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# Langerhans cell histiocytosis of the skull: Case report of a rare bone tumour

Rashmi Raveendran, Ganthimathy Sekhar*, Jayaganesh P

Department of Pathology, Saveetha Medical College, Saveetha Nagar, Thanadalam, Chennai - 602105 Tamil Nadu, India

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ABSTRACT

Langerhans cell Histiocytosis (LCH) constitutes a triad of diseases, which is clinically classified as unifocal-unisystem (Eosinophilic granuloma), multifocal-unisystem and multifocal-multisystem. The unifying feature of this group is the infiltration of the lesion by antigen-presenting cells of the accessory immune system known as the Langerhans cell. Eosinophilic granuloma is the most common and benign entity of the three, seen in children and affects the bones and less often, the lungs. In this report, we present this interesting case of Eosinophilic granuloma of the skull in a 2 year old girl, who presented with a painless scalp swelling of 2 weeks duration to our tertiary care centre and was diagnosed by histopathology and immunohistochemistry.

* Corresponding Author

Name: Dr. Ganthimathy Sekhar
Email: kanthisekhar1960@gmail.com

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## INTRODUCTION

Eosinophilic Granuloma is the most common benign lesion of a triad of conditions termed as Langerhans cell histiocytosis (LCH). The unifying feature of this group is the infiltration of the lesion by monocytic antigen-presenting cells of the accessory immune system known as the Langerhans cell. It is morphologically characterised by a distinct longitudinal, nuclear grooving. LCH is broadly divided into three types based on the extent of organ involvement which are unifocal-unisystem (Eosinophilic granuloma), multifocal-unisystem and multifocal-multisystem (Azouz EM *et al.,* 2005). Eosinophilic granuloma is one of the rarest bone tumours, representing less than 1% of all bone tumours. In 90% of the reported cases, it appears in children under the age of ten. There is a predilection to males in the ratio Approximately 10% of patients with unifocal eosinophilic granuloma of bone will develop the multifocal and extraosseous disease. Lung involvement usually occurs in an older age group of 2 : 1 (Ando A *et al.,* 2008).

(20–40 years) (Egeler RM *et al.,* 2010) and has a strong association with smoking in 20% of the patients with EG (Yang JT *et al.,* 1993; Kaul R *et al.,* 2009). Diffuse pulmonary infiltrates may be a manifestation of a covert osseous EG. The most common sites are skull, mandible, spine, ribs, humerus and femur (Azouz EM *et al.,* 2005).

**CASE REPORT**

A 2-year old girl was brought to the department of Paediatrics with complaints of swelling in the left side of the scalp for 2 weeks. The swelling was sudden in onset, progressively increasing in size and not associated with pain or discharge. There was no history of fever or trauma. Birth history and developmental history were normal. On local examination, swelling measured 3.0X3.0cms, over the left parietal region. On palpation, it was cystic, fluctuant, not warm, nor tender.

The child was clinically diagnosed as a case of dermoid cyst of the scalp. X-ray imaging of the skull showed an osteolytic lesion in the left parietal bone (Fig.1). A destructive lesion of left parietal bone with intracranial extension, extracranial soft tissue indenting the adjacent brain parenchyma with adjacent dural enhancement and no intracranial

lesions were noted on MRI brain (Fig.2). Radiological features were suggestive of malignancy. The child was transferred to neurosurgery and excision biopsy was done under general anaesthesia. Intra-op findings showed a soft, fleshy, moderately vascular tumour in the left frontal and left parietal extradural scalp with base towards superficial temporal artery, firmly adherent to the dura. Differential diagnoses included Eosinophilic Granuloma, metastatic lesions and Fibrous dysplasia.

