Journal of Clinical Orthopaedics and Trauma 10 (2019) 1038–1045

Contents lists available at ScienceDirect

Journal of Clinical Orthopaedics and Trauma

journal homepage: www.elsevier.com/locate/jcot

A diagnostic dilema in benign lytic lesions of clavicle - our experience of 37 patients

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ARTICLE INFO

Article history:
Received 9 March 2017
Received in revised form
19 May 2017
Accepted 29 June 2017
Available online 14 October 2019

Keywords:
Clavicle
Lytic lesions
Benign

ABSTRACT

Introduction: The studies on benign lytic lesion of clavicle are sparse. Asymptomatic nature of lesions, rare occurrence, the difficulty in interpretation of the X-rays because of the surrounding structures and striking similarities in various lesions further make the diagnosis of such atraumatic lytic lesions difficult.
Material and methods: Prompted by the rarity of lesion and scarcity of data regarding presentation and management, we performed a prospective study of benign lytic lesions of clavicle. The results of the lesions are categorised in infective, metabolic and neoplastic conditions.
Results: Infective lesions were most common cause of symptomatic painful benign lytic lesions. Metabolic lesions, like rickets, were the most common cause of painless swelling in clavicle. Neoplastic conditions although rare were an important differential.
Conclusion: It is important to differentiate and diagnose lytic lesions of clavicle. Early MRI and Biopsy of the lesion helps in preventing an undue delay in diagnosis. Most lesions when diagnosed in time have excellent results.

1. Introduction

Clavicle is a bone with numerous peculiarities. It is the first bone to ossify and has 2 primary and one secondary centre of ossification. It is the only long bone to lie in horizontal position, no well defined medullary canal and has a membranous ossification.[1,2] It is only ironic that a bone with so many unusual features is one of the least studied bones.[3] With the exception of traumatic lesions and tuberculosis of clavicle, most data on clavicle in literature is regarding its neoplastic lesions.[4-10] Even this data mostly revolves around the malignant lesions which are by far more common than benign lesions. The benign lesions are infrequent and most common is osteochondroma, which radiologically is bony outgrowth - pedunculated or sessile. The data on benign lytic lesion is however sparse. Asymptomatic nature of lesions, their rare occurrence, the difficulty to read the X-rays because of surrounding structures and striking similarities in various lesions further make the diagnosis of such atraumatic lytic lesions difficult.

Prompted by the rarity of lesion and scarcity of data regarding presentation and management, we performed a prospective study on benign lytic lesions of clavicle. The aim of this study was to establish etiological basis for benign lytic lesions presenting to our tertiary centre and identify clinical, radiological and pathological characteristics of these etiologies.

2. Materials and methods

A prospective study of benign lytic lesions of clavicle was performed from 2008 to 2013. Patients with all age group presenting with a lytic lesion in clavicle were included in the study. The patients with malignant lesions including multiple myeloma, traumatic lesions and metastasis were excluded from the study. All lesions that were benign and lytic with or without sclerotic component were included. Patients with less than 24 months of follow up were also excluded.

A thorough clinical examination was done in all patients presenting either with pain or swelling in or around clavicle. An informed consent was taken for their enrolment in study. All patients were subjected to routine investigations including complete blood count including ESR(erythrocyte sedimentation rate),

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https://doi.org/10.1016/j.jcot.2017.06.023
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baseline liver and renal function and Mantoux test, serum calcium, phosphorous and ALP (alkaline phosphate), CRP(C- reactive protein) and X-rays of bilateral clavicle. Serum uric acid was also investigated in adult patients. MRI (Magnetic resonance imaging) were ordered in all symptomatic lytic lesions of clavicle followed by a tru-cut biopsy when diagnosis was not clear. The material was sent for histopathology, pus culture and sensitivity, gram stain, acid fast stain and culture on Lowenstein-Jensen medium.

The objective assessment of function in pre and post treatment was done using University of California, Los Angeles (UCLA) shoulder rating scale.[11] The scale incorporated pain, movement, function and patient satisfaction. There were marked improvement in the scores with all patients achieving near normal functions and pre illness work status. We were not able to use scores in 1 patient with age 3 years and he was evaluated on pain and active shoulder movements which improved after anti-tubercular therapy. Visual analogue scale (VAS) was used for pain assessment.

The management was on the basis of the diagnosis of the lesion.

3. Results

The results of the 37 lesions of benign lytic lesion in our seies are categorised in infective, metabolic and neoplastic conditions and summarised in Table 1.

3.1. Infective lesion

Twelve of thirty seven lesions were infective with overall incidence of 32.3% in our series. They were further divided as tubercular or bacterial.

3.1.1. Tuberculosis Osteomyelitis

Tubercular osteomyelitis was the most common cause of lytic lesion in our series. There were nine cases of histopathologically proven tuberculosis. There were five females and four males. All cases were unilateral. The mean age of presentation was 23 years. The most common and earliest clinical feature was dull aching, deep seated moderate intensity pain with no obvious diurnal variation. This was followed by swelling in clavicular region. Two patients presented with an abscess over clavicle and one patient presented with a sinus. Five patients complained of constitutional symptoms like loss of weight, decreased appetite or low grade fever. The mean duration between onset of symptoms was 5 weeks (1 week −3 months). All patients in active stage had tenderness on direct palpation(Fig. 1a,b,1c,1d,1e).

