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Case Report

The great mimicker – Case report of eosinophilic granuloma of proximal radius and review of literature

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ABSTRACT

Eosinophilic granuloma is an uncommon bone tumour consisting of circumscribed lesions of the reticuloendothelial system usually confined to the bone. We present a case report of 28-year-old male who complaints of swelling over proximal end of radius associated with pain for a duration of 1 year. The patient was successfully treated with open biopsy followed curettage and intralesional methyl prednisolone injection using Boyd's approach. Histopathology reported the lesion as eosinophilic granuloma. Patient was followed up in our outpatient department and found to be symptom free with evidence of resolution of tumour. This case study adds to the current understanding and treatment of eosinophilic granuloma. Eosinophilic granuloma is always a diagnostic challenge for the surgeon. Clinical findings and investigations are usually non-specific. Histopathology and immunohistochemistry still remains the mainstay in diagnosis of EG. Always suspect it, lest you will miss it.

1. Introduction

Eosinophilic granuloma was the term first used by Lichtenstein and Jaffee in 1940.[1] Otani and Ehrlich have described the same lesion as the Solitary granuloma of the bone. Green and Farber in 1942 found that eosinophilic granuloma, Hand Schuller- Christian disease, and Letterer siwe's disease are presentation of the same pathological process.[1] While in 1953 Lichtenstein coined the term Histiocytosis X to describe the so mentioned three manifestations as the pathological common denominator was a specific inflammatory histiocytosis.[1] Eosinophilic granuloma (EG) is defined as a circumscribed lesion of the reticuloendothelial system usually confined to the bone but occasionally involving lymph node and pulmonary parenchyma, which belong to a subset of the spectrum of the disease called Histiocytosis X.[2] Diagnosis poses a dilemma to orthopaedician as neither the clinical nor the radiographic findings are specific for the disease. It is seen mainly in children and young adults approximately 2:1 male to female ratio, although usually single, the lesion may be multifocal. Any bone may be involved but there appears to be a predisposition to bones of the skull and the diaphysis of long bones. The disease presents with local symptoms varying from mild pain, swelling, and redness to those associated with pathological fracture. Systemic manifestations other than slight fever and malaise are rare. The radiological picture is that of a punched out, welldefined and often associated with periosteal thickening.[2] The biochemical values are usually undisturbed.

Infection or tumour are the commonest differential diagnosis made in patient with history of pain and tenderness.[3] Investigation modality like MRI and CT helps in evaluating the extent of the lesion but diagnosis is only confirmed by histopathology

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2. Case Report

A 28 -year old patient presented to the outpatient department with history of pain over right forearm since 1 year. It was dull aching in character, localised over proximal 3^{rd} of forearm, non- radiating type and aggravated with movements. Patient didn't have any history of trauma or associated constitutional symptoms. The patient had not taken any treatment except analgesics.

On clinical examination patient was afebrile with swelling of size 4x3 cm present over dorsal aspect of right forearm over radial border of proximal one third of radius associated with marked local tenderness and restriction of supination and pronation of forearm. There was no local rise of temperature and no neurovascular deficits. Imaging modalities like plain radiographs was done initially. It revealed well circumscribed lytic lesion over diaphyseal region of radius with no appreciable periosteal reaction. The lesion was 4.8cm from proximal articular surface of radius.

Laboratory investigations were found to be unaltered, Sr Ca – 8.8, Sr Phosphorus -2.60, Sr ALP 59, CRP – 0.80, TC – 7210, Hb- 15.90%, Neutrophils – 60. 80, Lymphocytes - 27.90, Eosinophils – 3.70 and ESR – 8. Subsequently a MRI was performed to delineate the lesion and to rule out any soft tissue involvement. It was reported as poorly defined slightly expansile intramedullary lesion noted in proximal metaphysis of radius measuring approximately 57 (CC) x 16 (TR) x 12 (AP) mm. The lesion showed T1 iso to hypo. T2 iso to hyperintense signal & STIR hyperintense signal with moderate inhomogeneous post contrast enhancement. There was cortical erosion and destruction at multiple areas with periosteal reaction. Matrix mineralisation was noted along the inferior aspect of the lesion. There was subperiosteal enhancement of soft tissue along lateral aspect of the lesion. There was no extension into articular surfaces or involvement of neurovascular bundles.

