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ORIGINAL STUDY

Primary epiphyseal and metaepiphyseal tubercular osteomyelitis in children A series of 8 cases

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Clinical series of primary epiphyseal and metaepiphyseal tubercular osteomyelitis are few. The purpose of our study was to retrospectively review the presentation, healing response and functional results of 8 such cases in children.

Material and methods : **The patients were evaluated for pain, deformity, range of motion, limb length discrepancy (if any) and recurrence. Serial radiographs of the region were studied to see remineralization, obliteration of radiological lesions, status of physis and remodeling of the growth plate.**

Results : **The mean patient age was 7.1 years. Average follow up was 3.7 years. The mean duration of symptom before presentation was 2.9 months (range, 0.5-8 months). Knee region was involved in 4, distal radius in 2, shoulder and distal fibula in 1 patient each. The lesions were either localized or diffuse depending upon physeal involvement and osseous destruction. At the last follow up, the involved joints were painfree and had useful range of motion. Limb length lengthening was seen in all knee patients. The diffuse variety resulted in premature physeal closure. The residual lucencies persisted for several years without any clinical manifestations.**

Conclusions : **Primary epiphyseal and metaepiphyseal tuberculosis was relatively uncommon. The clinical outcome was good following curettage and multidrug antitubercular therapy. The epiphyseal and metaphyseal lucencies persisted for several months even after successful treatment. The diffuse variety lead to premature physeal closure. Limb length lengthening was common sequelae of tuberculosis of knee region.**

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INTRODUCTION

Typical osseous lesions of tuberculosis in children are usually situated in the metaphyseal region. However, rarely the lesion can cross the physeal plate and involve the epiphysis especially in small children where the transphyseal vascular canals are open *(9,12,13,22)*. More infrequently, the lesion can be primary mycobacterial osteomyelitis of the epiphysis (mycobacterial POE) only *(22)*. This phenomenon, occurring probably due to the sluggish blood flow in epiphyseal sinusoids, is possible in any pediatric age group *(22)*.

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The advent of more sophisticated imaging modalities like CT and MRI has increased the detection and localization of such lesions *(8,22)*. The existing sparse literature on the subject offers conflicting views ranging from unfavorable clinical courses to benign long term outcomes *(8,9,13,22)*.

We retrospectively reviewed 8 cases of primary epiphyseal and metaepiphyseal tubercular osteomyelitis in children treated at our institution over a 7 year period. The purpose of our study was to further characterize the presentation, healing response and functional results in children following this pathology.

PATIENTS AND METHODS

This was a retrospective study in which we reviewed the clinical records and serial radiographs of 8 children (initial age ≤12 years) treated for primary epiphyseal and metaepiphyseal tubercular osteomyelitis between January 2009 and December 2015. The diagnosis of tuberculosis had been confirmed in all patients by microbiological/ histopathological examination. In each patient, the lesion was surgically curetted to remove pus and granulation tissue and obtain tissue for laboratory diagnosis. In two patients, autogenous bone grafting of the epiphyseal extension had been undertaken at the time of curettage (patients 4 and 5, Table I). Postoperative immobilization was provided by an appropriate splint for 4 to 6 weeks followed by passive and active range of exercises. Full weight bearing was permitted in lower limb affections by 12-16 weeks. Serial hematological and plain radiographs monitoring besides clinical examination was used during follow ups. Preoperatively, computed tomography (CT) scan (1 patient) or magnetic resonance imaging (MRI) could be obtained only in 4 patients due to financial restraints.

All patients had received an intensive phase multidrug antitubercular treatment [Isoniazid (10mg/kg/day), Rifampicin (10mg/kg/day), Pyrazinamide (25mg/kg/day) and Ethambutol (20mg/kg/day)] for 2 months and continuation phase [Isoniazid (10mg/kg/day), Rifampicin (10mg/kg/day)] for 10 months as per the institutional protocol.

The patients were evaluated for pain, deformity, range of motion, limb length discrepancy (if any) and recurrence at last evaluation. Antero-posterior and lateral radiographs of region were obtained to see remineralization, obliteration of radiological lesions, status of the physis and remodeling of the growth plate.