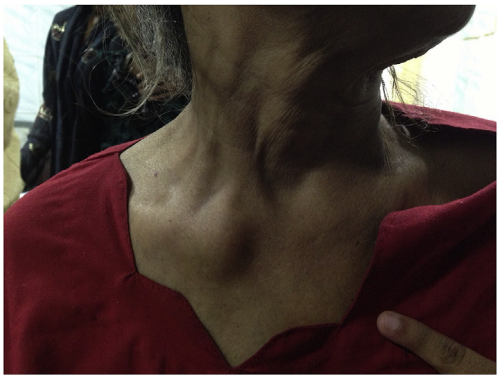


Fig. 1a. Clinical photograph of a 65 year old female presented with right sided swelling over medial end clavicle later proved to tuberculosis.

Table 1
Results summary of cases with lytic lesions of clavicle.

Etiology	Number of patients	Radiological features	Clinical feature	Histopathology	Average pre treatment/ post treatment UCLA*
Tubercular	9	Lytic lesion with bony destruction with osteoporosis MRI may show a soft tissue collection	Fever Pain Non progressive/slowly progreesive swelling	Caseous necrosis with giant cell granuloma	15/26
Osteomyelitis	3	Lytic lesion with surrounding sclerosis, may show sequestration	Fever Pain Non progressive/slowly progreesive swelling Sinus/abcess formation	Non specific inflammation Pus culture positive	13/25
Rickets	6	Mostly bilateral lytic lesion, with other characteristic features of rickets in other metaphyseal region	Stunted growth, Wide wrists Genu varum/valgum asymptomatic	Usually Not required	26/27
Gout	4	Usually a lytic area along with tophi at other usual sites	Episodic severe pain Tophi formation Asymptomatic	Usually not required	25/27
Hyperparathyroidism	3	Bony resorption, lytic areas along with brown tumor in other usual sites	Asymptomatic/features of hyperparathyroidism	Usually not required	22/27
Eosinophilic granuloma	3	A lyitic expansile lesion usually at metaphyseo-epiphyseal region	Pain Slowly progressive swelling	Langerhans cells with eosinophillic cytoplasm	18/26
Aneurysmal bone cyst	2	A lytic expansile lesion with trabeculation MRI shows fluid in cavities	Painful progressive swelling	cavernous blood filled spaces without endothelial lining with numerous giant cells and spindle cells	19/27
Giant cell tumor	1	Usually a metaphyseo-epiphseal lyic lesion in skeetally mature MRI show a solid tissue	Painful progressive swelling	multinucleated giant cells	17/27
CRMO	3	Multiple small lyitc areas witje surrounding sclerosis. Usually assossiated with similar features at other sites	Fever Swelling Relapsing course Involvement of other joints	Non specific chronic inflammatory cells with granuloma formation	19/26
Idiopathic	3	Non specific	Non specific	Non specific	

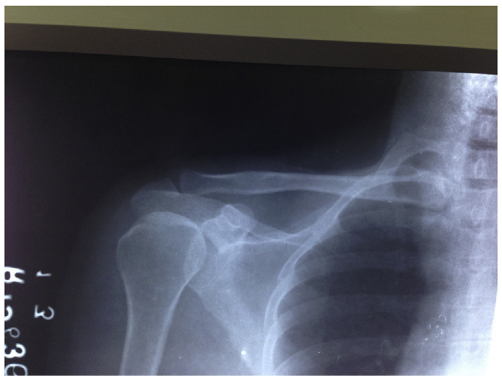


Fig. 1b. A plain AP radiograph of right clavicle showing lytic and expansile lesion on right side medial end clavicle.

The erythrocyte sedimentation rate (ESR) was elevated (mean: 68 mm/h) in all patients (range: 46–98 mm/h) whereas the full blood count (FBC) revealed a normocytic, normochromic anaemia (range: 7.9–11.3 gm/dl, mean: 10.1 gm/dl).

X-rays show either diffused thickening and honey combing or eccentric expansile lytic lesions with surrounding osteopenia. The most common site of presentation was medial end of clavicle. MRI showed area of destruction and any associated soft tissue abscess. MRI has greatly helped in identifying the lesions early.

All patients showed histopathology report suggestive of tuberculosis. The biopsy material revealed areas of central caseous necrosis numerous epithelioid cells with pale pink cytoplasm and indistinct boundaries with oval or elongated nucleous. There was presence of Langhans type giant cells with large mass of cytoplasm containing multiple small nuclei arranged peripherally. Stains for acid fast bacilli were positive in only three patients and two patients (17%) showed growth on Lowenstein-Jensen medium.

Patients with histopathological or culture proven tuberculosis were started on anti-tubercular therapy for 18 months. 4 drugs-Isoniazid 5 mg/kg, Rifampicin 10 mg/kg, Ethambutol 25 mg/kg and Pyrazinamide 15 mg/kg were given for initial 2–3 months. Depending on response, decrease in pain and decline in ESR, Pyrazinamide was stopped after 2–3 months and the other three drugs were continued for 6–9 months. Once pain was relieved and ESR approached near normal, Ethambutol was also stopped and two drug therapy was continued. Total duration of Anti tubercular therapy was kept for 18 months.