We performed 3D PET CT scan in siemens biography m-CT 128 slice Digital scanner after intravenous injection of 10 mci of FDG and it was reported as metabolically active lytic lesion noted in proximal shaft of right radius, measuring about 1.8 x 1.6x 2.2 cm with cortical thinning and anterior local breach. There was no evidence of periosteal reaction or osteoid matrix. A provisional diagnosis of Ewing sarcoma, eosinophilic granuloma was made, osteomyelitis or osteosarcoma were also considered Patient was taken up for the surgery – open biopsy followed by curettage and intralesional methyl prednisolone injection as an elective procedure using Boyd's approach. Intraoperatively we found irregular cortical thickening with friable greyish osseous material. A cortical window was made using 2mm drill and thorough curettage was done followed by intralesional methylprednisolone injection. Tissue curetted from the lesion was send for histopathological studies, aerobic culture sensitivity, mycobacterium and fungal culture sensitivity study. Cultures studies were found to be negative.

Histopathology showed dense inflammatory infiltrate of eosinophils, lymphocytes and neutrophils admixed with histiocytic cells arranged in clusters. Those cells exhibit oval nuclei with nuclear grooves and indistinct eosinophilic cytoplasm. Bony trabeculae with focal areas of necrosis were noted. These findings were consistent with that of eosinophilic granuloma.

The patient was followed up in our outpatient department for two months. Patient was symptomatically better and pain free. It was observed our line of management helped in resolution of this tumour and stimulated new bone formation in pre-existed zone of lysis in the serial radiographs. Patient was immobilized in an above elbow plaster for two months.

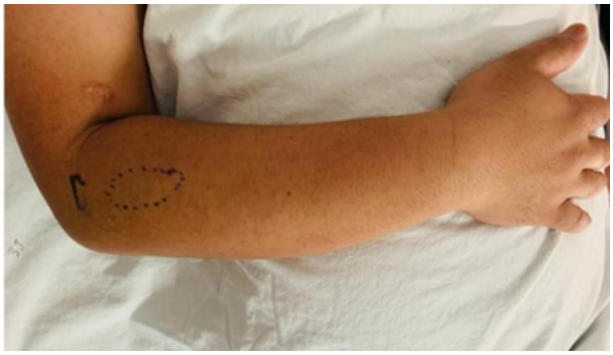

Fig. 1: Lesion depicted with dotted line while forearm in mid prone

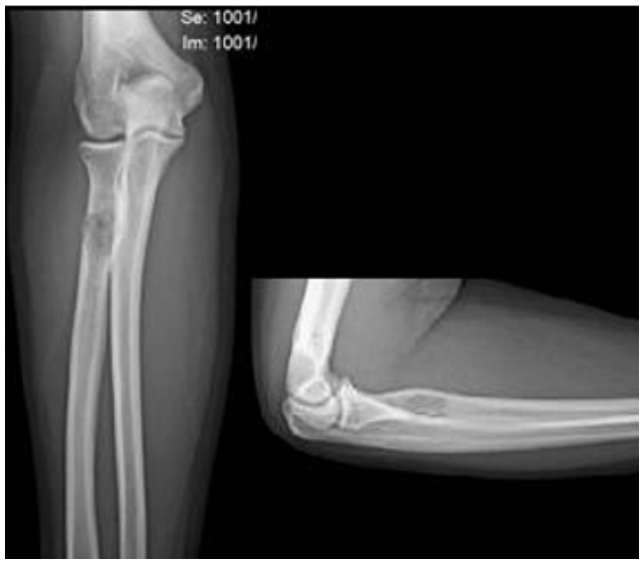

Fig. 2: Plain radiograph revealing lytic lesion present over proximal one third of radius

3. Discussion /Literature Review

EG is a uncommon bone tumor comprising less than 1% of all bone tumors. It is the commonest and mildest