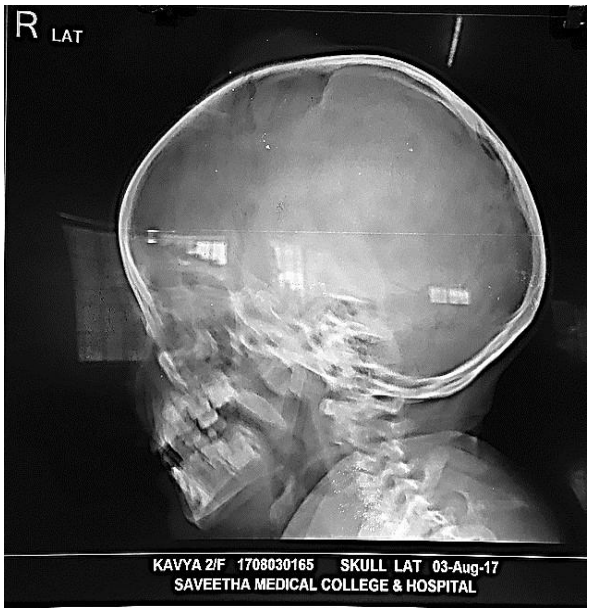


**Figure 1: Lateral X-ray of the skull shows an osteolytic lesion on the parietal bone.**

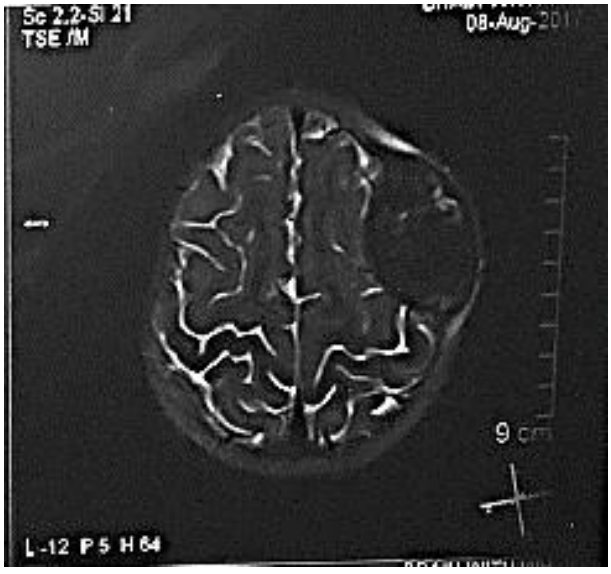


**Figure 2: MRI brain shows a hypoechoic lesion indenting brain parenchyma.**

Grossly, we received two containers. Multiple greys, soft brown tissue from frontal biopsy, on aggregate measuring 8.5×6.5×2cms from container A was partially embedded. A single grey, soft brown tissue from parietal biopsy measuring 2×2×0.5cms from container B was also partially embedded.

Microscopically, sections showed a lesion composed of sheets of round to oval cells having abundant eosinophilic cytoplasm and oval nuclei with distinct longitudinal grooves. Eosinophils, foam cells and multinucleated giant cells were also present amidst areas of fibrosis (Fig.3). No evidence of mitosis or necrosis noted. Immunohistochemistry showed strong positivity for S100 (Fig.4), CD1a (Fig.5) and positivity for macrophage marker CD68. Thus, we diagnosed this interesting case of scalp swelling in a 2 year old as a case of solitary Eosinophilic Granuloma.