The results of clavicle tuberculosis were uniformly good. Pain decreased in 2–3 months and swelling decreased in 7–9 months. Sinus healed in three months. Radiographs suggested mineralisation with decrease in size of lesion by 12–15 months. No recurrent abscess was seen in any of the case. No relapse of the disease has been seen in 2–5 year follow up after 18 months of anti tubercular therapy.

3.1.2. Bacteria osteomyelitis

Three cases – two males and one female, showed organism other than mycobacterium tuberculosis. The patients presented with deep boring pain, with one patient having a draining sinus. The biopsy material sent for culture revealed Staphylococcus aureus in all three cases. The biopsy were mostly non specific with

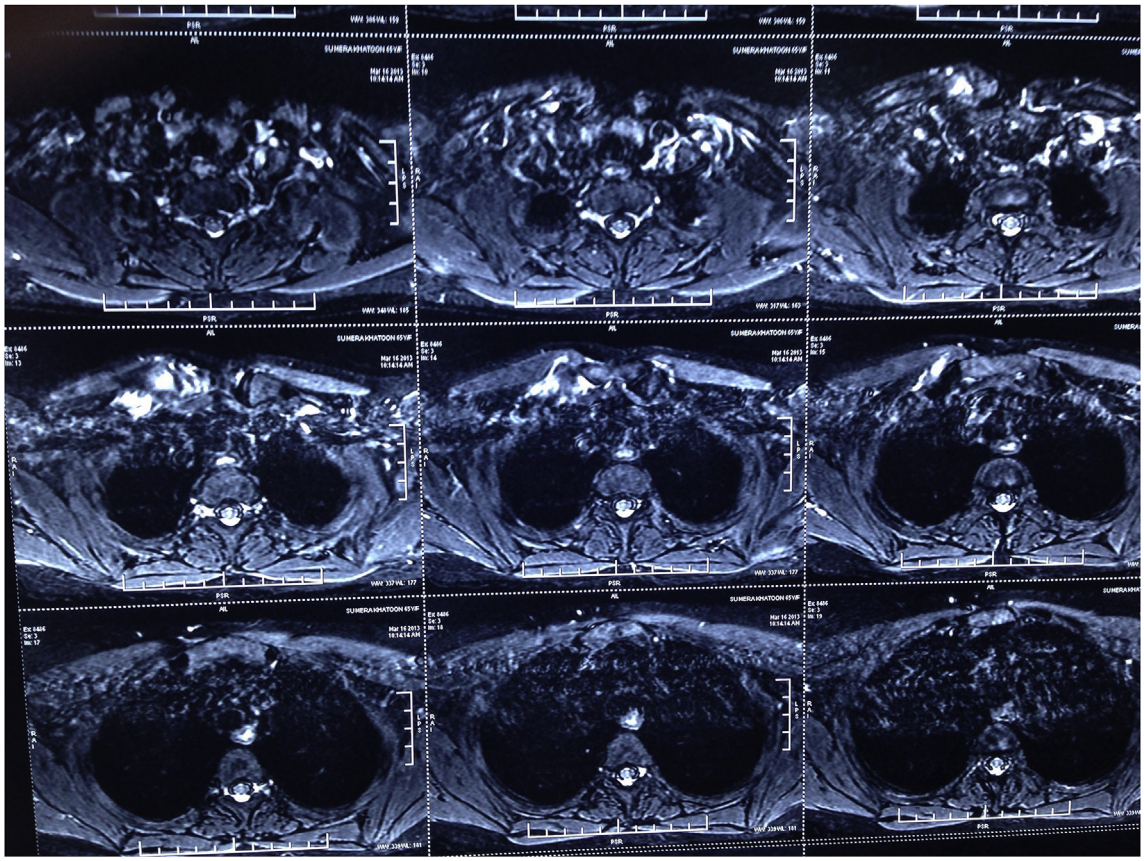


Fig. 1c. i T2 weighted image axial cut, ii: T2 weighted image sagittal cut, and figure iii: T1 weighted image axial cut showing marrow edema in right medial end clavicle with synovial effusion/thickening and assosiated small collection posterior to sterno-clavicular joint suggesting infective etiology which on biopsy proved tuberculosis.

