infection or subclinical exposure as well as recent past or remote past exposure. The result of tuberculin test should

be evaluated with various clinical and substitute investigative findings. After proper inoculation, readings of the transverse diameter of induration is taken after 48 hr and 72 hr with a transparent plastic ruler using the ball point pen technique and recorded meticulously in mm by the same observer.[7] The Induration of,

> 15 mm: always cosidered positive
> 10 mm: Consider positive in high prevalent area (i.e. India) , especially in children of less than 4 years
> 5 mm: Positive in HIV, Radiologically and clinically confirmed cases

The possibility of false negative result can be overcome by two step test were the positive test on subsequent occasion considered as past infection. But, in our country major limitation is false positive result. To avoid false positive interpretation, it is better to follow IUATLD Criteria for relevance of MT with diagnosis.[7]

Criterion	Score point in Age group	
	0-4 yr.	5-14 yr.
Close contact with a known case of TB	1	1
Mantoux skin test positive	2	3
Persistent cough	2	1
Low weight for age/weight loss	2	2
Unexplained / prolonged fever	3	3
Total score must equal / exceed	6	6

QuantiFERON®-TB Gold Test:

It is based on the stimulation of whole blood of patient with tuberculin and control antigen and subsequent detection of INF – ^{3} secreted by human lymphocytes if they are previously sensitized by exposure to M.Tb.

Advantages of the test are:

Like MT it is also demonstrating cell mediated immunity but it is in vitro test so many patient's factors interfering the results in MT can be bypassed. It requires a single patient visit to draw a blood sample.Results can be available within 24 hours.Is not subject to reader bias that can occur with TST. Is not affected by prior BCG (bacille Calmette-Guérin) vaccination.

Disadvantages and limitations of the test are:

Blood samples must be processed within 12 hours after collection while white blood cells are still viable. There are limited data on the use of QFT-G in children younger than 17 years of age, among persons recently exposed to M. tuberculosis, and in immunocompromised persons.

Adenosine Deaminase (ADA) assay:

ADA is an enzyme produced by Lymphocytes in the presence of intracelular tubercle bacilli. The same enzymes also produced by neutrophils and several other cells of the body. The highest value of ADA activity is observed in synovial fluid of patients with tubercular arthritis followed by rheumatoid, septic, osteo and post traumatic arthritis. Thus measurement of ADA activity in synovial fluid can be used as a parameter of differential diagnosis of arthritis specially tubercular in initial stages.[8]

The reported cutoff value for ADA varies

from 47 to 60 U/L. Specificity is increased when the lymphocyte/neutrophil ratio in the fluid (of > 0.75) is considered together with an ADA concentration of >50 U/L. The false-positive diagnoses by ADA level determination can be significantly reduced if ADA measurement is limited to lymphocytic fluids. In contrast to MT, in areas with a high prevalence of tuberculosis, the proportion of false-positive results will be lower. An elevated fluid ADA level predicts tuberculous effusion with a sensitivity of 90 % and a specificity of 89%.

ELISA: ELISA based method detection is rapid, but its sensitivity at best is not reported to be higher than 55%. Also the biggest drawback is the high rate of false positivity i.e., 20-30%, in both antigen and antibody detection assays in high prevalence regions like India. This makes results of ELISA very difficult to interpret for the physicians.

ESR: It is one of the commonest supportive investigations to be carried out in each patient. Though having very poor predictive value can help a lot when used in combination of various other clinical, radiological and laboratory parameters. It also provides a significant prognostic value in patient on therapy.

Mycobacterial species identification:

Tuberculosis is the most common mycobacterial infection(> 90 %) in our country. But a number of cases have been reported caused by MOTT. Few cases of infection with rapid grower mycobacteria (i.e. M.fortuitum, M.chelonei) also been reported in which the management is completely different. This warrants identification of mycobacterial species.

Species identification can best be done by conventional methods. Various commercial kits are available to provide identification of Mycobacteria grown on LJ or Middlebrook medium. NAP test with BACTEC 460 can differentiate MTb from MOTT. Nowadays PCR based and other molecular technologies provide perhaps the best option for rapid and reliable species identification.