OBSERVATIONS AND RESULTS

The mean age was 7.1 years (range, 4-12 years) with 6 male and 2 female patients. Table I shows the clinical, radiographic, and laboratory findings of the patients. Average follow up after completion of antitubercular therapy was 3.7 years (range, 1.5-7 years). Knee region was involved in 4, wrist in 2, shoulder and ankle in 1 patient each. The mean duration of symptoms before presentation to our institution was 2.9 months (range, 0.5-8 months). The diagnosis of tuberculosis was confirmed in all patients by microbiological/ histopathological examination. Culture for AFB was positive only in 2 patients (patient 2 and 7).

All patients presented with regional localized pain. In children with involvement around the knee, the swelling was minimal and range of motion was fairly preserved at initial presentation (figure 1a). Swelling of the adjacent joint and discharging sinus was present in both the patients having involvement of the radius (patient 6 and 7). The patient with involvement of proximal humerus had significant regional muscle atrophy (patient 8). Patient with involvement of the lower end of fibula had pain and swelling around the ankle (patient 3). One patient presented with skeletal tuberculosis at other sites as well (patient 7). Only two patients showed significant regional lymphadenopathy (patient 6 and 8). The average ESR (erythrocyte sedimentation rate) was 32 mm/hour (range, 23-55 mm/hour) at initial presentation. The Mantoux skin test was positive in 25% patients (2 out of 8). Only one patient (patient 7) had concomitant tubercular lesion in the lung. Radiologically, bony lesions were located in either the epiphysis (patient 1,3,8) (Figure 1,2,5) or spanned the physeal plate (transphyseal) to involve both epiphysis and metaphysis (patient 2,4,5-7) (Figure 3,7). Two

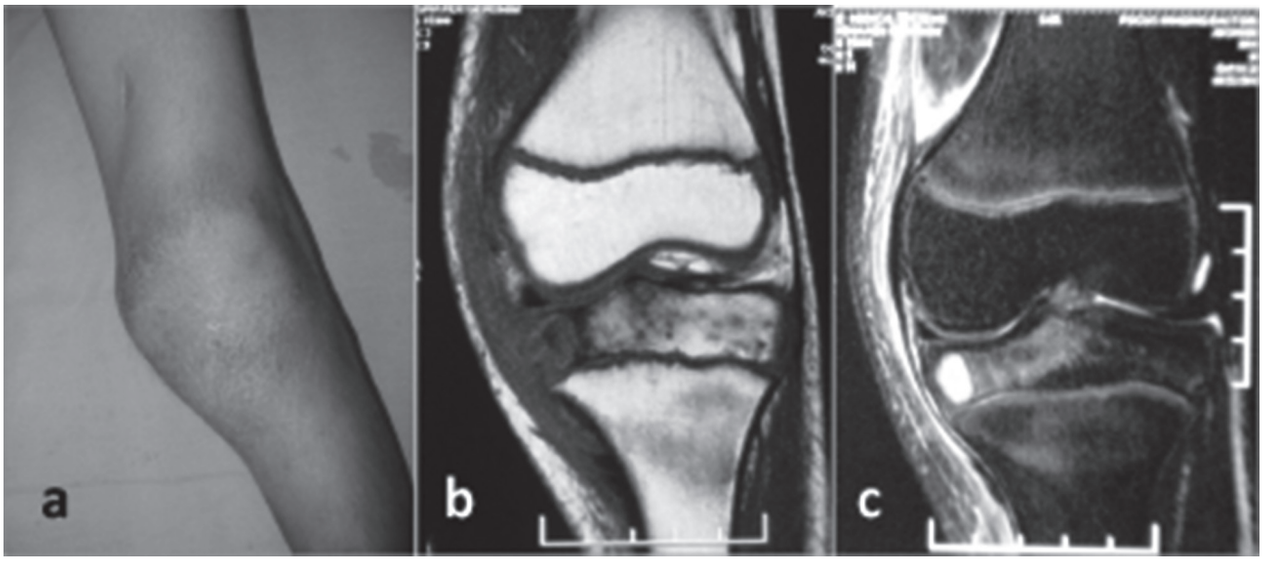

***Fig. 1.* —** Localized epiphyseal lesion (a) Presentation with localized knee swelling and pain. Knee range of motion was fairly well maintained in this patient (b,c) MRI delineated lesion precisely and helped surgical planning [see plain radiographs (figure 2a below)]