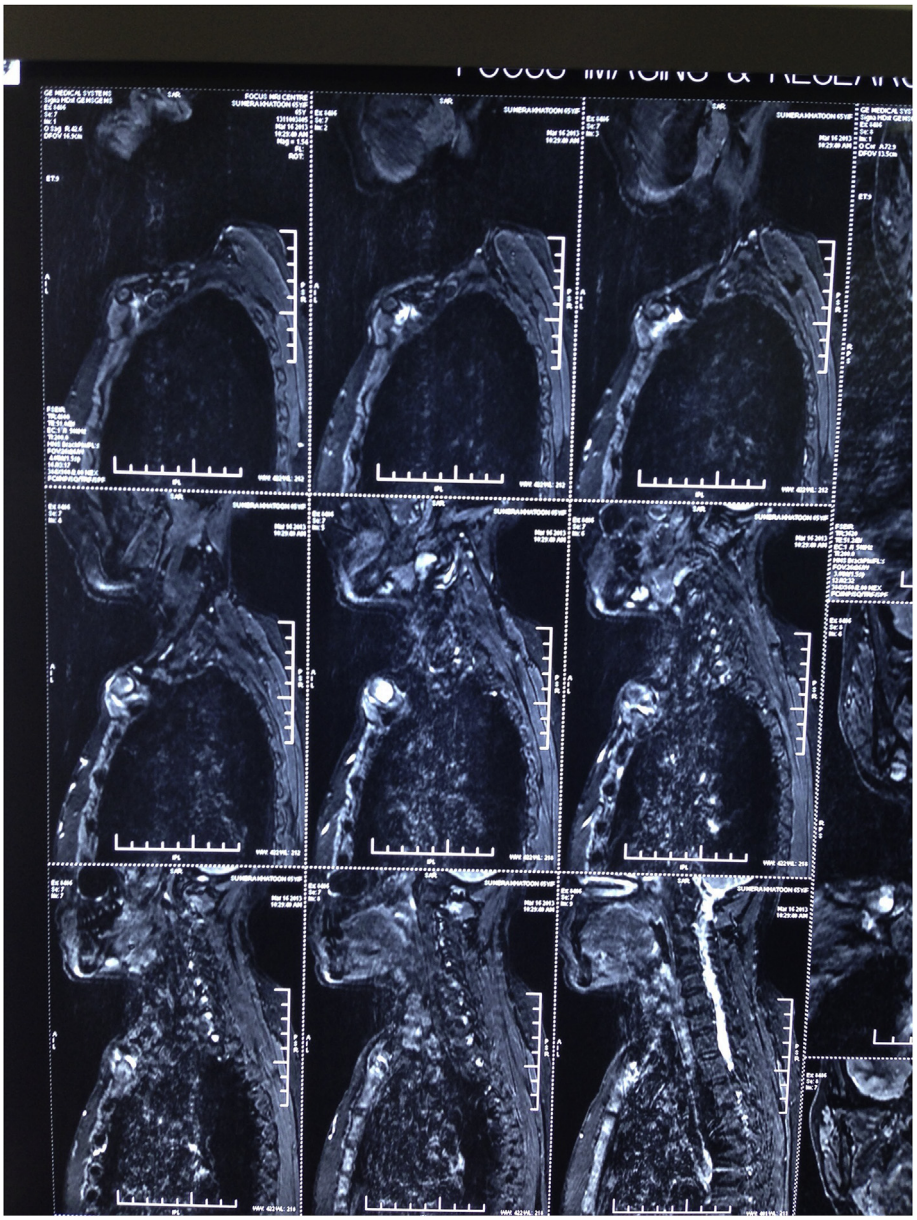


Fig. 1c. (*continued*).

chronic inflammatory changes. The radiological features showed a lytic lesion with surrounding periosteal reaction. One of the cases showed a central sequestrum lying in lytic lesion. All patients were given initial trial with antibiotics based on culture sensitivity. Two patients resolved on antibiotics alone with one requiring a curettage and removal of central sequestrum. No relapse were seen on 2 year follow up(Fig. 2a,b).

