Primary Epiphyseal Osteomyelitis (PEO) in 18 Children: A Rare Entity With Atypical Features

Maulin M. Shah, MBBS, MS Ortho, DNB Ortho, Gaurav Gupta, MS Orthopaedics,* Akash S. Makadia, MS Orthopaedics,† and Qaisur Rabbi, D-Ortho**

Objectives: The purpose of this study is to discuss the natural history and management of primary epiphyseal osteomyelitis (PEO), to differentiate clinico-radiologic features of PEO caused by Mycobacterium and other organisms, and to discuss their intermediate-term outcomes.

Methods: Between 2006 and 2017, 18 patients of PEO were managed at our center. Blood investigations, x-rays, and magnetic resonance imaging of affected part were carried out. Surgical drainage of lesions was done to retrieve infective fluid and tissue for examination. Antibiotics were administered for 1 year in Mycobacterial PEO and for 6 weeks in bacterial PEO. Average follow-up of patients was 5.5 years (range, 2 to 11 y).

Results: Boys were more commonly affected (11/18). Distal femur was the most common site involved (12/18). Eleven patients had *Mycobacterium tuberculosis* as the causative organism, 6 were positive for *Staphylococcus aureus*, and 1 for *Brucella*. Swelling and limp were predominant in patients with Tubercular PEO, whereas pain was more common in bacterial PEO. Nine of 11 patients with Tubercular PEO had penetration into the joint, whereas none in bacterial PEO. All patients recovered completely without residual movement restriction or growth alteration. On follow-up magnetic resonance imaging, 4 patients with Tubercular PEO had thinning of articular cartilage.

Conclusion: High index of suspicion is required for early diagnosis of PEO. It is important to differentiate Tubercular from other bacterial PEO as it has more subtle symptoms and poor prognosis if left untreated. Aggressive surgical treatment followed by antibiotic therapy of appropriate duration is required to avoid complications related to joint destruction. To our knowledge, this is the largest reported series with longest follow-up.

Key Words: primary, epiphyseal, osteomyelitis, children, mycobacterium, tuberculosis, bacterial, *Staphylococcus aureus*, *Brucella*

(*J Pediatr Orthop* 2020;40:361–366)

From the *OrthoKids Clinic; and †Health and Care Foundation, Ahmedabad, Gujrat, India.

M.M.S.: study design, performed measurements, statistical analysis, and manuscript preparation. G.G.: study design, performed measurements, and statistical analysis. A.S.M.: study design and performed measurements. Q.R.: statistical analysis and manuscript preparation.
No sources of support.
The authors declare no conflicts of interest.

Reprints: Maulin M. Shah, MBBS, MS Ortho, DNB Ortho, OrthoKids Clinic, 7th Floor, Golden Icon, Opp. Medilink Hospital, Near Shivranjini Flyover, Satellite, Ahmedabad, Gujrat 380015, India. E-mail: maulinmshah@gmail.com.

DOI: 10.1097/BPO.0000000000001551

Metaphyseal osteomyelitis is the most common type of bone infection seen in infants and children due to their typical vascular anatomy.[1] Epiphyseal osteomyelitis is a rare bone infection which is usually seen secondary to metaphyseal bone involvement. Infants are more prone to get epiphyseal involvement due to open transphyseal canals.[2] Primary epiphyseal osteomyelitis (PEO) is defined as isolated infection of the epiphysis without metaphyseal involvement. Epiphysis is directly supplied by the epiphyseal vessels which form sinusoids therein. Sluggish flow in the epiphyseal sinusoids make them prone to acute or subacute epiphyseal osteomyelitis.[1,3,4] Being independent of transphyseal blood vessels, it can present at any age of life.