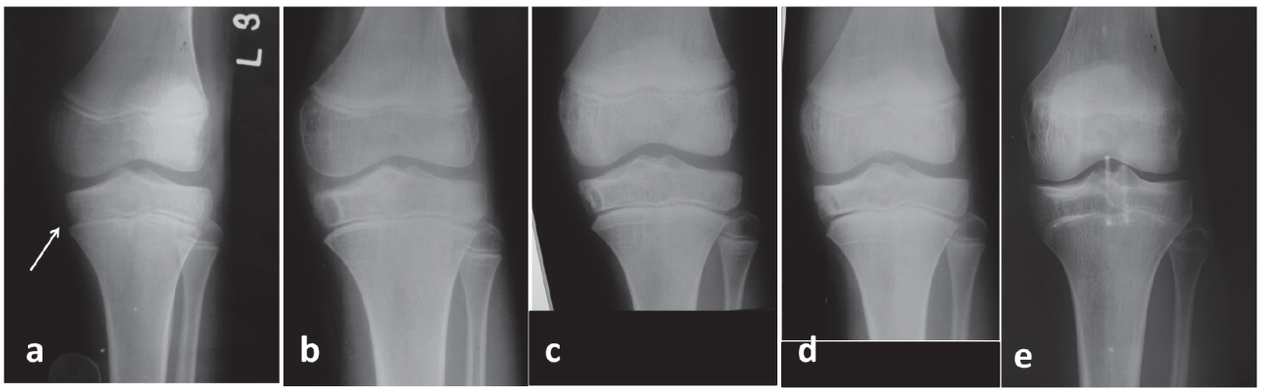

***Fig. 2.* —** Same patient as above (a) Plain radiographs showing radiolucent cyst in medial tibial condyle with ill defined margins (white arrow) (b) Margins of lesion became well defined after 6 months of chemotherapy (c) Progressive lesion obliteration seen 1 year after completion of chemotherapy (d) Follow up 3 years (e) Last follow up 5 years. Complete healing.

distinct radiological patterns were seen at the growing bone ends. The *localized* variety was either pure epiphyseal (patient 1,3,8; figure 1,2,5) or transphyseal and shaped like 'hourglass' (patient 4,5,7; Figure 3). The *diffuse* transphyseal variety had more extensive physeal plate involvement and osseous destruction (patient 2 and 6; Figure 7). Periarticular regional osteopenia was uniformly present in all patients.

At the last follow up, the involved joints were painfree. The useful range of motion recovered in all patients (Table 1, Figure 4,6). Limb length lengthening was seen in all patients with affection around the knee joint. There was premature physeal closure in both diffuse femur and radial involvement (patient 2 and 6; Figure 7). There was no clinical limb deformity in femur case but the patient with radial involvement had prominent ulnar styloid. In both patients, the joint was relatively preserved.

Radiologically, demineralization was first to recover following treatment (range, 6-12 weeks). The margins of lesions gradually became sclerotic