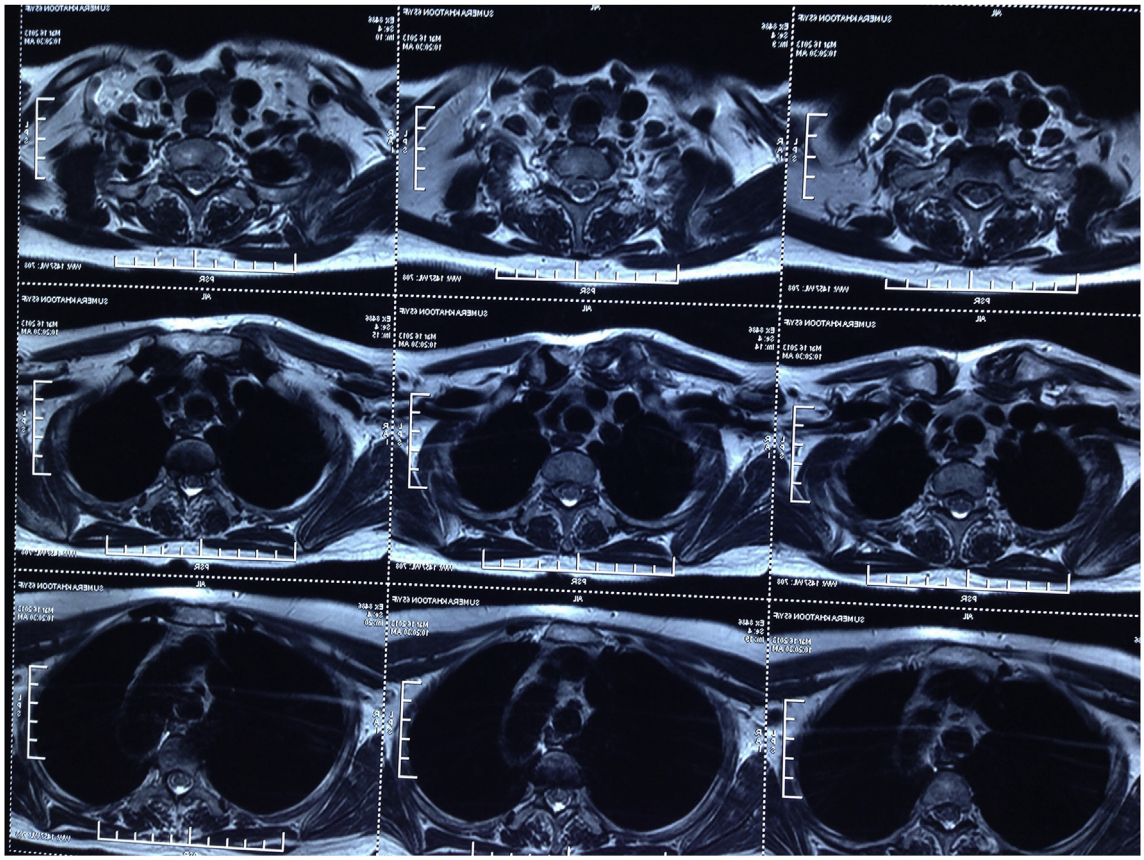
3.2. Metabolic lesion

Benign Lytic lesions were common in various metabolic lesions. 13 of our 37 patients (35.13%) were diagnosed of some metabolic disease. The patients were mostly asymptomatic except for their concern of a swelling over clavicle. Initial X-rays showed a lytic area without any sclerotic rim mostly on medial end of clavicle in all these conditions. Generally no surrounding osteoporosis were seen. On routine blood investigation six patients had rickets with an increased ALP, four patients had gout with increased uric acid level and atleast one painful joint showing uric acid crystal on microscopy and three patients had hyperparathyroidism with increased PTH levels. Resolving the primary condition resolved the lesion in all cases. No biopsy were done in any of these cases as all lesions resolved on treating primary condition(Fig. 3a,b,3c).

3.3. Neoplastic conditions

3.3.1. Eosinophilic granuloma

Three patients were diagnosed of eosinophilic granuloma in our series. Two patients were male and one was female with age of 3, 5, 11years. All three patients presented with a slowly progressive swelling on lateral aspect of clavicle. The swelling had been increasing in size and average duration of symptoms was six months before presentation. The swelling was non tender to touch and overlying skin was normal. There was no history of any other



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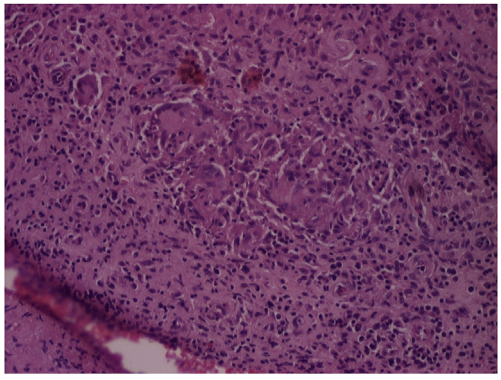

Fig. 1d. The histo-pathological sample of biopsy of clavicle with surrounding soft tissue showing tubercular granuloma with Langhans type giant cells and numerous epithiliod cells.

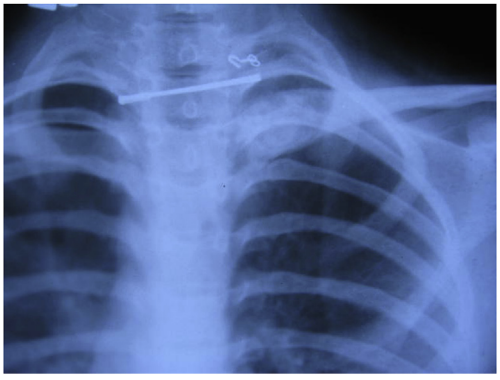

Fig. 1e. Plain X-ray AP view of right clavicle showing lesion at end of treatment with complete mineralisation.

swelling in the body. The X-ray showed expansile lytic lesion in lateral end of clavicle with normal soft tissue shadow. There was no breech in cortex. In one patient the cortex was thinned out. Biopsy of the specimen showed Langerhans cells which were mononuclear histocyte like cell with coffee bean nuclei(prominent central groove) and well defined eosinophilic cytoplasm, admixed in inflammatory cells with no nuclear atypia. CD-1A marker was done in all three cases and was found to be positive. Two cases with good cortex were managed conservatively with intra-lesional steroid and the third case with large lytic lesion with impending fracture was managed with curettage and allogenic bone grafting. Lesions healed in all three cases with excellent result and no recurrence was seen in 2 year follow up(Fig. 4a,b,c,d).