Detailed vascular anatomy of epiphysis has been explained by Morgan.[3] Through injection studies, he demonstrated that epiphyseal arteries enter the epiphysis near the capsular insertion and growth plate. These arteries successively branch and anastomose, reaching the growth plate and majorly communicate amongst them. Through the canals in the growth plate, these arteries form terminal loops and then turn back in to form large veins through the same or the other canal. These vessels do not penetrate the physeal cartilage. Trueta and Morgan[1] confirmed these findings and showed that the blood supply in the epiphysis is analogous to the metaphyseal circulation.

The most common causative organism causing PEO is *Staphylococcus aureus*.[2] Most of the cases of Bacterial Epiphyseal Osteomyelitis respond expeditiously to antibiotics and surgical drainage without any long-term complications.[5–8]

Mycobacterial Tuberculosis is a common cause of musculoskeletal infections not only in developing countries but also in developed countries where BCG (Bacillus Calmette Guerin) vaccination is carried out routinely.[9] Primary Mycobacterial Epiphyseal Osteomyelitis is rare and to date only 26 cases have been reported.[9] Because of the rarity of this disease, there are varied opinions regarding its natural course, severity and management. Treatment recommendations are divided between nonoperative[5] and operative management.[9]

We are presenting a retrospective case series of 18 patients (Tables 1, 2) affected by PEO who were treated at our center between 2006 and 2017. The purpose of this study was to differentiate the clinical features of Primary Tubercular Epiphyseal Osteomyelitis and other Bacterial Epiphyseal Osteomyelitis, to compare their radiologic features and to discuss their long-term outcomes after treatment.

TABLE 1. Patient Details

S. No.	Age (Years.Months)	Sex	Presenting Complaint	Site	Duration of Symptoms	TLC (1000/μL)	ESR (mm/h)	CRP (mg/L)
1.	3	M	L, S	D.F.	2 mo	11	18	4
2.	13	F	L, S	G.T. Femur	2.5 mo	10.2	25	6
3.	5	F	L, S	D.F.	36 mo	9	40	5
4.	3	M	P, L	D.F.	1 mo	12	15	8
5.	1.5	M	S, L	P.T.	1 mo	9.8	20	9
6.	4	F	F[1], P, L	D.T.	15 d	11	12	6
7.	7	M	P	D.F.	20 d	11.6	17	10
8.	8	M	L, S	D.F.	1.5 mo	9.2	18	5
9.	2.5	M	L, S	D.F.	1.5 mo	10.7	21	7
10.	1.8	M	L, S	D.F.	1.5 mo	10.1	23	3
11.	1	F	L, S	D.T.	8 mo	9.9	19	5
12.	14	F	P, L	D.F.	5 d	11.2	16	8
13.	2.7	F	P, L	D.F.	15 d	11.9	13	7.5
14.	4.5	M	P, L	D.F.	10 d	10.8	11	9.5
15.	5.10	M	P, L	D.F.	45 d	11.1	18	11
16.	1.1	M	L, S	D.F.	3 mo	9.7	19	5.5
17.	4.2	M	L, S	P.H.	25 d	10.3	24	6.5
18.	8.4	F	L, S	P.P.	2 mo	10.7	20	8.5

CRP indicates C Reactive Protein; D.F., Distal Femur; D.T., Distal Tibia; ESR, Erythrocyte Sedimentation Rate; F, Female; F[1], Fever; G.T., Greater tuberosity; L, Limp; M, Male; P, Pain; P.H., Proximal Humerus; P.P., Proximal Phalanx; P.T., Proximal Tibia; S, Swelling; TLC, Total leukocyte count.

