Unifocal Bony Lesion Of Langerhans Cell Histiocytosis Of Tibia In A Child Mimicking Osteomyelitis : A Diagnostic Challenge

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Abstracts: Langerhans cell histiocytosis (LCH) is a rare proliferative histiocytic disorder of unknown etiopathogenesis. The clinical presentations range from unifocal or multifocal bony lesions to disseminated form of the disease with multiorgan involvement. The unifocal bony lesion (Solitary eosinophilic granuloma) carries a good prognosis. We report such a case of unifocal bony lesion of LCH involving tibia in a 8 years old female child. The clinical and radiological manifestations were non specific, enlightening the suspicion of osteomyelitis. A curettage excision biopsy was performed which on microscopy revealed sheets of eosinophils in milieu of Langerhans cells, giant cells, lymphocytes and plasma cells. Langerhans cells showed strong immunoreactivity for S-100 and CD1a antigen thus establishing the diagnosis of LCH. LCH of long bones may be a rare entity but it must be kept in mind as a differential diagnosis whenever a child presents with features of osteomyelitis.[Singh P et al NJIRM 2012; 3(5) : 147-150]

Key words : Langerhans cell histiocytosis, Osteomyelitis, Tibia.

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Introduction: Langerhans cell Histiocytosis (LCH) previously known as histiocytosis X, encompasses three classic clinical entities, which are now considered to be variations of the same disease: Eosinophilic granuloma (localized lesions in bones); Hand-Schüller-Christian disease (multiple organ involvement with the classic triad of skull defects, diabetes insipidus , and exophthalmos); and Letterer-Siwe disease (visceral lesions involving multiple organs). [1]

A fourth clinical entity termed congenital self-healing reticulohistiocytosis (Hashimoto- Pritzker variant) has been described in which skin lesions are present at birth, accompanied in rare cases by systemic findings, and with complete spontaneous involution within 2 to 3 months . [2] The localised LCH (the monostatic or multifocal eosinophilic granuloma) is the least severe form of the disease characterized by solitary or multiple skeletal lesions without extra-skeletal involvement. It commonly affects children and young adults with overall good prognosis. Eosinophilic granuloma has a predilection for flat bones with one third of the lesions occurring in long bones where clinically and radiologically may mimic primary and metastatic bone tumors and even osteomyelitis. The clinical findings and imaging studies are insufficient to make a conclusive diagnosis.[3]

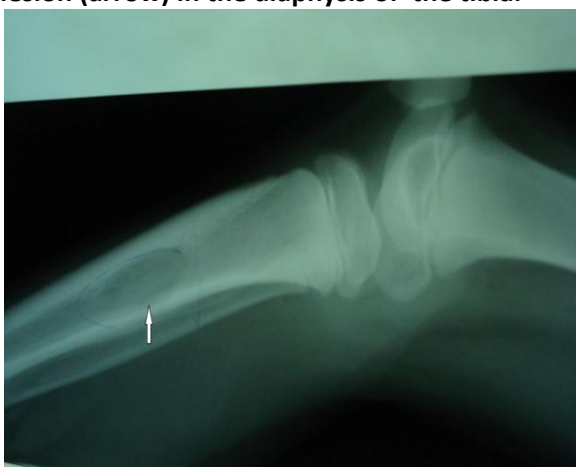
We present a case of 8 years old girl who presented with clinical and radiological features of osteomyelitis but subsequent biopsy of the lesion supplemented by immmunohistochemistry established the diagnosis of Langerhans cell Histiocytosis.

Case report:Eight years old female child reported to our institute with pain in the anteromedial aspect of upper part of left leg of one month duration following a trivial trauma while playing in the school. She developed redness at the site of injury followed by low grade fever. Pain and fever used to subside after taking symptomatic treatment. There was no past or family history of tuberculosis and also no loss of weight was noticed.