3.3.2. Giant cell tumor

One patients was diagnosed of giant cell tumor. Patient was 23 year old female with painful lytic lesion in medial end of clavicle. Plain radiograph showed a epiphysio-metaphyseal lytic area on medial aspect of clavicle. The lesion was geographic type and showed no periosteal reaction. There were no calcification in the matrix. MRI showed a solid component lesion in medial aspect of clavicle with low to intermediate signal density in T1 and heterogeneous intermediate density in T2 with no soft tissue component and no soft tissue component. Histology sections of the lesion revealed a cellular lesion comprising predominantly of sheets of

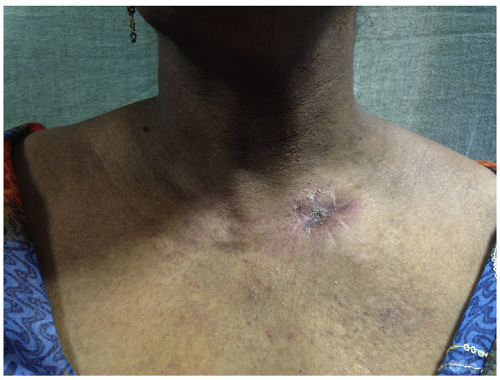

Fig. 2a. Clinical photograph of a 35 year old female presented with a draining sinus proved to be caused by Staph aureus on culture report.

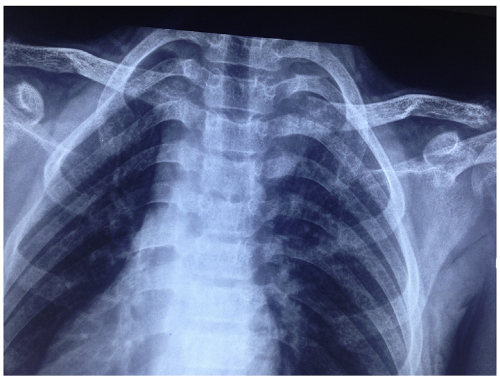

Fig. 3b. AP X-ray of bilateral clavicle showing bilateral lytic lesions on medial side due to rickets.

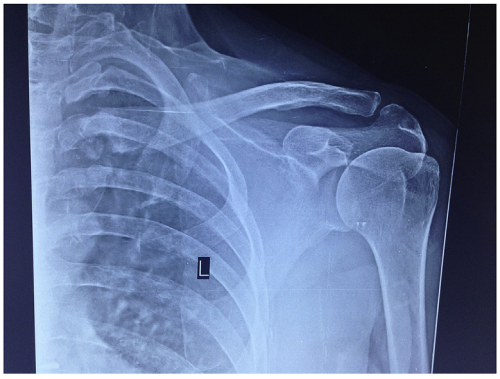

Fig. 2b. plain AP X-ray of left clavicle showing a sequestrated lesion on medial end of clavicle. Sequestrated part is shown by X-ray.

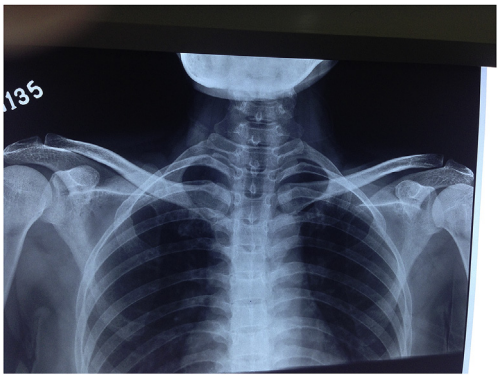

Fig. 3c. AP Xray of bilateral clavicle showing a lytic lesion on medial aspect on left side due to gout.

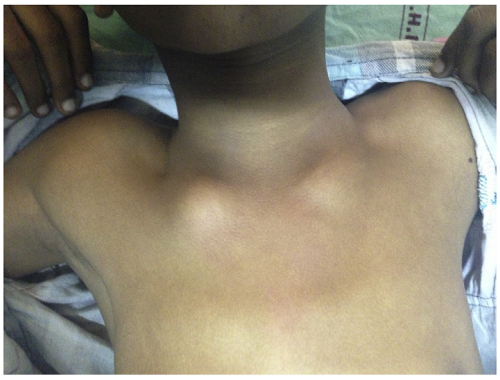

Fig. 3a. Clinical photograph of a 15 year old boy presented with bilateral medial end swelling. The patient was later proved to have rickets.

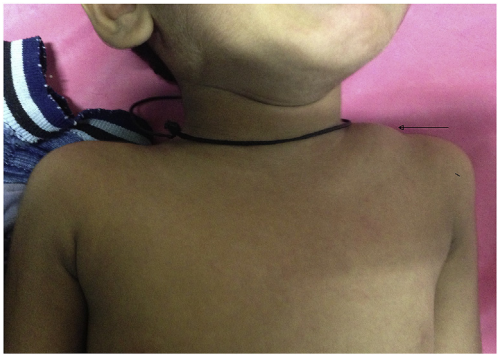

Fig. 4a. clinical photograph of 3 year old boy showing lesion on lateral end of clavicle.

plump, oval, mononuclear cells with mild pleomorphism. The cells had moderate amount of eosinophilic cytoplasm, oval to elongated nucleus with moderate anisokaryosis with irregular nuclear membrane, vesicular nucleus and 0–1 nucleolus. Admixed amongst these, many multinucleated giant cells were seen distributed in a regular and uniform fashion.