METHODS

Between 2006 and 2017, 400 cases of acute and chronic osteomyelitis in pediatric age group have presented at our tertiary care center. Out of these, 18 were diagnosed with PEO (Tables 1, 2). There were 11 boys and 7 girls. The average age at presentation was 5 years (range, 1 to 14 y). Institutional review board approval was obtained for the study. Clinical history, general physical examination and local examination were done. Preoperative blood investigations, radiograph and magnetic resonance imaging (MRI) of the involved extremity were carried out in all cases. Open debridement was carried out in all patients. Fluid retrieved was sent for microscopic examination, culture and sensitivity testing. Curetted tissue was subjected to histopathologic examination. Gene X-pert testing was done when Acid Fast Bacilli was found in microscopy or Tuberculous granuloma was detected in histopathologic examination. Gene X-pert is a cartridge-based nucleic acid amplification test for simultaneous rapid tuberculosis diagnosis and antibiotics sensitivity testing.[10]

Inclusion Criteria

(1) All patients with x-ray/MRI evidence of primary epiphyseal involvement with or without extension into the joint and evidence of infection in culture of fluid or histopathologic examination.

TABLE 2. Disease Spread, Outcome, and Complications

S. No	Organism on Culture/Biopsy	Duration of Follow-up (Years.Months)	Joint Penetration	ROM	Arthrotomy	Complications
1.	*M. tb*	8.10	Yes	Full	Yes	Thinning of A.C.
2.	*M. tb*	11	No	Full	No	None
3.	*M. tb*	8.1	Yes	Full	Yes	Complete erosion of femoral articular cartilage and penetration into patellar cartilage
4.	*S. aureus*	7.4	No	Full	No	Thinning of A.C.
5.	*M. tb*	8.1	Yes	Full	Yes	Thinning of A.C.
6.	*S. aureus*	6.1	No	Full	No	None
7.	*S. aureus*	6.4	No	Full	No	None
8.	*M. tb*	4.8	No	Full	No	None
9.	*M. tb*	5.5	Yes	Full	Yes	Thinning of A.C.
10.	*M. tb*	2.8	Yes	Full	Yes	None
11.	*M. tb*	2.6	Yes	Full	Yes	None
12.	*S. aureus*	2.6	No	Full	No	None
13.	*S. aureus*	2.1	No	Full	No	None
14.	*B. brucellae*	2.7	No	Full	No	None
15.	*S. aureus*	2.7	No	Full	No	None
16.	*M. tb*	2	Yes	Full	Yes	None
17.	*M. tb*	7.4	Yes	Full	Yes	None
18.	*M. tb*	9.2	Yes	Full	Yes	None

A.C. indicates articular cartilage; *B.brucellae*, *Brucella brucellae*; M. tb, *Mycobacterium tuberculosis*; ROM, range of motion; *S. aureus*, *Staphylococcus aureus*.

(2) All patients with complete record and minimum 1 year of follow-up.
(3) Patients having epiphyseal osteomyelitis in association with open fractures and primary metaphyseal osteomyelitis was excluded from the study.

Procedure

Patients were operated following routine surgical preparation. The lesion was localized under image intensifier and a small incision was placed just above the localized lesion. Epiphysis was exposed, and a small window was made by multiple drill holes. The pus was collected for culture/sensitivity and curettings for histopathologic examination. Arthrotomy, debridement and decompression were done in patients with preoperative evidence of joint collection. A probe was used to assess the articular cartilage and presence or absence of epiphyseal rent communicating with the joint.

Patients were then followed every 3 months till growth maturation. Patients who were positive for *M. tuberculosis* were prescribed antitubercular treatment for 1 year. Gene X-pert testing was done to rule out resistance to Rifampicin and Isoniazid. Patients affected from Bacterial PEO were given oral antibiotics for 6 weeks according to sensitivity of the organism.

RESULTS

The majority of patients in our series were male with male to female ratio of 1.57:1.

Distal femoral epiphysis was the most common site of involvement (12 cases) in our series (Figs. 1, 2) followed by proximal tibia (3 cases). We also found involvement of few uncommon sites like proximal humerus, proximal phalanx of great toe, distal tibia, and greater trochanter of femur (Fig. 3).