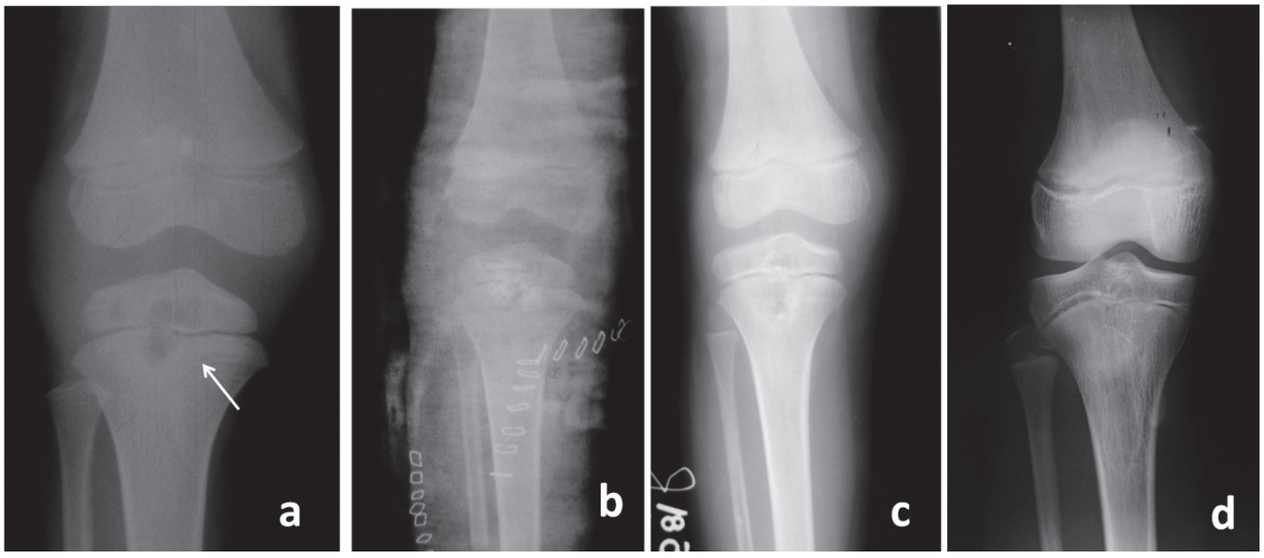

***Fig. 3.* —** Localized transphyseal 'hourglass' lesion (a) Plain radiographs of knee showing hourglass (white arrow) lytic lesion in tibia with involvement of epiphysis and metaphysis transgressing physis (b) After curettage and epiphyseal bone grafting (c) Residual radiolucencies 2 years after completion of chemotherapy. Sclerosis of the margins can be appreciated indicating healing of the lesion (d) Last follow up 6 years. Some residual lucencies still persist.

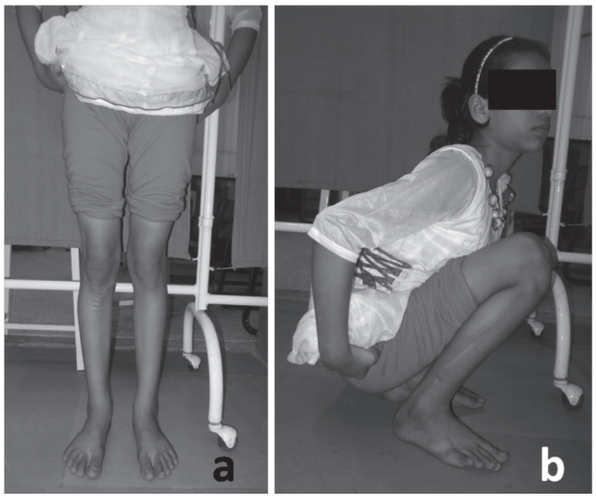

***Fig. 4.* —** Same patient as above at last follow up (a, b) Painless full range of motion, no deformity, limb length lengthening 2 cm.

during healing (Figure 2b, 3c, 7c). Even after healing of the disease after the full course of antitubercular treatment, some areas of lucency persisted for several years, probably being filled by fibrous tissue (Figure 2c,d; 3d, 7d). In patient 1, it took 5 years after completion of chemotherapy for the radiological lucency to resolve. Radiologically, the joint space was not reduced at the time of initial presentation and it remained so during the course of treatment and subsequent follow up (Figure 2,3). No recurrences were noted in the available follow up.

DISCUSSION

Primary tubercular epiphyseal and metaepiphyseal osteomyelitis, although known, is an uncommon entity *(1-3,5-7,9,11-13,15-19,21,22)*. Our institution is a tertiary care referral centre for children up to twelve years of age that covers a large geographic area. About 500 cases of tuberculosis are treated annually here, of which 30 to 50 cases fall into the category of osteoarticular tuberculosis. Epiphyseal tuberculosis just accounts for approximately 8/350 (2.2%, calculated over a period of 7 years) of all cases of osteoarticular tuberculosis seen annually. To the best of our knowledge, except for two series by Yoo et al (2005-2012) and Kao et al (1990-2008), no other exclusive paediatric clinical series for epiphyseal tuberculosis have been reported in past 50 years *(12,22)*!

Primary tubercular epiphyseal and metaepiphyseal osteomyelitis in children has certain distinct characteristics. Being uncommon and less symptomatic, the diagnosis is often delayed *(5,9)*. There was delay upto 8 months before diagnosis in our own series (patient 8). Moreover, tubercular etiology in the differential diagnosis is not easily considered. The epiphyseal lesions prompted several other differential diagnosis such as primary epiphyseal or apophyseal subacute osteomyelitis (PEASAO) *(4,8)*, chronic osteomyelitis, simple and aneurysmal bone cysts, cartilaginous tumours, osteoid osteoma, granulomatous lesions, haematological disease, and certain malignant tumours *(5,6,21)*. Variants of tuberculous osteomyelitis such as BCG vaccine-induced lesions, although extremely rare now, may present similarly *(18)*. The clinical presentation of these lesions was usually subacute with mild localized pain and soft tissue swelling *(5,8,22)*. When the lesion was localized within the epiphysis or adjacent metaphysis, there was sometimes very little inflammatory reaction (Figure 1a) and joint function remained preserved for a long time. Uzel et al reported multiple lesions in proximal tibial epiphysis with duration of symptoms of 2 years and a normal knee joint space *(21)*. In our patients also, the joint space was found maintained at presentation and during treatment (Figure 2,3). When the abscess extended into the joint or periarticular soft tissues, the swelling and pain increased and range of motion of joint decreased (patient 3 and 6).