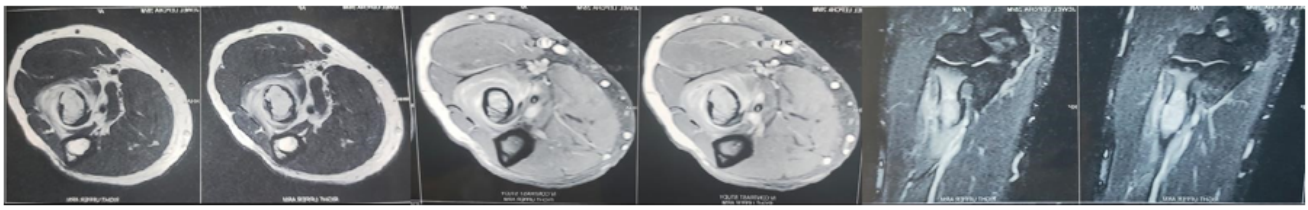

Fig. 3: MRI shows poorly defined slightly expansile intramedullary lesion noted in proximal metaphysis of radius

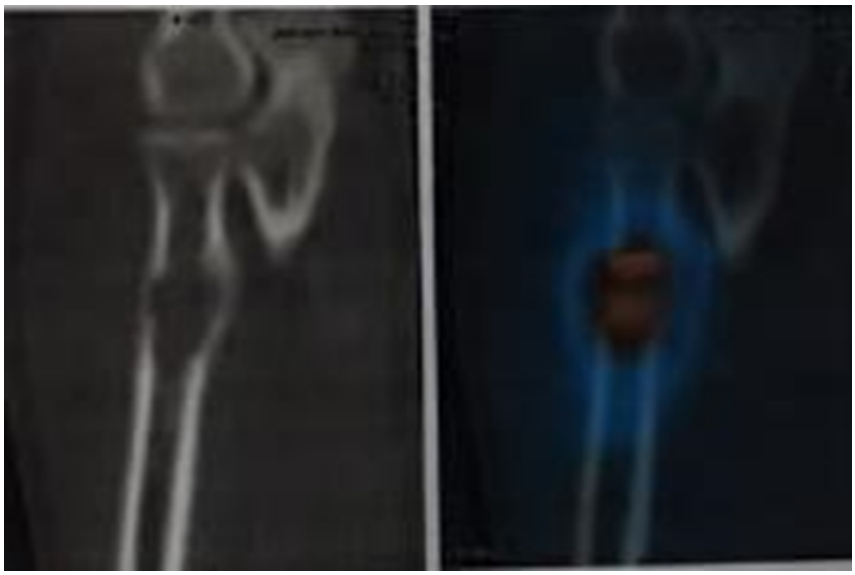

Fig. 4: FDG PET Scan showing increased FDG concentrationin proximal radius

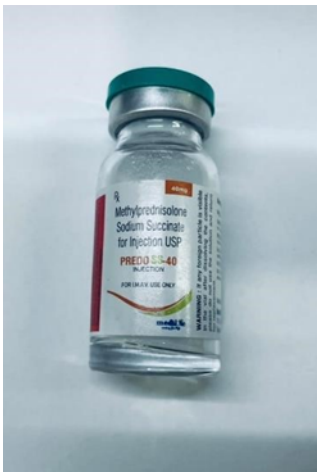

Fig. 5: Methylprednisolo ne 40 mg

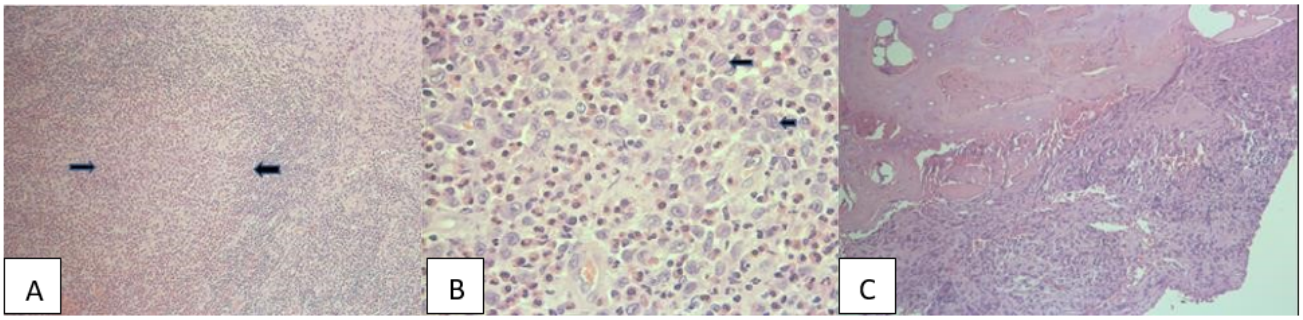

Fig. 6: Histopathology slide **A:** Shows histiocytic cells with oval nuclei, nuclear grooves(arrow) and indistinct eosinophilic cytoplasm admixed with eosinophils; **B:** Shows histiocytic cells with oval nuclei, nuclear grooves(arrow) and indistinct eosinophilic cytoplasm admixed with eosinophils; **C:** shows bony trabeculae focally showing involvement by the neoplasm

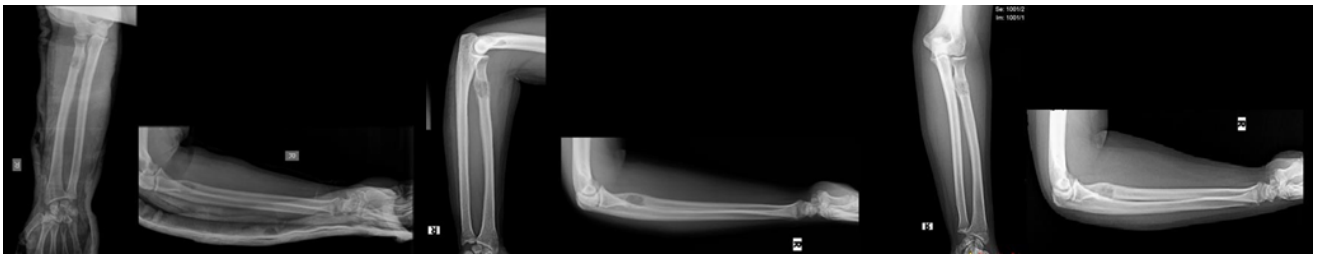

Fig. 7: A and B – Immediate post-operative x-ray, **C and D** – follow up after 1 month, **E-F** – follow up after 2 months

form of LHC. It usually affects children and young adults, predominantly males.[1] The common sites of bony involvement are the skull (34%), spine (15%), ribs (7%), and long bones (15%). However, almost any bone may be affected. In long bones, the diaphysis is most commonly affected (58%) than metaphysis.[2] However, in our case, it was metaphysio-diaphyseal junction. The etiology of LCH is unknown. There is ongoing debate whether the condition is neoplastic or nonneoplastic. Senechal et al. proposed that enhanced cell survival than the uncontrolled LC proliferation, is likely to play a major role in the maintenance and dissemination of this tumors.[3] The immune response against these LCs is inhibited by accumulation of T regulator cells, which lie in contact with immature LC. This leads to better survival and granuloma maintenance and dissemination.[3] Increased understanding of the pathogenesis of this disease is important for better management. Patients usually have a history of pain and swelling over bony lesions and often localized Tenderness[4] similar to our case.

Patients with EG are categorized into two groups - disease restricted to either bone or soft tissue or a combination of both. LCH can have a benign course or can present with diffuse disease.[1] LCH can be divided into three clinicopathological entities - acute unifocal disseminated LCH (Letterer- Side disease) and multifocal uni-system LCH (EG), multisystem LCH (Hand Schuller Christian disease).[5]

Solitary EG of bone can present dilemmas of both diagnosis and treatment.[4] Laboratory findings are mostly non-specific except for a moderate rise in erythrocyte sedimentation rate. Skeleton involvement is best evaluated with plain radiographs.