Preoperative blood investigations (including Complete hemogram, C-Reactive Protein, Erythrocyte Sedimentation Rate) were equivocal in all the patients. Eleven patients in our series were positive for *M. tuberculosis*, 6 for *S. aureus*, and 1 for *Brucella*. The average follow-up in our series was 66 months (range, 24 to 132 mo). Gene Xpert testing was negative in all mycobacterium cases suggestive of sensitivity to the first line antitubercular drugs. At final follow-up, all the patients achieved full range of motion with no complaint of persistent pain, limp, physeal arrest and recurrence. The average duration of symptoms before presentation was 5.4 months in tubercular epiphyseal osteomyelitis with an outlier of 3 years as patient was lost to follow-up in between. Patients with tubercular epiphyseal osteomyelitis presented later with predominant symptoms of limp and swelling and mild or no pain, whereas patients with Staphylococcus epiphyseal osteomyelitis presented comparatively earlier (within 3 weeks) with predominant complaint of severe pain and inability to bear weight over the affected limb.

DISCUSSION

PEO is a rare disease most commonly caused by *S. aureus*,[2,11] whereas a European report of 14 cases has shown Kingella Kingae to be the most common organism involved.[12] However, *M. tuberculosis* has also been found as a causative organism in several case reports.[13,14] To our knowledge, around 26 cases of Primary Mycobacterial Epiphyseal Osteomyelitis have been reported in the English literature since 1975.[9,13–16] The longest case series described in previous literature is of 8 cases by Yoo et al.[9] The largest follow-up reported in literature is of 9 years.[17] Till date, this is the largest series of PEO and Mycobacterial Epiphyseal Osteomyelitis with the longest follow-up. The most common site of involvement was distal lateral femoral epiphysis correlating with the previous literature.[10,15,17,18] We also encountered cases of proximal phalangeal and distal tibial epiphyseal involvement which has not been described earlier. Predominant

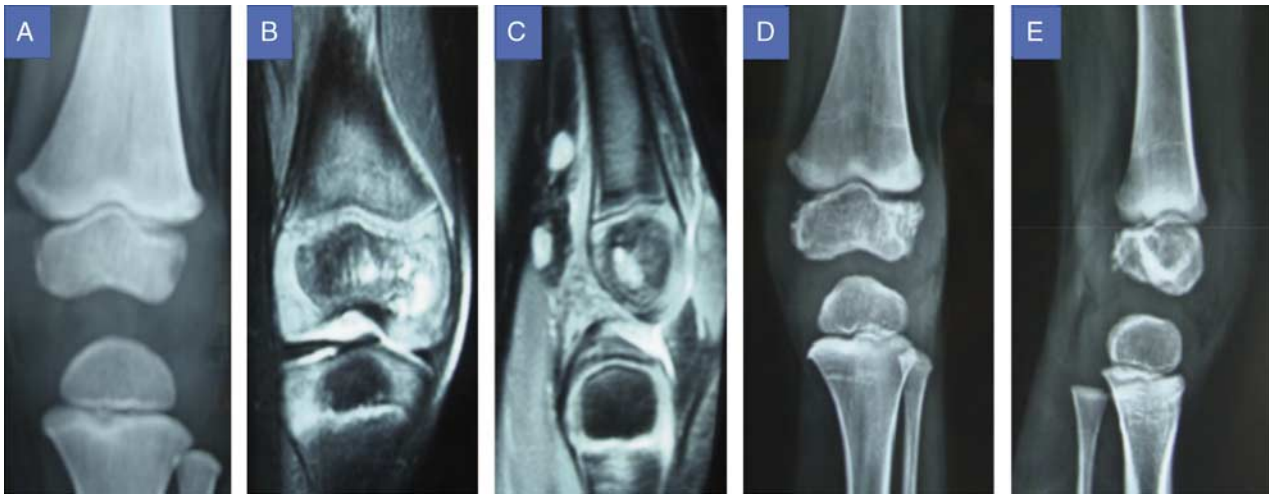

FIGURE 1. Primary epiphyseal osteomyelitis of Distal Femur Case 1. A, X-ray Knee AP view at the time of presentation. B and C, MRI Knee Coronal and Sagittal section. D and E, Two year follow-up x-ray knee antero-posterior and lateral view. MRI indicates magnetic resonance imaging. full color online