The patient was treated with extended curettage and bone graft. No recurrence is noted at 2 year follow up.

3.3.3. *Aneurysmal bone cyst*

We had an opportunity to see 2 aneurysmal bone cyst in clavicle in our study. Both patients were female and aged 12 years and 14 years. The lesion was located in medial end in one patient and lateral end in other patient. Both complained of tender progressive bony swelling. Examination revealed mildly tender bony mass continuous with clavicle. Radiographs showed a lytic expansile lesions with trabeculations in the lyric area. Computed tomography (CT) revealed a thin-walled multiloculated lesion in the clavicle. MRI did not reveal any soft tissue extension(Fig. 5).

The biopsy showed characteristic cavernous blood filled spaces without endothelial lining with numerous giant cells and spindle cells. The lesions were treated with curettage and grafting and had excellent out come.

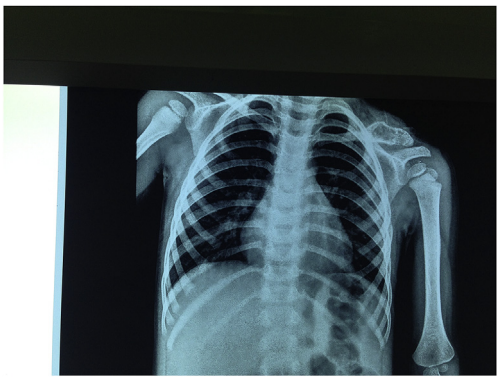

Fig. 4b. Plain AP radiograph of clavicle showing an expansile lytic lesion on lateral end of clavicle.

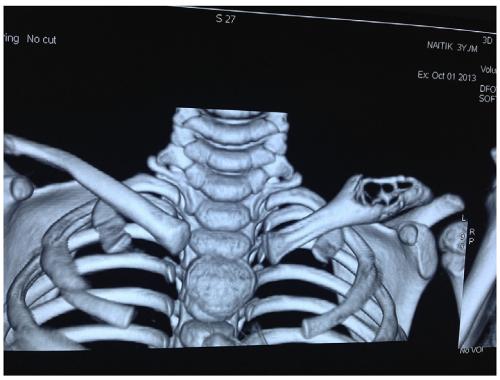

Fig. 5. CT scan of chest showing a lytic lesion with trabeculations which on biopsy proved to be aneurysmal bone cyst.

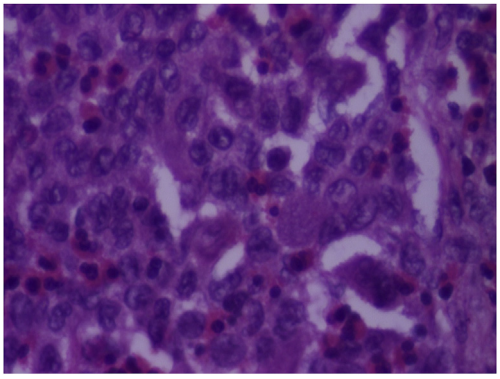

Fig. 4c. histological sample of same patient showing Langerhans cells in patient with eosinophilic granuloma.

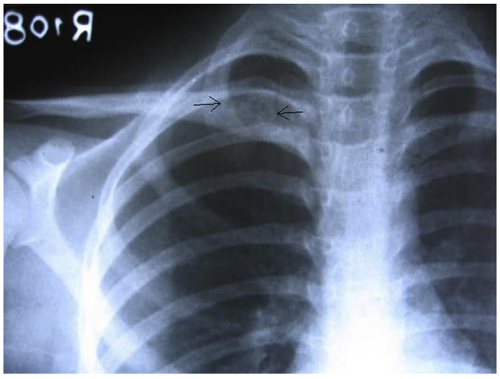

Fig. 6. a plain X-ray of chest showing two areas of lytic lesion on medial end of clavicle diagnosed as CRMO.

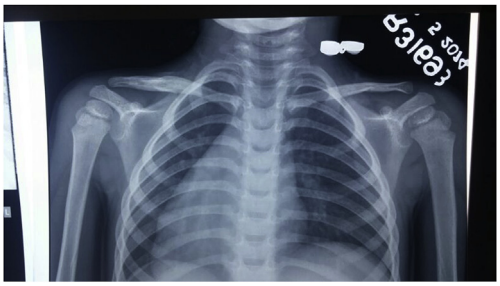

Fig. 4d. 1 year follow up X-ray of patient of eosinophilic granuloma treated with curettage and bone grafting.