AKT sensitivity

On LJ medium AKT sensitivity can be performed by 1% proportional method, resistant ratio method or absolute concentration method. This usually takes 12 to 16 weeks. Since these traditional methods are time consuming and may delay the treatment by at least 2 to 4 months, newer and rapid methods of culture and sensitivity of the mycobacteria have been developed. Newer rapid radiometric BACTEC 460 TB System for culture and drug sensitivity gives early results, thereby immensely aiding in early institution of correct therapy. Equally good results can be provided by BacT Alert 3 D and MGIT. Identification of gene conferring resistance to mycobacteria can be detected by PCR. Mutated resistant gene confirming resistance to rifampicin, isoniazide and streptomycin can be detected by PCR from Mycobacterial growth or strong positive clinical sample. It requires less than 2 days for the results. It is now established that the mutations conferring multiple drug resistance in the Indian strains of Mycobacterium tuberculosis are different from the western strains and PCR protocols, which can pick up the novel Indian mutations have been standardized in various

reference laboratories of India.

Comparision of results obtained by 5 different laboratory methods.[1]

N=103	AFB Smear		Histopath		L J		Automated culture		PCR	
	Pos	Neg	Pos	Neg	Pos	Neg	Pos	Neg	Pos	Neg
Definite TB (47)	25	22	33	14	35	12	46	01	44	03
Probable TB (16)	06	10	16	0	0	16	01	15	14	02
Possible TB (19)	0	19	0	19	0	19	0	19	06	13
Clinically suspected TB(11)	0	11	0	11	0	11	0	11	01	10
Non TB controls	0	10	0	10	0	10	0	10	0	10

Whenever sample from site of the infection is possible, mycobacterial cultures using liquid media with susceptibility should form the backbone of management of osteoarticular TB. Automated culture can reduce turnaround time. PCR enhances the sensitivity if performed in addition to culture and provide early diagnosis. When proper sample can not be obtained, IFN – ^{3} assay can provide the best information. Whenever proper biopsy material taken, histopathology will provide good information. If only synovial fluid can be possible, Cytology and ADA assay will improve clinical judgment. Other laboratory facilities can be useful in particular clinical situations for diagnosis and prognosis if carefully selected.

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CHAPTER 19

OSTEOMYELITIS IN SICKLE CELL ANEMIA

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GENERAL OVERVIEW

Osteomyelitis is a pathological definition of infection of bone and its marrow. It can occur in anyone irrespective of age, gender and geographic location. However, it is more common in children under 10 years old,[1] diabetics, immunocompromised patients and those with sickle cell disease (SCD).[2]

The incidence of its complicated chronic variant is commoner in the under-developed countries because of poverty, shortage of trained and qualified staff and delayed presentation to hospitals.[3]

It is also more complicated in patients with SCD because of recurrent bone infarction. The diagnosis in SCD may be challenging because of bone pain from recurrent infarctions.[4,5]

Early diagnosis with prompt and aggressive treatment is associated with good prognosis. Therefore, any patient with bone pain and fever should be considered as acute osteomyelitis until proven otherwise[1].

INTRODUCTION

SCD refers to a group of autosomal recessive red cell disorders first described in medical literature by Herrick in 1910[6].The characteristic sickle-shaped red blood cells (RBC) seen on blood film result from the presence of Haemoglobin S (**HbS**), a variant of normal adult haemoglobin, caused by the substitution of valine for glutamic acid at position 6 of the beta globin chain. The homozygous form of SCD, HbSS, or sickle cell anaemia (SCA) is the commonest and most severe type. Compound heterozygous states may also occur where HbS is present

with other variant haemoglobins such as haemoglobin C, D, O-Arab or beta thalassemia[7].

SCD affects millions of people worldwide and has been recognized by the World Health Organization as a major public health problem. About 5% of the world's population carries genes responsible for haemoglobinopathies and each year about 300,000 infants are born with major haemoglobin disorders[8]. In populations of African Ethnic origin, SCA represents 70% of cases of SCD[9].

EPIDEMIOLOGY OF SCD

The global distribution of HbS reflects the survival advantage in malaria endemic regions and subsequent migration[7,9]. Even though there are conflicting reports regarding the former[10], the fact that it is commonest in sub-Saharan Africa lends credence. 8% of African-Americans carry the gene responsible for sickle-cell disease. About 40% in some African tribes also carry this gene[9,11]. The Bhopal experience in India showed 7% out of a total of 500 samples carrying the sickling gene. Of this 45.71% carried Sb*/Sb. The sickling trait was seen in about 20%[12].