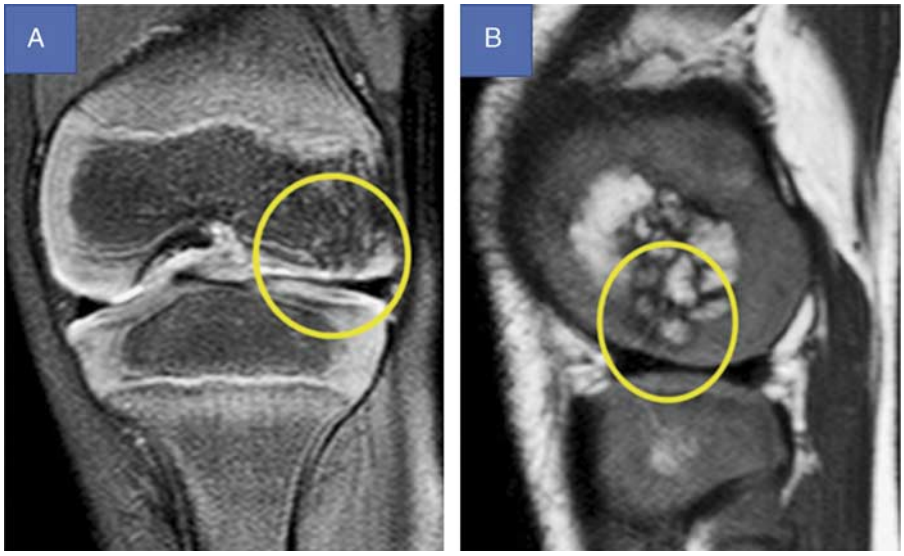

FIGURE 2. Two year follow-up of Case 1. A and B, MRI coronal and sagittal section at 2 year follow-up showing thinning of cartilage. MRI indicates magnetic resonance imaging. full color online

presenting symptom in Bacterial Epiphyseal Osteomyelitis was pain, while Mycobacterial Epiphyseal Osteomyelitis patients were mostly painless. Their common complaints were local swelling and limp while walking. The destruction is gradual in cases of Mycobacterial Epiphyseal Osteomyelitis and so the initial x-rays may look benign with minimal or no abnormality. Some of the cases reported were in the cartilaginous area of epiphysis which cannot be picked up by an x-ray. A high index of suspicion is required, and an MRI of the affected area can be diagnostic. MRI helps in localizing the lesion, delineating its extent and preoperative planning. MRI also differentiates infections from bone tumors like Eosinophilic Granuloma and Chondroblastoma. We strongly recommend MRI in patients who are under suspicion of PEO. Open biopsy and decompression help in retrieving material and detecting penetration of the joint. Joint lavage can be added if it is found contaminated. Early diagnosis and prompt treatment results in good prognosis with no long-term complications. In contrast to other published series,[9] 9 of 11 cases of Tubercular PEO had joint penetration in current series. Penetration of the joint was more common in cases which presented late. We believe that this case example (Figs. 4, 5) explains the natural history of undiagnosed and untreated Tuberculous PEO. Although in the world literature, PEO is considered as benign localized disease, this case report warrants attention, as if it remains untreated, it will lead to joint destruction.

Delay in treatment can lead to joint destruction as shown in the case above. In contrast to the study by Yoo et al,[9] none of the patients deteriorated after surgical drainage or required additional surgery. After a mean follow-up of 5.5 years (range, 2 to 11 y), there was no case of focal physeal damage or clinical growth disturbance. However, as 7 of 18 cases in our study had <3 years of follow-up and majority of cases have not reached skeletal maturity, we cannot comment on the final effect of PEO on growth arrest, limb length discrepancy and deformity.