Such lesions have been described mainly from knee region *(1,2,5-7,9,11-13,16,17,19,22)*, although involvement of other epiphysis like proximal femur *(12,15,19)*, distal tibia, fibula, humerus *(12)*, radius *(19)* and ulna *(3)* have also been reported by various authors. The probable reason for predominant tubercular seeding of knee region seems to be the large epiphysis of distal femur and proximal tibia, rich vascularity of the region and potential knee trauma in infants and toddlers. Involvement of proximal humerus epiphysis was also noted in our series (Table I, Figure 5). Despite the fact that tubercular lesions can transgress the physeal plate, the physis probably offered some resistance to the spread of infection as manifested by transphyseal 'hourglass' appearance in some patients (patient 4,5 and 7) (Figure 3). The infective focus in combined metaepiphyseal lesion still remains debated although both primary mycobacterial metaphyseal and epiphyseal lesions are known to occur *(1,12,22)*.

The initial diagnosis of these lesions was mainly based on clinical symptomatology and plain radiographs. CT and MRI delineated the lesion more precisely and in the planning of subsequent tissue procurement for diagnosis and

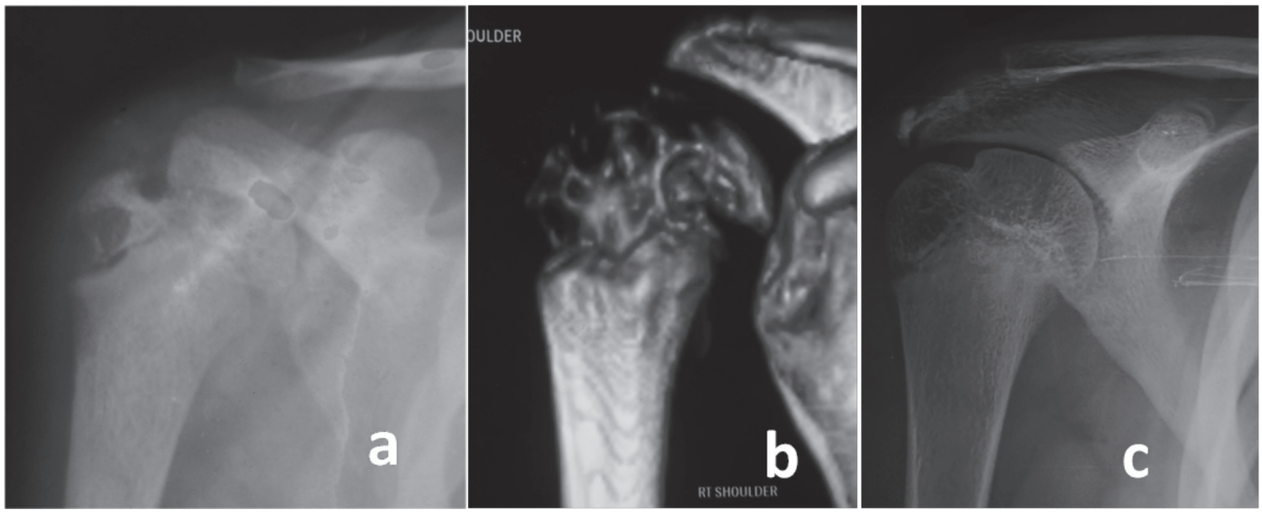

***Fig. 5.* —** Localized epiphyseal lesion (a,b) Plain radiographs and CT of shoulder showing multiple lytic lesions involving whole of the epiphysis (c) Last follow up 5 years. Complete healing.