PATHOGENESIS OF SCD

There is a genetic mutation of the b-globin chain of haemoglobin at position 6, where the amino acid glutamine is replaced by valine. This produces hydrophobic haemoglobin, which in the presence of decreased oxygen tension crystallizes. The crystallization produces a polymer nucleus that enlarges to fill the erythrocyte and in the process, distorts its architecture and flexibility. This causes 2 major pathophysiological processes: micro vascular vaso-occlusion with ischaemia-reperfusion injury and haemolytic anaemia. The exact mechanism of micro vascular occlusion has not been full explained. It seems the production of less deformable erythrocytes to navigate the micro-vascular channels is only part of the process. Recent studies have implicated inflammatory complexes of leucocytes and erythrocytes as well as complex interactions between the red cell membrane and vascular endothelium.

The clinical manifestation is of anaemia, jaundice, recurrent vaso-occlusive crisis and recurrent infection due to organic and functional asplenia.

The rate and extent of polymerization correlates with the extent and duration of deoxygenation, the intracellular concentration of HbS and the presence and concentration of Fetal Haemoglobin[7].

It would seem that the concentration of HbF is the most significant. The higher the HbF, the less the HbS and hence, the lower the rate and extent of polymerization[7]. For the same reason, the compound heterozygous forms like HbSC, HbSb-Thalassaemia etc confer better prognosis than the homozygous HbSS form. However, there are conflicting reports of the beneficial effect of a higher HbF concentration. Even though Powars' initial work did not concur with this assertion, they later showed benefit only beyond a threshold level. The Orissa experience demonstrated benefit[13,14]. This will explain why the Indian sickling population suffers

fewer complications than their African and Jamaican counterparts.

ETIOLOGY:

Bacteria, viruses and fungi may cause osteomyelitis. In the general population, Staph aureus remains the commonest cause. The generation old conflict about the commonest organism in SCA has still not been resolved. Some studies have found Salmonella to be the commonest whilst others have found Staph aureus to be. There is a trend from the vast number of publications that there are geographic differences [15,16]. Studies from the North Americas and England suggest Salmonella as the commonest culprit. Studies from Sub-Sahara Africa where SCA is commonest, lean towards Staph. Even then, there are conflicting reports[17]. Some studies have also demonstrated mixed organisms. It will take about 48 hours for culture results to be available no matter where we find ourselves. This means that we would have started antibiotic therapy before we get these culture and sensitivity results. The prevailing organisms cultured in our geographical area guide our choice of antibiotic. Even then, blood culture yield is about 30-40% and aspiration yield is about 60-70% [1]. The essence is that the yield is never 100%. There is anecdotal evidence in support of combination antibiotics for SCA to cover both Salmonella and Staph while waiting for the results13[17].

Other organisms are Streptococcus, haemophilus influenza, and E-coli. In theory, all pathogens may cause osteomyelitis in the SCA patient.

ROUTE

The haematogenous route still remains the commonest documented yet[2]. In this case, there is a remote site of infection as in ear infections, URTI and Staph skin lesions. The organisms enter the blood stream and are transported to distant sites. Spread may be from adjacent structures like septic arthritis of knee spreading to cause osteomyelitis of proximal tibia. It may be by direct inoculation as seen in open fractures and thorn pricks on the farm [18].

Unfortunately, it may be of iatrogenic cause from open reduction internal fixation, emergent intra-osseous infusions and transfusions and femoral vessels venepunctures.

SITES

Osteomyelitis may affect any bone in the body, from the long bones to vertebrae, ribs and even the cranium [19]. Osei-Yeboah and Neequaye reported osteomyelitis of the frontal bone [20]. However, it most commonly affects the long bones [2,17].

It may also affect any part of the long bone, but again its preference is for the metaphyses [1] because of its peculiar blood supply. The physeal plate is cartilaginous and avascular. Its nutrition therefore is by diffusion. For diffusion to occur, the blood flow must of necessity be slow. The metaphyses has predominantly cancellous bone with a large surface area and a rich network of vascular sinusoids. These conspire to reduce the rate of flow of blood, which has a lower oxygen tension. This increases the risk of polymerization, which in turn leads to vaso-

occlusion with consequent bone marrow and endosteal necrosis. Thus, a good medium is created for the organisms to thrive and multiply. This is aggravated by their reduced ability to fight infection from functional and organic asplenia. Studies have shown that in about 30% of cases there is a history of trauma[1] around the metaphyses. Trauma with bleeding causes haematoma, which is good pabulum for establishment of infection.