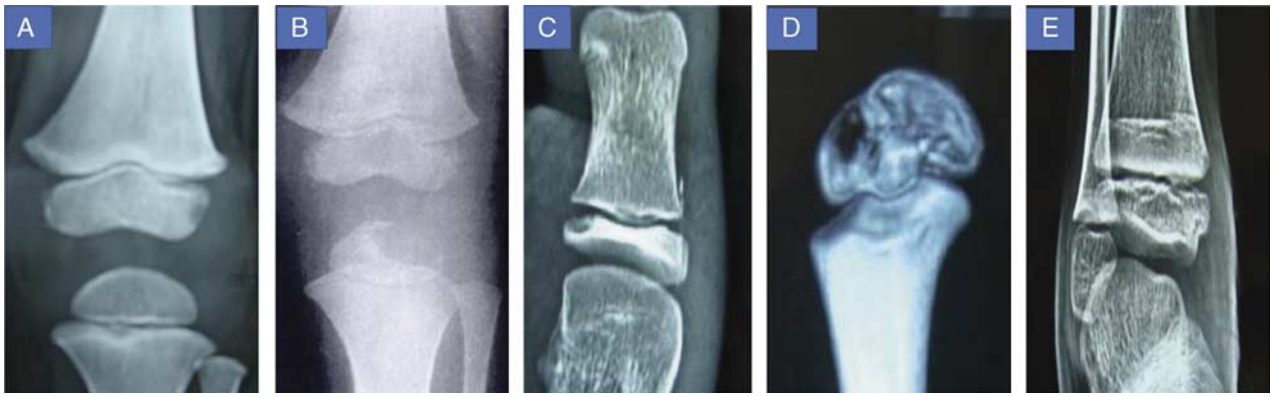

FIGURE 3. Different sites of affection. A, Distal Femoral condyle. B, Proximal Tibia. C, Proximal phalanx. D, Proximal Humerus. E, Distal Tibia. full color online

