

Orbital Manifestation of Langerhans Cell Histiocytosis in a Child - A Diagnostic Dilemma

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Abstract

Langerhans Cell Histiocytosis (LCH) is a rare and variable disease process that mimics inflammatory and sometimes malignant disease. Diagnosis is challenging as it may simulate abscess, hematoma, acute dacryocystitis and neuroblastoma in young children. We describe here a case of Langerhans cell histiocytosis in a young child, who presented with right superolateral orbital swelling and proptosis. He was initially treated as subcutaneous abscess with antibiotic and partially responded for a brief duration. Subsequently, he was confirmed LCH by radiological imaging and immunohistochemical marking. Thus, clinicians should consider Langerhans cell histiocytosis in their differential diagnosis, particularly in young children with similar presentation.

children younger than 2 to 3 years of age suffer more often from multi-system LCH which harbors a more unfavorable outcome [5].

LCH of the orbit usually presents as an isolated bone lesion with an associated soft tissue mass, although it can also be associated with multifocal or multi systemic disease [6]. It occurs predominantly in the superior or superolateral orbital roof and exhibits other features depending on the location of the Langerhans cell infiltrate such as a visible mass with ptosis and erythematous swelling if located in the anterior orbit. This may be misinterpreted as an infectious process [4]. We present here a case of eosinophilic granuloma, the most common and least morbid form of LCH, initially treated as infection and responded briefly to antibiotics.

Case Report

A 6-month old boy presented with superolateral orbital swelling of the right side, progressively increasing in size for a week duration. The patient also had low grade fever with watery eye. There was no eye redness, discharge or pain. There was no history of trauma, insect bite or other swelling elsewhere.

Physical examination revealed a non-tender, firm, well defined, immobile mass over the superolateral region of the right orbit, measured approximately 3 x 2cm in size. No pus discharge or obvious vessels noted at the mass. His visual acuity were 6/12 with both eyes opened using cardiff test. Both conjunctiva were white. Anterior chamber examination was unremarkable with normal intraocular pressure. Fundus examination revealed pink optic disc, cup to disc ratio 0.2 with normal macula. No retinal mass was observed. Extraocular muscles movement was in full range. The patient was active, with no palpable lymph node or organomegaly detected.

Keywords: Langerhans Cell Histiocytosis; Superolateral Orbital Swelling; Child

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Introduction

Langerhans Cell Histiocytosis (LCH) is an uncommon disease affecting predominantly children and young adults but can be found in any age group [1]. The disorder is characterized by abnormal, clonal proliferation and accumulation of antigen-presenting dendritic cells, the Langerhans cells, associated with immunosurveillance and immune regulation [2]. They may manifest as unisystem (unifocal or multifocal) or multisystem disease, predominantly in children [3, 4]. In particular, small