In the medulla, it starts as an acute inflammation with inflammatory oedema. This coupled with the bone marrow necrosis and oedema from vaso-occlusion, will cause an elevation in the intramedullary pressure. This process takes about 72 hours. If the diagnosis is made and aggressive appropriate treatment started, the process may be completely aborted without recourse to surgery. If however this window of opportunity is missed, the transudate is converted to exudate. This usually would require surgical drainage[1].

With increasing intramedullary pressure, there is tamponade of the endosteal vessels. There is also septic embolization of the vessels. The exudate forces its way through the porous bony cortex into the subperiosteal space. This denudes the cortex of its blood supply. Sometimes the organisms may be so virulent that they destroy the periosteum completely.

The bony cortex thus denuded of blood supply becomes necrosed and is then referred to as sequestrum. The elevated periosteum lays down new bone, which is referred to as involucrum. At this point it has progressed from acute osteomyelitis to chronic osteomyelitis.
Complications arising thereof include leg length discrepancy, deformity, persistent discharging sinuses, sepsis and pathological fractures.

CLINICAL PRESENTATION

This may be acute, sub-acute, chronic and acute-on-chronic.The acutely presenting patient is toxic, febrile, anaemic with limb pain and swelling[1]. There is usually jaundice. In the under-developed countries, this may be the first time to diagnose SCA because newborn screening is not routine[21].

In chronic osteomyelitis, the patient is usually not toxic and febrile. He/she may present with chronic discharging sinuses, leg length discrepancy and deformity. There may be an acute exacerbation of a chronic osteomyelitis as in acute-on-chronic. Chronic osteomyelitis arises mainly from misdiagnosed, undiagnosed and mismanaged acute episode. It may arise de novo as in Brodie's abscess or by the very nature of the organism causing it as in Tuberculosis and fungi infections.

TIME OF PRESENTATION

In the developed countries, the first port of call is usually the hospital. This is not so in most developing nations. A lot of patients will report to herbalists and traditional bonesetters first. The shortage of trained staff does not help either. Poverty and ignorance also cause delay in reporting[3]. Evidence exists of the good prognostic effects of early presentation, diagnosis and treatment.

LABORATORY INVESTIGATIONS

Haemoglobin count is about 6-8g/dl for most

SCA.The **ESR** is elevated usually above 40mm/hr. **CRP** is elevated in the acute phase. There is leucocytosis with relative neutrophilia.Blood culture samples should be taken at the peaks of fever to improve yield. Sub-periosteal aspiration is done for gram staining and culture.

RADIOLOGICAL

X-Rays: In acute osteomyelitis, there are no evident changes. The experienced eyes may see soft tissue haziness. It is important however to get one to rule out fractures, bone tumours and also to act as baseline to which others are compared. It takes 10-14 days for bone changes (of involucrum and sequestrum) to be visible by which time it has become chronic osteomyelitis [9].X-rays are cheap, and readily available even in the most poor economies.

Ultrasonogram: This may show subperiosteal collection and elevation, medullary abscesses and cortical erosions. It will also aid in guided needle aspiration for gram staining and culture. It is also fairly affordable and available. However, it is user dependant and would therefore require an experienced ultrasonographer.

Radionuclide scans: A 3-phase Technetium99 scan will show an increased uptake on the bone crystallization phase in acute osteomyelitis. There are reported false negatives. It is sensitive but not specific. The yield may be enhanced by white cell tagged radiopharmaceuticals. It is also not readily available in most centres in poor countries.

CT scan: This is not used routinely in acute osteomyelitis for diagnosis. It may help in the acute phase when there is pus collection. It is of use in the chronic phase for planning reconstruction surgeries.

MRI: This is very sensitive but not specific. It shows marrow inflammation and oedema[1]. It is however very expensive and not readily available.

PET scan: It is not readily available. It is expensive. Its use is mainly to distinguish between vaso-occlusive bone crisis and osteomyelitis [22].

IS IT VASO-OCCLUSIVE BONE PAIN OR OSTEOMYELITIS?

Early diagnosis and treatment confer good outcomes is well established.

It is therefore important to differentiate between vaso-occlusive bone pain and osteomyelitis. There are several publications but we do not have proper randomized controlled trials to settle this matter. At best the articles are of level III evidence.