The radiographic appearance alters with the phase of the disease and site of involvement. In general, the acutephase or early-stage lesions appear rapidly, are lytic and aggressive lesion with poorly defined margins. It is difficult to differentiate from malignancy, such as Ewing sarcoma or infection.[5] LCH primarily presents as a small area of medullary destruction in the long bones. This may either progress to cause endosteal scalloping, cortical erosion, periosteal reaction (single layered or laminated), and soft-tissue production or regress to a well -defined lesion with sclerotic margins. Chronic-phase lesions and lesions in flat bones are well defined. Early spontaneous healing is suggested by a reactive sclerosis around the lesion and it favours good prognosis.[5] Bone scintigraphy has poor reliability.[6] MRI is appropriate for demonstrating any bone marrow involvement or accompanying soft tissue mass in EG of bone. Though MRI is highly sensitive, the findings remain non-specific.[3]

Biopsy remains the key to diagnosis in EG since clinical and radiological findings are not specific enough for diagnosis.[3] Histopathological EG is characterized by clonal proliferation of Langerhans type histiocytes, which is pathognomonic. These contain Birbeck granules (electron

microscopic feature) whose role is yet unidentified. While Eosinophils, lymphocytes, fibroblasts, foam cells are not diagnostic. Morphologically the important feature is the identification of Langerhans cells with characteristic grooved, folded or indented nuclei in the appropriate milieu that includes variable numbers of eosinophils & histiocytes including multinucleated forms. An ultrastructural hallmark of LCH is the characteristics tennis racket-shaped Birbeck granules seen in the cytoplasm. Immunohistochemically LCH is positive for CD1a and s100 protein, Langerin (CD207), MCH class II, PNA (peanut agglutinin). CD1a is diagnostic.[7]

Differential diagnoses are osteomyelitis, lymphoma, chondroblastoma, Ewings sarcoma, metastatic carcinoma. Osteomyelitis is the most important differential diagnosis particularly in our country where it is common. In case of lymphoma, presence of eosinophilic and histiocytes can mimic hodgkins lymphoma but identification of Reed Sternberg cell should be mandatory for diagnosis of the disease. Chondroblastoma there will be bi-morphic population of chondroblasts and osteoclastic giant cell. In Ewing sarcoma there will be characteristic small round cell morphology makes it easily distinguishable from LCH. Metastatic carcinoma especially renal cell carcinoma exhibits a clustered cell morphology and epithelial feature.

Prognostic factors include the extent of disease and age at presentation. Children less than 2 years with involvement of vital organ have a poorer prognosis than those with the localized form of disease and older than 2 years at presentation. Overall, the patients with LCH have a variable prognosis and somewhat unpredictable.[5]

Treatment of EG is controversial with different therapeutic approaches claiming effectiveness. A minimally invasive form of treatment with a low rate of complications is desirable since the clinical course of the disease is usually benign.[4] Spontaneous remission is usually seen in solitary EG of bone.[3] Symptomatic and surgically accessible solitary EG are managed by biopsy, curettage and bone grafting if required. A single curettage usually helps in healing. Scaglietti et al[8] described that corticosteroids injections will help in immediate pain relief and causes healing response within 2 months after injection. Irradiation is rarely used because of late latent neoplasms. The use of chemotherapy and oral corticosteroids alone or in combination is indicated in systemic disease but rarely in a solitary lesion due to the toxic and oncogenic risk.[3]

4. Conclusion

Eosinophilic granuloma is always a diagnostic challenge for the surgeon. Clinical findings and investigations are usually non-specific. Histopathology and immunohistochemistry still remain as the mainstay in diagnosis of EG. Curettage with intralesional injection of corticosteroid is desirable and helped in resolution of the tumor and enhance new bone formation. We conclude by rule of thumb, suspect it, lest you will miss it.

5. Conflicts of Interest

Declaration by each author. There are no conflicts of interest associated with this publication and there has been no significant financial support for this work thatcould have influenced its outcome.

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