

A Rare Case of Orbital Langerhans Cell Histiocytosis in a Child

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Abstract: Orbital Langerhans Cell Histiocytosis (LCH) is a rare disease, generally affects younger age group [1]. Presentation may resemble infective and malignant diseases, hence making diagnosis more challenging. We report a case of a young girl with sudden progressive right upper eyelid mechanical ptosis with superotemporal orbital swelling, which was highly suspicious of orbital childhood malignancy. Surprisingly, tissue biopsy confirmed an Orbital LCH. This 3 year-old Malay girl developed painless, sudden progressive drooping of right upper eyelid of three weeks duration, associated with swelling over superotemporal orbit and acute subconjunctival hemorrhage (SCH) three days prior to presentation. She had no history of fever, recent trauma or surgery prior to that. Her vision was normal. There was right upper eyelid and superotemporal fullness with no overlying inflammation, mild non-axial proptosis and SCH temporal and inferiorly. Fundus and left eye examination was unremarkable. Computed Tomography (CT) of brain and orbit revealed extraconal mass at lateral aspect of the right orbit, eroding adjacent lateral wall of orbit. Magnetic Resonance Imaging (MRI) showed hemorrhagic and enhancing mass at superolateral aspect of right orbit with adjacent bony erosion. Histopathological Examination (HPE) of the incisional biopsied tissues confirmed Orbital LCH. Chemotherapy was started according to the LCH therapy guidelines and she responded with marked improvement clinically and radiologically. Although Orbital LCH is rare, several cases have been reported with almost similar presentation [2,3]. Thus, it may be suspected in a child with orbital mass, but confirmation with tissue biopsy is mandatory.

Keywords: Orbital Langerhans Cell Histiocytosis, Childhood malignancies, orbital mass in a child.

INTRODUCTION

Langerhans Cell Histiocytosis (LCH) is an uncommon disease, characterized by a common histopathologic pattern, which is accumulation of dendritic cells (Langerhans cells) with features similar to epidermal Langerhans cells in various organs [4]. LCH falls into class I diseases in the classification of the Histiocytosis Of Childhood [2].

Newer classifications focus on unifocal or multifocal disease and unisystem or multisystem disease involvement [5]. Several organ systems, including the lungs, bone, skin, pituitary gland, liver, lymph nodes, and thyroid gland, may be involved in LCH, but in patients presenting with orbital disease, usually no other organ systems are involved (unifocal – unisystem disease) [1]. Among those organs that can be affected, more frequently involvement are seen the

skeleton (80% of cases), the skin (33%), and the pituitary (25%) [4]. LCH predominantly affects infants and children but few cases have been reported in adults [1].

Ocular LCH can be both the result of direct infiltration of tissue by the histiocytic cells or secondary effects resulting from infiltration in the surrounding structures [6]. Direct involvement has been known to occur in the orbit, eyelids, epibulbar conjunctiva, cornea, iris, vitreous, choroid, and optic nerve [6,7]. Orbital LCH accounts for less than 1% of all orbital tumors [8] and up to 20% of cases of LCH presented with orbital involvement [6, 9]. Intraocular involvement is rare [9]. From observation, osseous LCH is largely confined to the pediatric population [1].

Patients frequently presented with proptosis, thus, the differential diagnosis may include inflammatory lesions such as orbital cellulitis, idiopathic inflammatory orbital pseudotumor, conjunctivitis, allergic edema, and childhood tumours particularly Rhabdomyosarcoma, neuroblastoma, orbital capillary hemangioma, lymphangioma, Langerhans cell histiocytosis, and others [10]. Orbital LCH is usually characterized by osteolytic bone lesions with sclerotic margins. Involvement of the zygomaticofrontal suture has been thought to be highly characteristic [2]. Majority of the cases reported that, orbital involvement has been centered in the frontal bone, with few reported cases involving the sphenoid bone of the orbit and the ethmoid bone [1,2].