On examination she was found to be of moderate build and nutrition. There was no lymphadenopathy ,pallor or hepatosplenomegaly. Systemic examination was remarkably normal. On local examination there was redness and induration in the region of upper half of (Lt) tibia with marked tenderness. Regional lymph nodes were not enlarged. Movements of knee joint were painful. Results of routine investigations were within normal limits, except raised erythrocyte sedimentation rate (ESR) of 32 mm in 1st hour. Serum electrophoresis revealed no M band. Chest radiograph was normal. Plain radiograph of the left leg revealed an osteolytic lesion involving diaphysis of tibia (Figure.1). She was clinically diagnosed as a case of subacute osteomyelitis and

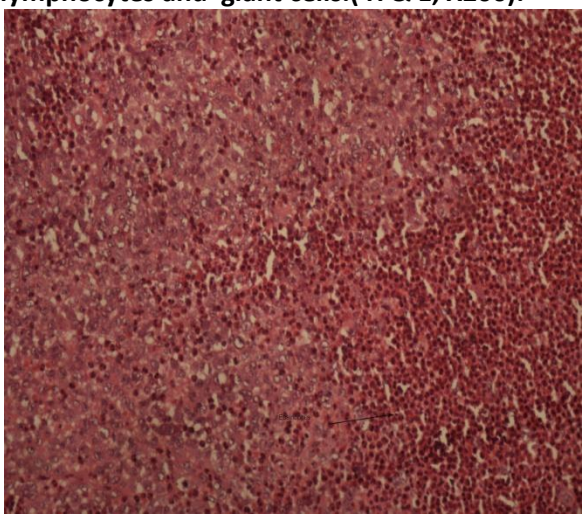
was put on conservative treatment. Since there was no significant improvement a diagnostic open biopsy with curettage of the lytic lesion was performed which revealed grayish white friable fragments resembling granulation tissue.

Figure.1. Plain radiograph shows a lytic lesion (arrow) in the diaphysis of the tibia.



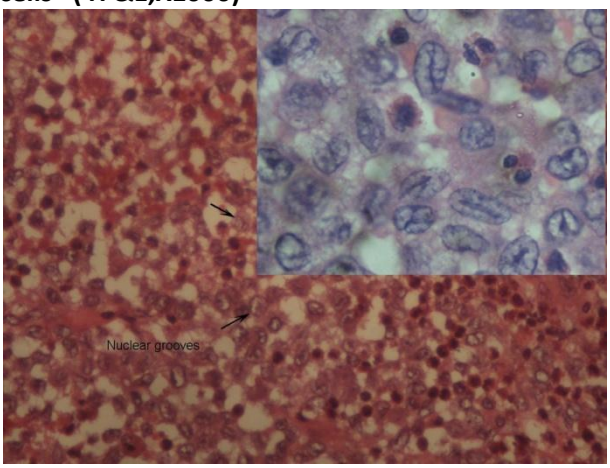
Pathology: Histological examination of curetting showed polymorphous population of cells comprising of numerous eosinophils, lymphocytes, Langerhans cells and multinucleated giant cells (Figure, 2).

Figure. 2. Photomicrograph showing mixed population of histiocytoid cells, eosinophils, lymphocytes and giant cells.(H & E, X200).



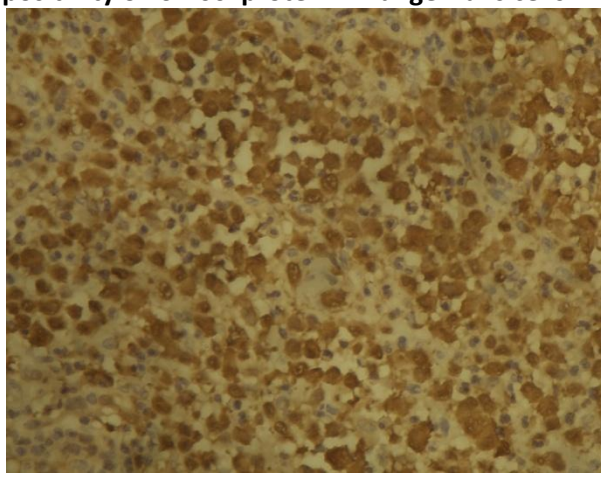
A high power view showed Langerhans cells with moderate to abundant eosinophilic cytoplasm and folded,indented, grooved nuclei with a `coffee-bean` appearance (Figure.3, Inset.).