3.4. Chronic recurrent multifocal osteomyelitis (CRMO)

Three patients in our series were diagnosed with chronic recurrent multifocal osteomyelitis. The average age was 23 years and 2 were male and one female. Two patients presented within 6 months of symptoms and one presented at 9 months of onset. Mild discomfort and localised swelling were present in all. Two patients gave history of fever. The symptoms were present in atleast one more area except clavicle most common being metaphysis of distal femur. The plain Xrays revealed small lytic areas in clavicle one in medial end and 2 in lateral end of clavicle. The patients who presented early had a single lesion and were started on antibiotics after biopsy which showed non specific osteomyelitis with granuloma. The culture revealed no growth. These two patients developed new lesions even under treatment and the diagnosis of CRMO was made in retrospect The patient who presented at 9 months had a second episode at presentation with a symptom free interval in between 2 episodes. The second lesion developed on medial end of clavicle. The patients were managed conservatively and are being regularly followed up(Fig. 6).

3.5. Idiopathic

In spite an extensive search for diagnosis, no diagnosis could be made in 3 patients with lytic lesions of clavicle. The biopsy in all 3 patients showed chronic inflammatory cell and was non specific. Patients were managed conservatively with symptomatic treatment. The patients are under follow up and the lesion or symptoms have not progressed and all 3 patients are asymptomatic.

4. Discussion

The non-traumatic lesions of clavicle are rare and always pose a diagnostic challenge. The area is difficult to radiograph as it is surrounded by other bony structures and patients are mostly asymptomatic for long time. Also a wide array of pathologies have striking radiographic similarities and all these aspects make the diagnosis of lesion difficult. Further since most lesions in clavicle are malignant it becomes very essential to differentiate the benign lesions at an early stage.[1,2] A good clinical history and examination along with lab investigations and X-rays and MRI generally helps in forming a diagnosis which in case of any doubt must be confirmed histologically. Infective lesions generally have history of fever with elevated ESR and CRP. MRI in most occasions show soft tissue

collection, mostly an abscess, along with bony erosions and biopsy and culture reports can confirm diagnosis. Metabolic lesions on most occasions are asymptomatic and careful history and evaluation of other joints give a clue to diagnosis which may be confirmed on blood tests. Usually no biopsy is required in such cases. A painful or even painless swelling that has increased in size requires an aggressive approach as most tumours are malignant. Age usually helps in diagnosis with eosinophilic granuloma and ABC being most common lesions in 1st two decades. The other possibilities are non ossifying fibroma and simple bone cysts. These can be differentiated easily by radiological and pathological reports. GCT, osteoid osteoma and fibrous dysplasia, though very rare may be the differential in adult patients.[8–10]

Metabolic abnormalities were also a common cause of lytic lesions. Rickets, hyperparathyroidism and gout were most common disorders that were found in our series to cause such lesions. The lesion in these cases are often asymptomatic. However finding of such lesion followed by a good clinical work up was helpful in the diagnosis of underlying lesion. The treatment of underlying lesion in most cases resolved the lytic lesion as well. Radiological features of gout in bone includes lytic lesion and reports of such lesions mimicking tumours have been mentioned in literature.[3] Rickets and hyperparathyroidism are known to cause bony resorption and lytic lesions. However clavicle is rare sites for such lesions and therefore it is important to keep such metabolic conditions as differential diagnosis while dealing with lytic area in clavicle.

Tuberculosis of clavicle was single most common cause of symptomatic benign lytic lesion. %). Most of the patients presented with pain and swelling of involved region. The lesion was most common in medial end of clavicle. Similar results were observed by Tuli et al. in their description of 7 cases.[4–6]

X-rays show either diffuse thickening and honey combing, or eccentric expansile lytic lesions with surrounding osteopenia However it was observed that plain radiographs were inconclusive to define the lesion primarily due to overlying anatomical structures. Similar observations were made by Aggarwal et al. CT or magnetic resonance imaging(MRI) provide better assessment of the lesion.[5,6] On CT, destructive changes are better appreciated. On MRI, they are seen as a breach in the normally hypointense rim formed by the cortices of the bones. MRI is useful for determining the extent of the lesion and soft tissue involvement. All imaging methods provide complementary information.

The results were uniformly good with conservative management on Anti tubercular treatment for 18 months.[4–6]

Osteomyelitis of clavicle is rare and presents most commonly with painful swelling. Staph aureus was found to be most common causative organism and results of antibiotics were good similar results are seen in literature also.[7]

Clavicle is the bone of peculiarities. Apart from morphological and embryological uniqueness, clavicle also presents radiological irregularities. The usual benign lesions may appear aggressive in clavicle. Gersovich et al. have hypothesized that several factors including the bone's unusual shape, with its irregular ridges and rough cortical surface and the variable thickness of its cortex (thicker in the middle third) may contribute to this uncharacteristic response. Further the authors believe that direct membrenous ossification of this bone make it prone for exuberant bone formation in response to trauma or tumor giving an aggressive picture for relatively mild etiologies.[12,13] However, elaborate history and clinical examination coupled with early MRI and biopsy may help to differentiate benign lesions from malignant ones.

5. Conclusion

The benign lytic lesions of clavicle are very rare. It is important to differentiate and diagnose such lesions. Asymptomatic lesions may be a clue for underlying metabolic condition. Tuberculosis of clavicle is important differential of all lytic lesion and single most common cause. Early MRI and Biopsy of the lesion helps in preventing an undue delay in diagnosis. Most lesions when diagnosed in time have excellent results.

Declaration of competing interest

No conflict of interest.

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