Often, the diagnosis of Orbital LCH is usually lower down the list after more worrying diagnosis have been ruled out due to its benign nature and low prevalence. The overall prognosis for Orbital LCH is excellent and treatment is started based on the pre-treatment clinical evaluation as listed in the treatment guidelines [5]. Here, we discuss a case of a child with sudden progressive right upper eyelid mechanical ptosis, superotemporal orbital swelling and proptosis, which initially was suspected of childhood malignancy. Surprisingly, tissue biopsy confirmed a rare Orbital LCH.

CASE REPORT

A 3 year old previously healthy girl was brought in by her parents with a complaint of painless sudden progressive drooping and swelling of right upper eyelid, associated with swelling at superotemporal aspect of the right orbit of three weeks duration. Three days prior to presentation, parents noted right eye redness that was increasing in severity. There was no history of recent trauma or surgery prior to this. There was absence of fever or any symptoms of infection prior to the onset of swelling.

Her visual acuity in both eyes was 3/3 with Kay Pictures with no afferent pupillary defect. Extraocular motility was normal in all direction of gazes. There was right upper eyelid and superotemporal fullness causing mechanical ptosis that was just covering the visual axis. Mild non-axial proptosis of the right eye was observed, in which the eye appeared hypo and esotropia but not to the extent of causing lagophthalmos. There was presence of SCH over temporal conjunctiva extending towards inferior fornix, which was increasing in severity over few days but no adjacent dilated conjunctival vessels was observed (Figure 1A and 1B). The upper eyelid swelling was firm and non-tender with no overlying inflammation. Fundus assessment and left eye examination were unremarkable.



Fig-1A



Fig-1B

Figure 1A and 1B: Photographs showing the child upon presentation with right upper eyelid and superotemporal fullness, partial ptosis and subconjunctival hemorrhage.

Full blood count and coagulation profile were normal. An urgent CT scan of the brain and orbit showed presence of extraconal mass at lateral aspect of right orbit eroding adjacent roof and lateral wall of the orbit with small intracranial epidural extension (Figure 2A and 2B).



Fig-2A



Fig-2B

Figure 2A and 2B (axial view CT images of the brain and orbit in bone setting): CT scan images showing extraconal mass at lateral aspect of right orbit with adjacent bony erosion.

MRI of the brain and orbit showed a heterogeneously enhancing solid mass in the superolateral aspect of right orbit, extraconal in location and causing compression to the globe. The mass extended laterally through the zygomaticofrontal suture causing widening of the suture and superiorly, it is causing erosion of the floor of anterior cranial fossa. Gradient echo sequence exhibit susceptibility artefact indicating intratumoral hemorrhage (Figure 3A, 3B and 3C).

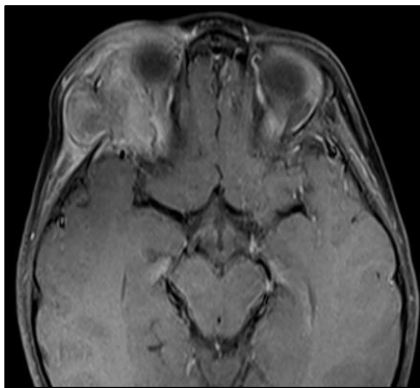


Fig-3A

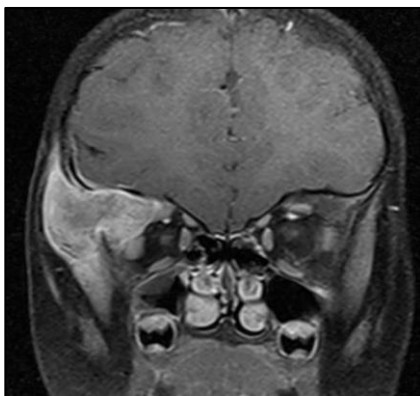


Fig-3B



Fig-3C

Figure 3A and 3B (Axial and coronal view post contrast images): MRI scan images showing heterogenous enhancement of superotemporal extraconal mass compressing on right globe. Figure 3C: Axial gradient echo sequence exhibit susceptibility artefact indicating hemorrhage.