Table I. — Patient data (n=8)

S. no.	Age (yrs)	Sex	Side	Main clinical findings	Location and type of lesion	Duration of symptoms (months)	Other lesions	Lab.Investigations	Final follow up					
									Follow up (in years)	Pain	Adjacent joint ROM	Deformity	LLD (in cm)	X - rays
1	10	M	Lt.	Localized pain and swelling	Medial tibial epiphysis, localized	3	-	Leukocytosis, normal ESR	5	-	Knee Full ROM	None	+ 2	Complete healing
2	9	M	Rt.	Localized pain and swelling	Femur epiphysis and metaphysis, diffuse	0.5	-	Leukocystosis, ESR↑	3	-	Knee 0 – 120 degrees	None	+3	Premature physeal closure
3	4	F	Lt.	Localized pain and ankle swelling	Distal fibular epiphysis, localized	3	-	Leukocystosis, ESR↑	1.5	-	Ankle Full ROM	None	-	Remodeled epiphysis
4	5	F	Rt.	Pain in leg, knee ROM preserved	Tibia epiphysis and metaphysis, localized transphyseal hourglass	3	-	Normal leukocyte count, ESR↑	6	-	Knee Full ROM	None	+2	Residual lucencies
5	5	M	Lt.	Pain in knee region, knee ROM preserved	Distal femur epiphysis and metaphysis, localized transphyseal hourglass	4	-	Leukocystosis, ESR↑	2	-	Knee Full ROM	None	+3	Residual lucencies
6	12	M	Lt.	Localized pain and swelling, discharging sinus	Distal radius epiphysis and metaphysis, diffuse	1	-	Leukocystosis, ESR↑	2	-	Wrist Dorsiflexion palmar flexion arc -80 to +80 degrees	Prominent ulnar styloid	-	Positive ulnar variance, premature physeal closure, residual lucencies
7	5	M	Rt.	Localized pain and swelling, discharging sinus	Distal radius epiphysis and metaphysis, localized transphyseal hourglass	1	Rt. distal humerus, Lt. proximal ulna, Lt. 3rd MC, Lt. 5th MC, Lt. tibia, C1 Lt. lateral mass and facet of C2	Normal leukocyte count, ESR	5	-	Wrist Full ROM	None	-	Residual lucencies
8	7	F	Rt.	Stiff shoulder, regional muscle atrophy	Proximal humeral epiphysis, localized	8	-	Normal leukocyte count, ESR	5	-	Shoulder Full ROM	None	-	Complete healing

Abbreviations: M – Male; F – Female; Rt. – Right; Lt. – Left; MC- Metacarpal; ROM – Range of movement; LLD – Limb length discrepancy.

therapy (Figure 1,5) *(8,22)*. The confirmation of tubercular diagnosis however came only through histopathology (6 patients) or microbiological cultures (2 patients). It is suggested to obtain samples from multiple locations in the lesion and send all the pus/ granulation tissue/ curettage for all likely or possible laboratory tests *(5)*. This will reduce the likelihood of negative diagnostic results and the need for additional investigative procedures.

Surgical curettage was performed in all our patients along with multidrug tubercular chemotherapy. However, in two patients additional autogenous bone grafting of the epiphyseal component was done where subchondral thinning was obvious after curettage of the lytic lesion (patient 4 and 5) *(12,14)*. The rationale was to prevent subsequent collapse of epiphysis due to subchondral softening resulting from infective process and curettage. The physeal plate was carefully preserved using an autogenous fat pad in these patients (Figure 3). More recently, Takashi et al has recommended a minimally invasive endoscopic technique to minimize physeal damage during surgical curettage of hourglass lesions *(20)*.

During the available follow up, all patients had recovered useful adjacent painfree joint motion. Diffuse lesions resulted in premature physeal closure. Limb length discrepancies were observed in all four patients with involvement around the knee. The cause of lengthening may be temporary stimulation of growth plate due to juxta physeal focus. Radiologically, after institution of chemotherapy, lytic lesions with ill defined edges became more clearly defined (Figure 2b, 3c, 7b). The