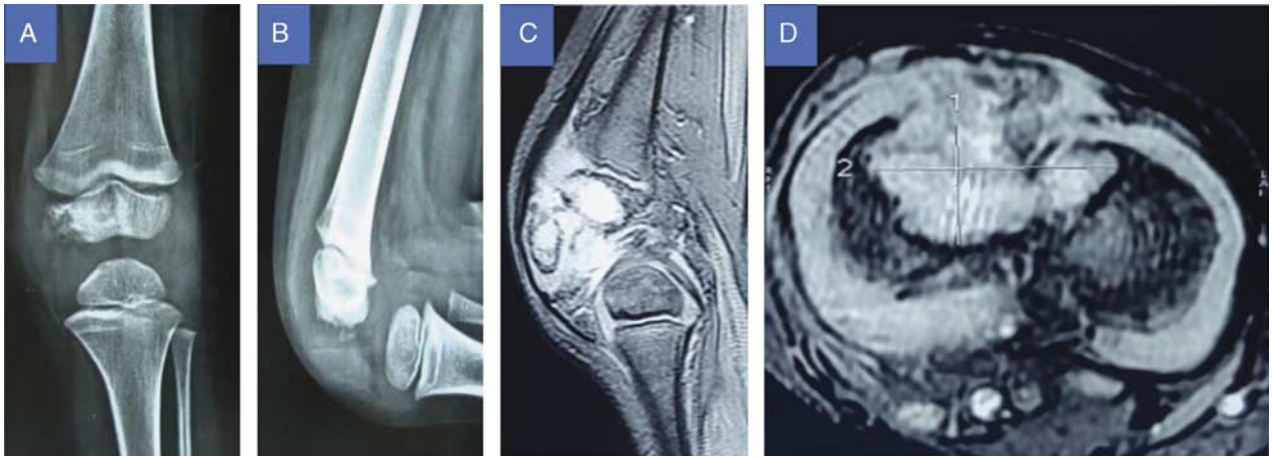

FIGURE 4. Primary Tubercular Epiphyseal Osteomyelitis of Distal Femur (Case 3). This 5-year-old girl initially presented to us with complaint of limp and swelling over right knee since 3 months. X-ray of the right knee showed lytic lesion in the distal femoral epiphysis (A and B). Patient was advised MRI of the involved joint followed by biopsy and debridement, but patient denied surgery and was lost to follow-up. After 3 years, patient again presented to us with complaint of right knee fixed flexion deformity of 40 degrees. MRI revealed lytic lesion of right distal femoral epiphysis penetrating the right knee joint along with complete erosion of articular cartilage of femoral trochlea and corresponding surface of the patella (C and D). On exploring the joint, we found purulent collection and breech in the femoral articular surface communicating with epiphysis. There was severe erosion of femoral trochlea and patellar medial facet. The joint was thoroughly lavaged and debrided. A blunt probe was passed from the articular surface of femur into the femoral epiphysis and surrounding area was curetted out. Pus culture was positive for *Mycobacterium tuberculosis*. The child was given 4 drugs Antitubercular treatment for 3 months followed by 3 drugs for further 9 months. Splint was removed after 2 weeks at the time of suture removal and gentle exercises were started. Gradual weight bearing was started after 1 month. After 8 years of follow-up, the child has full range of motion and function with no limb length discrepancy. This case suggests that untreated PEO of Tubercular etiology can lead to severe destruction of the joint. MRI indicates magnetic resonance imaging; PEO, primary epiphyseal osteomyelitis. full color online

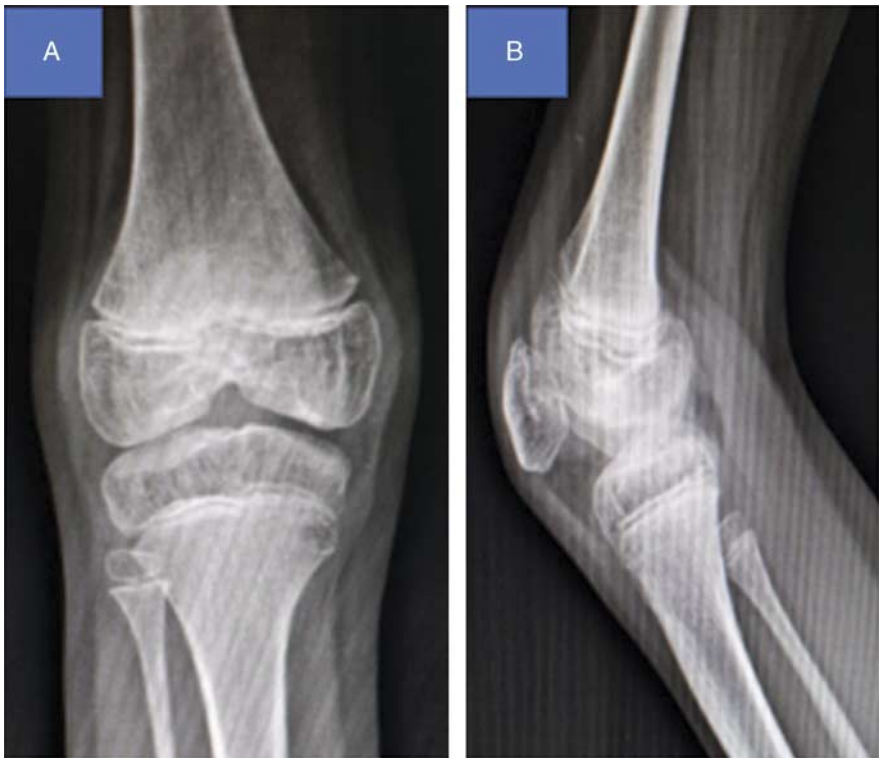

FIGURE 5. Seven year follow-up of Case 3. A and B, Antero-posterior and lateral x-rays of affected knee at 7 years follow-up. full color online

CONCLUSION

High index of suspicion is required for early diagnosis of PEO. It is important to differentiate Tubercular from other Bacterial PEO as it has more subtle symptoms and poor prognosis if left untreated. Aggressive surgical treatment followed by antibiotic therapy of appropriate duration is required to avoid complications related to joint destruction.