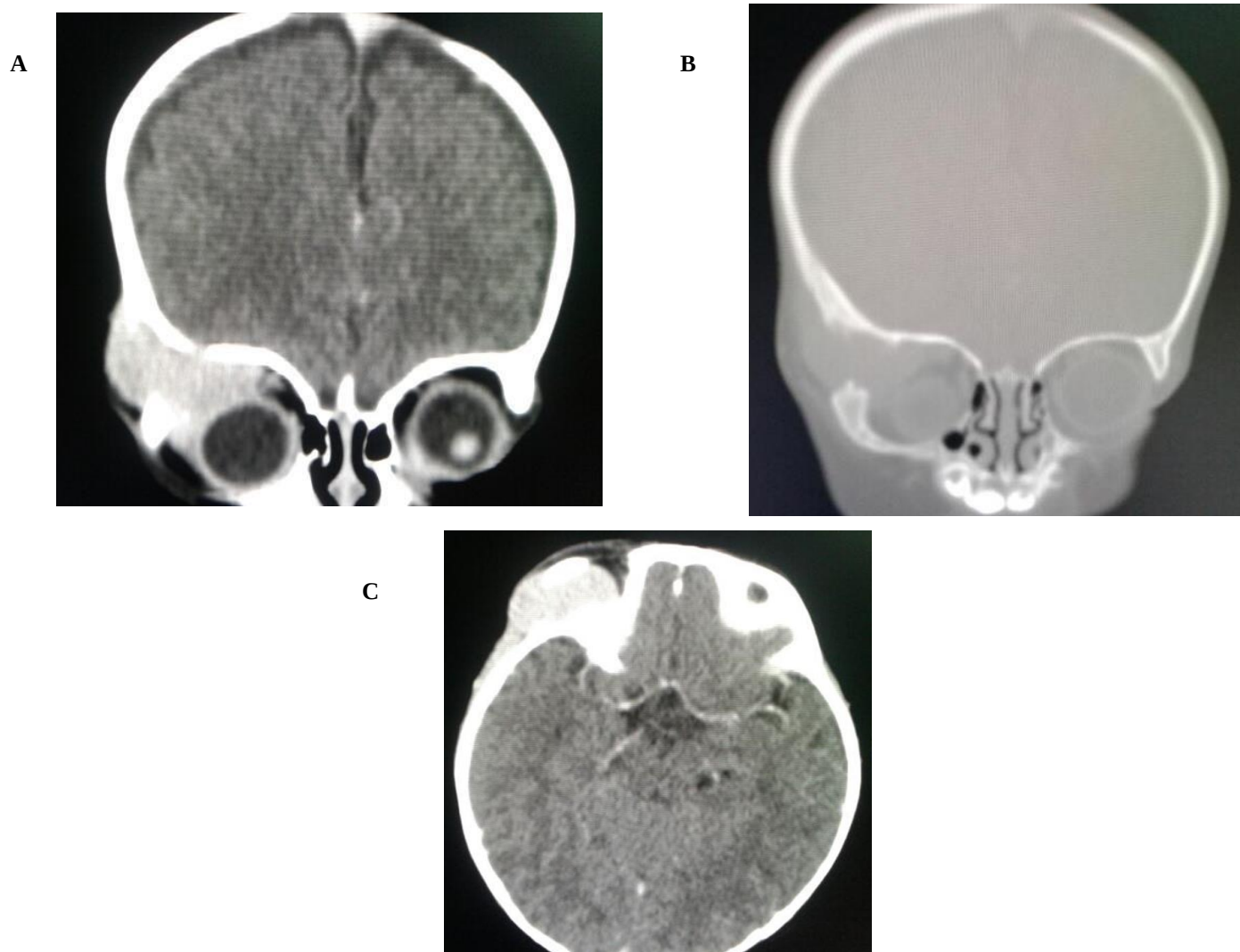
We treated the patient for subcutaneous abscess with syrup cloxacillin 200mg 6 hourly for a week. Although initially the swelling reduced with treatment, upon completion of antibiotic the swelling noted to increase. The patient developed hypotropia and mild non-axial proptosis on day 3 post completion of oral antibiotic (Figure 1A). Systemic examination was unremarkable. Full blood count was normal. He was admitted and started on intravenous Augmentin 200mg 12 hourly.

Computer Tomography (CT) scan brain and orbit showed homogenously enhancing soft tissue lesion occupying the superolateral region of right orbit with lytic lesion of the adjacent bones (Figure 2 A, B and C). These features were suggestive of right superolateral orbital region mass, likely bony in origin. Differential diagnoses included LCH and neuroblastoma metastasis. Ultrasound abdomen showed no significant abnormality.

Figure 1A: Photograph showing superolateral mass of the right orbit with mild proptosis



Figure 2A, 2B (Coronal oblique) and **2C** (axial contrast enhanced CT images of the orbit and brain, in soft tissue and bone setting): showing an enhancing lesion at superotemporal region of right globe with adjacent bony erosion



Excisional biopsy of the mass was performed, and the bulk of the excised mass was submitted for histological examination which revealed Langerhans cell infiltrate with giant cells, eosinophils, lymphocytes and plasma cells. The Langerhans cells were positive for S100 and CD1a. These findings are compatible with LCH.