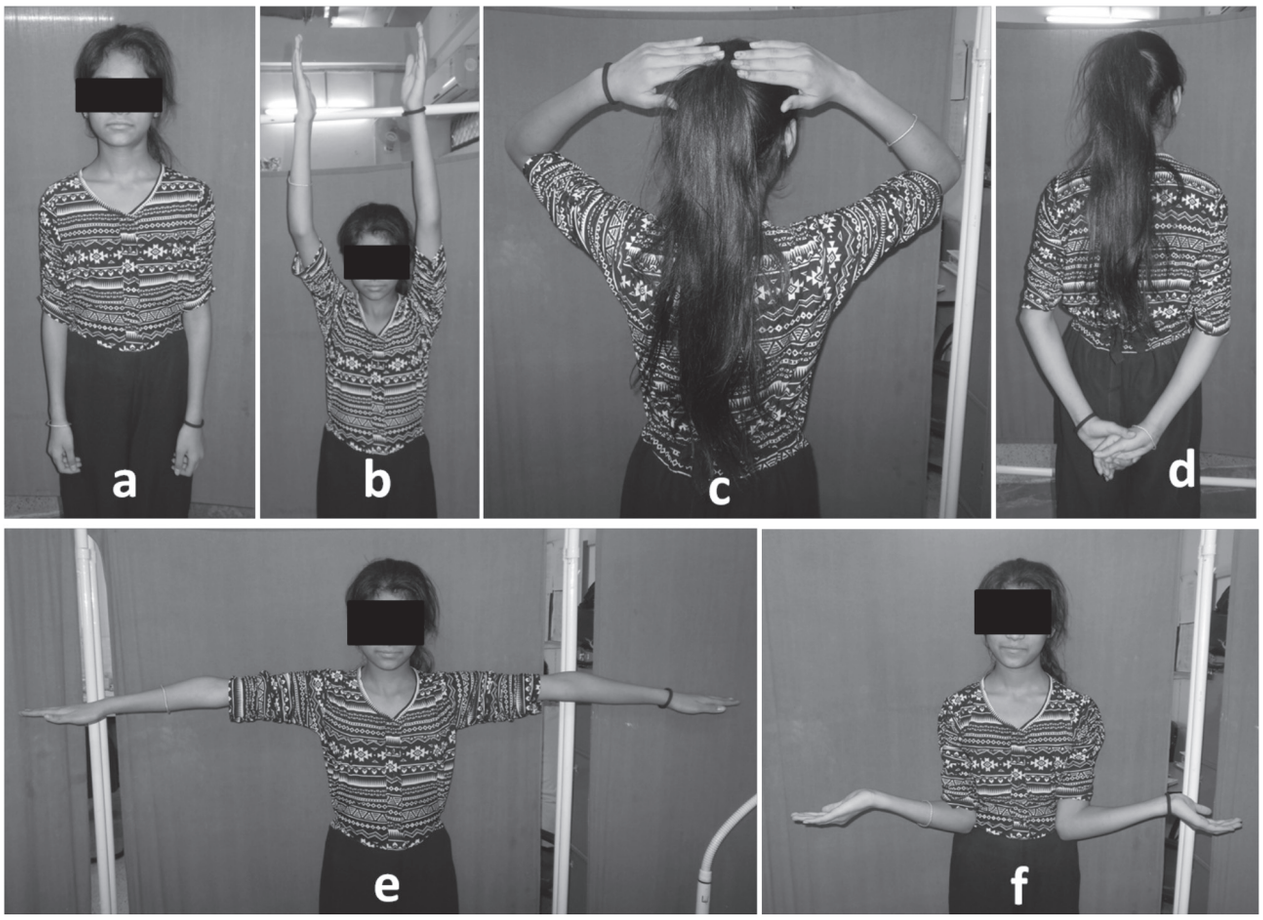

***Fig. 6.* —** Same patient as above at last follow up (a,b,c,d,e,f) Painless full range of shoulder motion, no deformity.