ACKNOWLEDGMENTS

The authors thank Dr Dhiren Ganjwala and Dr Atul Bhaskar for their suggestions in preparing and editing this manuscript.

REFERENCES

1. Trueta J, Morgan JD. The vascular contribution to osteogenesis. I. Studies by the injection method. *J Bone Joint Surgery Br*. 1960;42: 97–109.
2. Rosenbaum DM, Blumhagen JD. Acute epiphyseal osteomyelitis in children. *Radiology*. 1985;156:89–92.
3. Trueta J. The three types of acute haematogenous osteomyelitis: a clinical and vascular study. *J Bone Joint Surg Br*. 1959;41:671–680.
4. Brookes M. The vascularization of long bones in the human foetus. *J Anat*. 1958;92:261–267.
5. Ezra E, Cohen N, Segev E, et al. Primary subacute epiphyseal osteomyelitis: role of conservative treatment. *J Pediatr Orthop*. 2002;22:333–337.
6. Green NE, Beauchamp RD, Griffin PP. Primary subacute epiphyseal osteomyelitis. *J Bone Joint Surg Am*. 1981;63:107–114.
7. Ross ER, Cole WG. Treatment of subacute osteomyelitis in childhood. *J Bone Joint Surg Br*. 1985;67:443–448.
8. Macnicol MF. Patterns of musculoskeletal infection in childhood. *J Bone Joint Surg Br*. 2001;83:1–2.
9. Yoo WJ, Choi IH, Yun YH, et al. Primary epiphyseal osteomyelitis caused by mycobacterium species in otherwise healthy toddlers. *J Bone Joint Surg Am*. 2014;96:e145.1–9.
10. Hillemann D, Rusch-Gerdes S, Boehme C, et al. Rapid molecular detection of extrapulmonary tuberculosis by the automated GeneXpert MTB/RIF system. *J Clin Microbiol*. 2011;49:1202–1205.
11. Kao FC, Lee ZL, Kao HC, et al. Acute primary hematogenous osteomyelitis of the epiphysis: report of two cases. *Chang Gung Med J*. 2003;26:851–856.
12. Ceroni D, Belaieff W, Cherkaoui A, et al. Primary epiphyseal or apophyseal subacute osteomyelitis in the pediatric population: a report of fourteen cases and a systematic review of the literature. *J Bone Joint Surg Am*. 2014;96:1570–1575.
13. Gardner DJ, Azouz EM. Solitary lucent epiphyseal lesions in children. *Skeletal Radiol*. 1988;17:497–504.
14. Rasool MN, Govender S, Naidoo KS. Cystic tuberculosis of bone in children. *J Bone Joint Surg Br*. 1994;76:113–117.
15. El Houmami N, Minodier P, Bouvier C, et al. Primary subacute epiphyseal osteomyelitis caused by Mycobacterium species in young children: a modern diagnostic approach. *Eur J Clin Microbiol Infect Dis*. 2017;36:771–777.
16. Peltola H, Salmi I, Vahvanen V, et al. BCG vaccination as a cause of osteomyelitis and subcutaneous abscess. *Arch Dis Child*. 1984; 59:157–161.
17. Sorensen T, Hedeboe J, Christensen E. Primary epiphyseal osteomyelitis in children: report of three cases and review of the literature. *J Bone Joint Surg Br*. 1988;70-B:818–820.
18. Hempfing A, Placzek R, Göttsche T, et al. Primary subacute epiphyseal and metaepiphyseal osteomyelitis in children diagnosis and treatment guided by MRI. *J Bone Joint Surg Br*. 2003;85-B: 559–564.