Bone infarcts are 50 times more common than osteomyelitis in patients with SCD. The treatment is rehydration and analgesia. In osteomyelitis, there is more prolonged hospital stay. Intravenous antibiotics are used and surgical drainage may be indicated. We may presumptively treat all cases of bone pain empirically as acute osteomyelitis until culture and gram stain results are available, and when they are negative do we just discontinue antibiotics? A negative culture does not necessarily mean there is no infection. These are anxious moments for patients, parents and us. For these reasons, it is important to distinguish between infarcts

and osteomyelitis.

There is no single well-validated entity to distinguish between the vaso-occlusive bone pain and osteomyelitis. For instance, history alone will not suffice. Unifocal bone pain is more likely to be due to osteomyelitis, but there are many exceptions. Temperature is usually above 38.4□C for osteomyelitis but there have been cases of osteomyelitis with lower temperatures during their whole hospital stay. There is more leucocytosis in osteomyelitis.

Radionuclide scans are helpful but not sacrosanct. The sulfur colloid scan and white cell labeled radiopharmaceutical enhance the yield.

In one study using ultrasound scan, they found that all patients with osteomyelitis had bony changes where as there were no changes in bone infarction. Contrast enhanced MRI may also help [5]. It is important that we use a combination of modalities to rule out bone infarction [23].

TREATMENT OF ACUTE OSTEOMYELITIS:

The patient is admitted, rehydrated and given intravenous analgesia. The affected limb is splinted. Intravenous antibiotic is started, the choice determined by the most likely organisms. It is generally agreed that we start with intravenous antibiotics and observe the following parameters; heart rate, temperature, white cell count, CRP and patient's general condition[1]. If there is no improvement and temperature continues to swing in 36 hours, then there is pus present which needs to be surgically evacuated. In underdeveloped countries where patients present late, it is our experience that pus has already collected by the time these patients present.

CHOICE OF ANTIBIOTICS:

There is no single well-powered level I trial to determine this. Most are recommendations based on retrospective trials[24.] In a French study, there was consistency among paediatric residents and newly qualified paediatricians. Their prescribing patterns reflected current microbiological trends[25]. Again there was no consensus about mono-therapy or combination therapy.

ROUTE OF ADMINISTRATION:

Generally, most people will start with the intravenous route of administration. There are cases where oral administration was used at the beginning with similar results [26]. There has not been any head to head comparison. The generally held view of starting with intravenous route is more popular and consistent and indeed may be the common sense thing to do in the circumstances where a patient is very toxic, anorexic and vomiting.

DURATION OF ANTIBIOTIC THERAPY

In the French study one thing was conspicuous- that we are far from a consensus[25]. In the past the standard was 6 weeks of intravenous antibiotics. Prolonged antibiotic use comes with complications[27]. There was a switch from that to 3 weeks intravenous followed by 3 weeks oral. The orthopaedic community is moving more towards shorter duration of intravenous and following up with oral [26,28]. We have still not settled on the parameters to determine when

to switch. There are many success reports with short-term intravenous antibiotics [29]. A proper trial is desperately needed to put this matter to rest [30].

TREATMENT OF CHRONIC OSTEOMYELITIS:

This is an area that will continue to generate a lot of controversy and discussion. This is because there are no proper trials. The pathology is that of dead bone because it has been denuded of blood supply so antibiotics will not get to it. This acts as a platform for organisms to thrive. Laboratory investigations tend to be unreliable. Culture of the sinus tracts usually yields superficial contaminants. There are a few unpublished reports showing spontaneous resolution. The general trend is to wait for the involucrum to mature and then surgically remove the sequestrum and curette the medullary canal until active bleeding is seen. This process is referred to as sequestrectomy. It may be necessary to do saucerization when a sequestrum is not obvious.

After these procedures, a defect may be created which is usually filled with cancellous bone and covered with muscle as described by Papineau[31]. The acute-on-chronic is managed just like in the acute setting. Once the acute phase has subsided, the chronic phase is treated as described above.

CONCLUSION:

Osteomyelitis in SCA is common. A high index of suspicion is needed to make an early diagnosis. To distinguish it from vaso-occlusive bone infarction is challenging. Early diagnosis and prompt treatment are crucial for a favourable outcome. There is a paucity of high-level trials and therefore, we have to rely on retrospective studies to guide our approach to management.

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