Figure. 3. Higher magnification. Langerhans cells with nuclear grooves. (H&E, X400), Inset.A typical `coffee- bean` appearance of Lagerhans cells (H &E,X1000)



Immunohistochemical stains revealed strong positivity of Langerhans cells for S-100 protein (Figure.4) and CD1a (Figure.5). Further skeletal survey did not reveal any other bony lesion. The child recovered completely after curettage of the lesion and no recurrence was noticed**.**

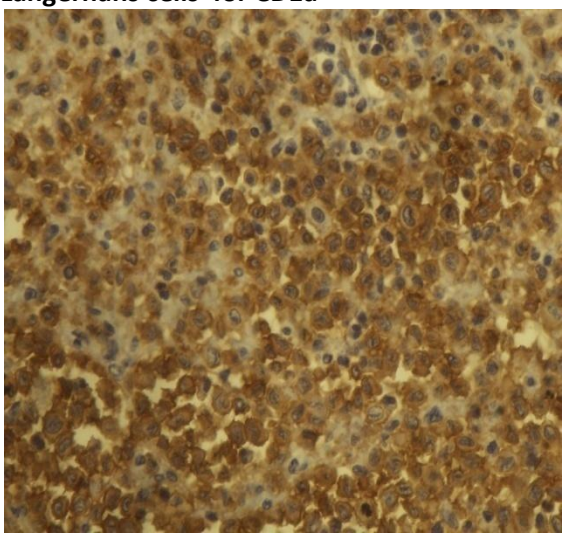
Figure. 4 Immunohistochemical stain: Strong positivity of S-100 protein in Langerhans cells.



Discussion : LCH is a proliferative histiocytic disorder which affects children and young adults with incidence of about five per million. [4] The median age at diagnosis is 3.8 years (2 months to

13.7years) with 69% of the children being afflicted with single systemic disease with a predilection for males (male : female ratio 3.7:1).[5] In contrast to above data our patient was a 8 years old female child .

Figure. 5 Strong membrane positivity of Langerhans cells for CD1a



Solitary eosinophilic granuloma accounts for the majority of LCH patients usually involving bone in 60 to 80% of cases (Unifocal LCH) and less commonly the lymph node, skin or lungs. [6] The usual sites of bony involvement are the skull (34%), spine (15%), ribs (7%) and long bones (15%).The diaphysis is most commonly affected site in the long bones (58%), as seen in our case followed by metaphysis. [7] Clinically the patient may present with persistent pain, localized swelling and less commonly a pathological fracture. The clinical and radiological findings are not specific for the disease.Laboratory findings may show mildly elevated ESR. Radiographic appearance is variable among different patients with different locations and phase of the disease.

In acute phase the lesions of LCH have an aggressive permeative and lytic appearance with poorly defined margins and may resemble variety of other bony lesions such as tuberculous osteomyelitis, chondroblastoma ,Ewing's sarcoma,lymphoma and metastatic renal cell carcinoma. [8] As the lesion regresses it is better delineated and is surrounded by a reactive sclerosis. [9] In our reported case there was a diaphyseal involvement by an osteolytic lesion. A possibility of osteomyelitis especially of tuberculous nature is most likely differential diagnosis of a unifocal bone lesion, when accompanied by soft tissue involvement ; particularly in countries like India where tuberculosis is endemic.

With absence of pathognomonic signs and specific laboratory and radiological investigations the diagnosis of LCH can only be established by biopsy and histopathological examination .The histological findings characteristically reveal Langerhans cells in a milieu of histiocytes , multinucleated giant cells with variable number of eosinophils ,lymphocytes and neutrophils. Langerhans cells characteristically reveal folded, indented,grooved nuclei with `coffee-bean` appearance. Immunohistochemically these are identified by the presence of the antigens S-100 , CD1a and Langerin. Eosinophilic infiltrate may consist of sheet like masses of cells. LCH basically is not a malignant disease.The CD1a + Langerhans cells overexpress inflammatory chemokines which are important for T cell recruitment. Release of cytokines like interleukins,tumor necrosis factor-a ,interferon and colony stimulating factor facilitate in bone resorption , necrosis and fibrosis in LCH. [10]

Treatment modalities for LCH in unifocal bone lesion are variable according to location, extension and number of lesions. Usually these patients have good prognosis with 100% survival. Surgical curettage with removal of entire lesion may suffice. Concurrently filling of defect after curettage by PMMA (Poly-methyl-methacrylate) cement which produces local exothermic reaction has added advantage. Patients with multifocal involvement and systemic disease will need radiotherapy and systemic chemotherapy.[9] Our patient responded well to local curettage because of a small unifocal lesion and a consequent two years follow up did not reveal any recurrence.

Conclusion: Unifocal bony lesion of LCH (solitary eosinophilic granuloma) is a rare disease of

children and young adults and could mimic osteomyelitis clinically and radiologically. Final diagnosis is established by HPE supplemented by immunohistochemistry. Therefore in children with bone pains this entity must be kept in mind as a differential diagnosis.

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