**Figure 3: H&E stained sections (40X) show Langerhans cells with scattered eosinophils and giant cells.**

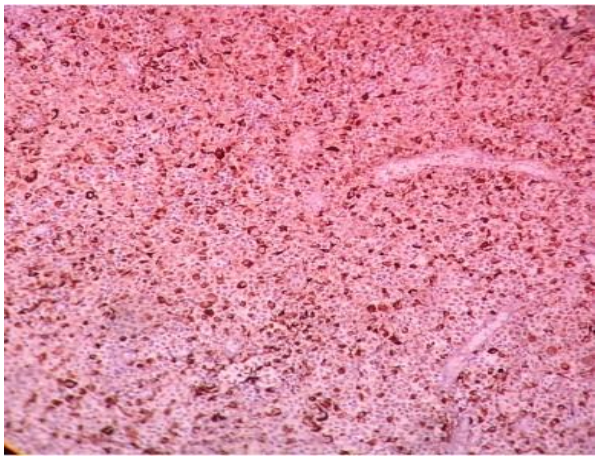

**Figure 4: Immunohistochemistry (10X): S100 stained sections show mild positivity.**

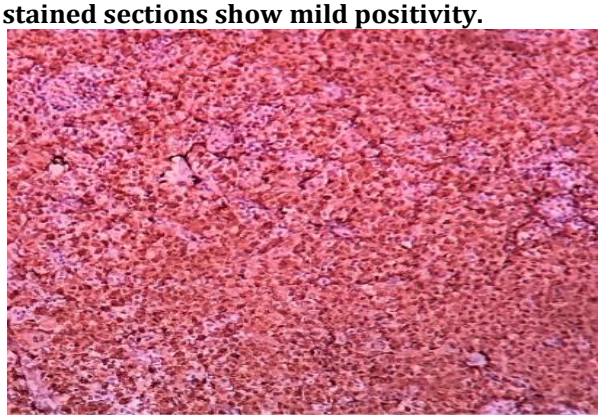

**Figure 5: Immunohistochemistry (10X): CD1a stained sections show diffuse positivity.**

**DISCUSSION**

Langerhans cell histiocytosis (LCH)is a complex disease entity comprised of three distinct clinical syndromes that demonstrate indistinguishable histology. It is classified under Class I of WHO classification of Histiocytosis, under dendritic cell disorders (Satter EK, High WA 2008). The origin and nature of LCH have remained controversial, although scientists have discovered a number of mutations in its pathogenesis, most commonly the Valine to Glutamate substitution at residue 600 in BRAF gene (Badalian-Very *et al.,* 2010; Grana N 2014). Recently, MAP2K1 gene mutations have been known to occur in about 75% of patients, especially in BRAF-negative cases (Brown, N.A *et al.,* 2014). The hallmark of LCH is the abnormal monoclonal proliferation of a unique type of dendritic cell in the monocyte-macrophage cell line known as the Langerhans cell, (Somach SC 2016) named after medical student Paul Langerhans who first described it in 1868 (Fernandes L *et al.,* 2015). Morphologically, Langerhans cell can be identified by the oval, indented and longitudinally grooved nuclei with finely dispersed chromatin, single nucleolus and abundant, eosinophilic cytoplasm. Characteristic plasma membrane invaginations are known as 'Birbeck's Granules' that appear as rod-like structures with a dilated ends or "tennis rackets", are observed in the cytoplasm of the Langerhans cell under electron microscopy. Other cells like eosinophils, neutrophils, foamy cells and giant cells are present in variable proportions accompanied by areas of fibrosis. Important differential diagnoses include another histiocytosis such as Rosai-Dorfman disease and Erdheim-Chester disease, Kimura's disease, cat-scratch disease, parasitic infections and some forms of malignant lymphomas. Diagnostic immunohistochemical (IHC) markers are S-100 protein, CD1a, CD207 (langerin).LCH can be divided clinically into three major categories based on type and extent of organ involvement. Unisystem lesions are traditionally termed as Eosinophilic granuloma (EG), introduced by Lichtenstein and Jaffe in 1940. It can be monostotic (unifocal) or polyostotic (multifocal). Solitary EGis the most common and self-limiting entity of the Langerhans cell Histiocytosis. Primarily affects children and young adults, particularly males. It usually involves the bone, and to a lesser extent, the lungs, lymph nodes or skin (Jain A *et al.,* 2008). Most common sites in the bones are skull, mandible, humerus, femur, and ribs in descending frequency. The spine is involved less frequently. Almost all bones can be affected with the possible exception of hands and feet. Clinically, they may be asymptomatic or cause pain and swelling as they expand. Extension into the medullary cavity may lead to pathological fractures (Kaul R *et al.,* 2009). Radiologically, they present as an osteolytic, 'punched out' lesion with reactive sclerosis in the metaphysis of long bones. Endosteal scalloping, cortical thinning, intracortical tunnelling and widening of the medullary cavity are other common features. A less common finding is a permeative pattern with or without periosteal reaction. They can be confused with metastatic carcinoma or Ewing sarcoma. Mixed osteolytic and osteosclerotic lesion maybe encountered in chronic lesions in healing. Involvement of mandible may result in imaging of 'floating teeth' within an expansile osteolytic mass. EG may regress spontaneously or can be removed by surgical intervention. Recurrences may develop in the soft tissue after surgery. They are extremely radio-sensitive and can be cured even with small amounts of radiation, especially recurrences (Yang JT *et al.,* 1993). Long-term prognosis is excellent.

Isolated pulmonary lesions are an uncommon phenomenon, frequently associated with smoking in young adults of 20 years of age. Smoking cessation can result in the improvement of respiratory symptoms and the spontaneous resolution of pulmonary LCH (Grana N 2014; Elia D *et al.,* 2015). Multiple bone lesions are defined as development of new osseous lesions within 1-2 years of initial diagnosis and are also termed as polyostotic Eosinophilic granuloma. Physicians need to be aware that additional EG of the bone occurring as long as four years after initial diagnosis, should be interpreted as a localised form (Yang JT *et al.,* 1993). Depending on the location, bony infiltration may result in proptosis, diabetes insipidus, chronic otitis media or a combination of these conditions (Marchand, I *et al.,* 2011). The collective term of the Hand-Schuller-Christian disease has been applied to this variety. It is characterized by a prolonged course, often marked by alternating episodes of recurrences and regressions. Treatment is the same as for solitary bone involvement (Al-Grawi *et al.,* 2018). The eventual outcome is favourable in most cases. Due to its erratic nature, the term is seldom used nowadays.

Multisystem variety of LCH is an acute, aggressive, disseminated disease referred to as Letterer-Siwe disease. It is an autosomal recessive condition with multi-organ involvement, commonly involving the skeletal system, skin and lungs. Frequently affects children less than 2 years who present with seborrhoeic eruptions on trunk and face and pulmonary lesions (Gloster Jr HM *et al.,* 2016). Bad prognostic factors include under 18 months of age at the time of diagnosis, hepatosplenomegaly, anaemia, thrombocytopenia, bone marrow involvement and haemorrhagic skin lesions.

Treatment requires chemotherapy with vinblastine or etoposide. Prognosis is often poor, with 50% chance of 5 year survival (Gadner, H *et al.,* 2013).

## CONCLUSION

Eosinophilic Granuloma is a rare bone tumour, commonly seen in the paediatric age group with a clinically benign course that forms part of a triad of diseases called Langerhans Cell Histiocytosis. It is mandatory for the clinician, the radiologist and the pathologist to consider the various conditions that resemble Eosinophil Granuloma before conclusion and for the pathologist to utilise the newer modalities like immunohistochemistry and electron microscopy for a confirmatory diagnosis.

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