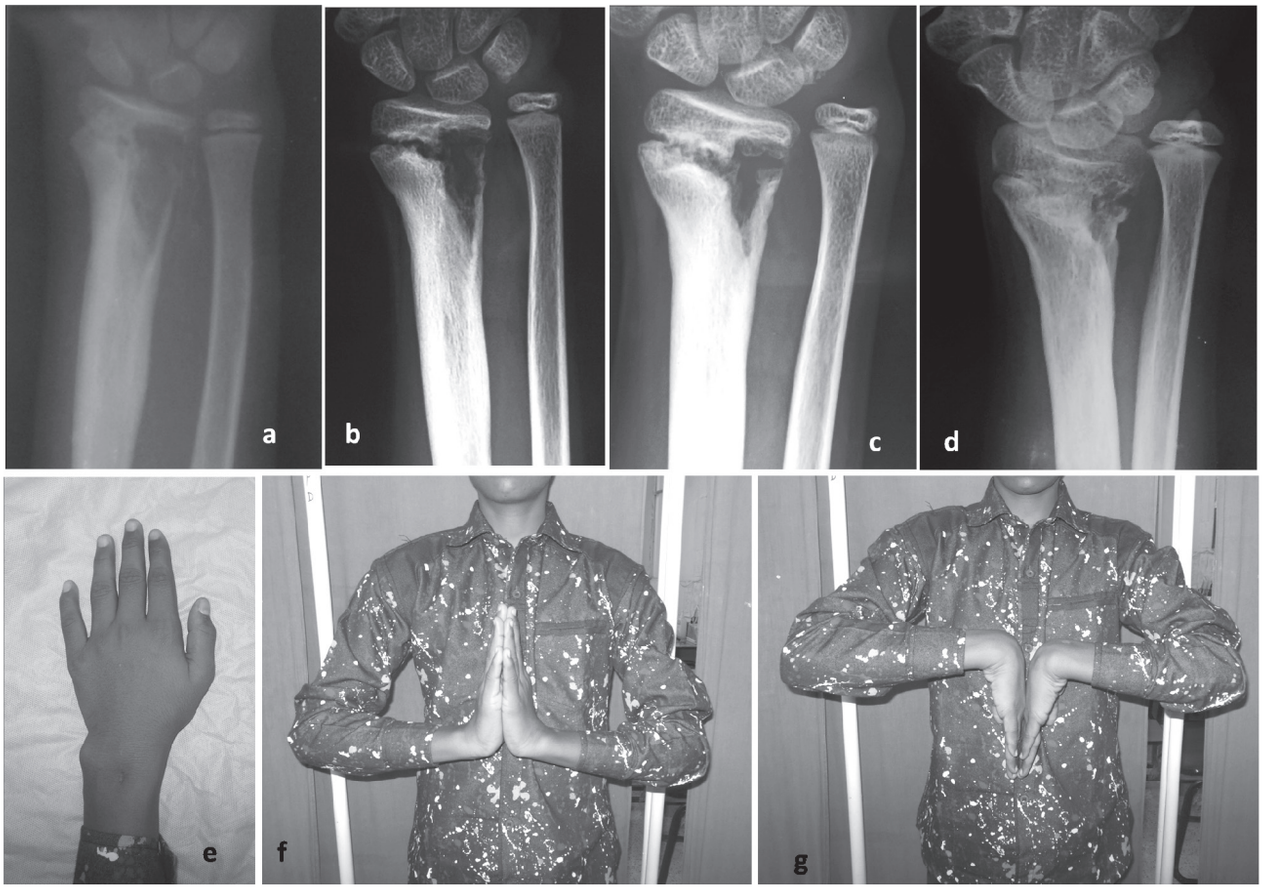

***Fig. 7.* —** Diffuse lesion (a) Plain radiographs of wrist showing transphyseal diffuse lesion in radius (b) After completion of antitubercular treatment. Sclerosis of the margins can be appreciated indicating healing of the lesion (c) One year post chemotherapy (d) Last follow up 2 years. Premature physeal closure. Some residual lucencies still persist. Except for ulnar prominence (e), the wrist function was preserved well (f,g).

'hourglass' physeal breach was not an unfavourable prognosticator in our series as the lesions healed without physeal bar formation as also reported by many authors (Figure 3d) *(5,10,12,16,17)*. The residual lytic radiological lucencies took longer time for complete obliteration (Figure 2b,c,d). However, the persistence of these lucencies was probably not of great clinical significance. No recurrences were noticed till the last available follow up in these patients.

The ability of epiphyseal and metaepiphyseal tuberculosis to mimic other diseases, combined with a lack of awareness to this clinicoradiological presentation, can lead to deterioration of the symptoms and subsequent delay in starting appropriate therapy *(5,8,9)*. Good prognosticators in these lesions have been young age of onset *(3,5,12,16)*, early diagnosis using advanced imaging *(9,22)* and treatment with curettage and multidrug chemotherapy *(5,9,12,19)*. Our study also supports the same findings. In our small series, transphyseal 'localized hourglass' lesions also resulted in favorable functional outcome *(5,12)*. This was very different from the transphyseal 'diffuse' variety with premature physeal closure. The bone grafting of the epiphyseal lesions in select patients also had favourable results. The residual epiphyseal and metaphyseal lucencies may persist for several months even after successful treatment. The final outcome in adult life in tuberculosis of these

growing bone ends can be influenced by both disease sequelae and effects of growth. It is therefore highly desirable to keep children in regular follow up.

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