Postoperatively, he made an uneventful recovery with a good cosmetic result. The swelling and proptosis resolved completely one week post-surgery (Figure 1B). The patient was referred to a pediatric oncologist. However parents refused for further assessment. He was planned for a repeat CT brain and orbit in a month time.

Figure 1B: Photograph showing postoperative appearance



Discussion

LCH or eosinophilic granuloma is the most common form of histiocytosis, with an annual incidence of 4-5 per million [7]. It has a peak incidence of 5 to 10 years of age, and has a male predominance [3]. The skull is affected in more than 50% of cases and approximately 20% occur in the orbital region involving the frontal bone [3, 8]. Orbital LCH typically affect the superolateral anterior orbit with painful, tender, erythematous swelling in the upper eyelid causing eyelid edema and ptosis [9]. Proptosis, ocular motility disturbances, cranial nerve palsies, and papilledema can also occur with more posterior orbital involvement if the lesion extends to lateral orbital wall or sphenoid bone [10-12].

The clinical differential diagnosis need to be considered includes periorbital cellulitis, acute dacryocystitis, ruptured dermoid cyst, hematoma, inflammatory pseudotumor, pilomatrixoma, leukemia, sarcoma, metastatic neuroblastoma, and rhabdomyosarcoma. Some of these lesions may be differentiated from LCH by the absence of lytic bony erosions that are typical for LCH [13]. There have been several reported cases of LCH where children presented with a preseptal cellulitis picture and initially treated with antibiotics [14, 15].

Our patient, a 6-month old boy presented with focal swelling of right superolateral region of the orbit. He was initially treated as subcutaneous abscess and treated with antibiotic. The correct diagnosis of LCH was confounded further in this case, as

in others, by a variable response to antibiotic therapy. Hypotropia and mild proptosis were the alarming signs of further mandatory work-up.

Radiological imaging is advised in those without proper response to antibiotics or those with recurrence as in our case. This including computed tomography and magnetic resonance imaging. It usually reveals well-defined bony lesions with a classic 'punched-out' lytic appearance that are often accompanied by soft tissue involvement in the orbit [16]. Although these findings are nonspecific and can mimic metastatic tumors, they may aid an early diagnosis [11].

Ultimately, the diagnosis is histological and confirmed by CD1a positivity, the presence of Birbeck granules that are pathognomonic for LCH, or both. Adequate specimens may be obtained by fine needle aspiration biopsy or trucut biopsy. Langerhans cells are large cells with abundant eosinophilic cytoplasm. They have round or indented nuclei with marked nuclear folds, which giving them a pink coffee bean appearance on hematoxylin-eosin stain. They contain Birbeck granules, which are rod or racket shaped cytoplasmic structures seen on electron microscopy [3]. Immunohistochemical staining is often positive for S-100 and CD1a. The monoclonal CD1 antibody identifies the CD1 antigen, which is only expressed by the proliferating monoclonal population of Langerhans histiocytes. Lymphocytes and macrophages do not express this antigen or the S-100 protein [15].

In ophthalmic practice, the current trend in the management of isolated eosinophilic granuloma is increasingly becoming minimal intervention including incisional biopsy for diagnosis and curettage [17]. Intralesional injection of methylprednisolone into superficial lesions has been reported to promote early pain relief and osseous healing. Low-dose radiation therapy and systemic chemotherapy too are reported to be effective, however carry significant risks [11, 12]. All patients diagnosed with LCH need follow-up to monitor local recurrence or systemic involvement. Radiographic imaging should be performed every 6 months for at least 1 to 2 years following diagnosis, concentrating on the original site of the lesion and any other suspicious areas [3].

In conclusion, all pediatric patients presenting with orbital swelling and proptosis should undergo a thorough examination, and LCH should be considered in the differential diagnosis although it is rare. It should be kept in mind that early diagnosis of LCH is possible with careful clinical assessment and radiologic imaging to aid for early treatment.

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