This unfortunate child underwent urgent open incisional biopsy after the MRI scan. HPE of the biopsied tissues showed Langerhans cells that display grooved and irregularly contorted nuclei with delicate chromatin and inconspicuous nucleoli, with presence of eosinophilic cytoplasm. Staining was positive for CD1a, therefore confirmed of Langerhan Cell Histiocytosis (Figure 4A and 4B). No other organs involvement identified. She was subsequently referred to the Paediatric and Paediatric Oncology team for further management.

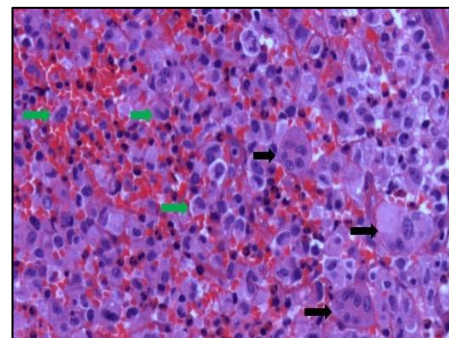


Fig-4A

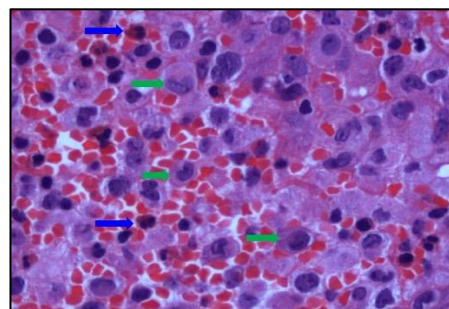


Fig-4B

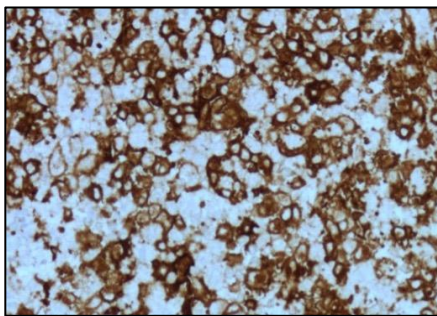


Fig-4C

Figure 4A, 4B and 4C (Histopathologic pictures from the biopsied tissue): The lesional tissue is composed of sheets of Langerhans cells (green arrows) admixed with red blood cells and variable amount of eosinophils (blue arrows). The cells display grooved and irregularly contorted nuclei with delicate chromatin and inconspicuous nucleoli. The cytoplasm is abundant and eosinophilic. Multinucleated giant cells (black arrows) are easily seen in some areas. Figure 4C showed positive immunohistochemical staining for CD1a.

Based on LCH-III Group 3 'localised special site' (Eye and craniofacial) protocol, chemotherapy was commenced, which includes oral Prednisolone and Intravenous Vinblastine for six cycles.

Upon completion of the chemotherapy, there was no more swelling observed or palpable at superotemporal part of the right orbit. Right upper eyelid ptosis and SCH had resolved completely (Figure 5A ad 5B).



Fig-5A



Fig-5B

Figure 5A and 5B: Photographs of the child upon completion of chemotherapy showing resolved right upper eyelid ptosis, superotemporal swelling of the right orbit and subconjunctival hemorrhage.

A repeated MRI was performed upon completion of the 6th cycle of chemotherapy, showed previous right superotemporal mass has markedly reduced in size with residual lesion. No more blooming artifact seen to suggest residual calcification or hemorrhage (Figure 6A and 6B).

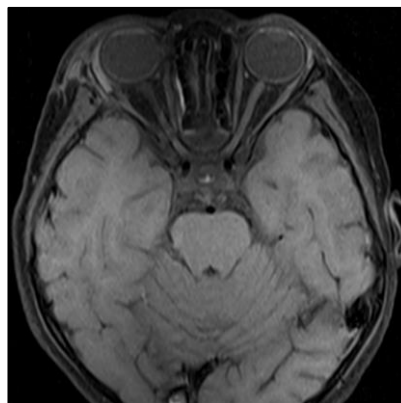


Fig-6A

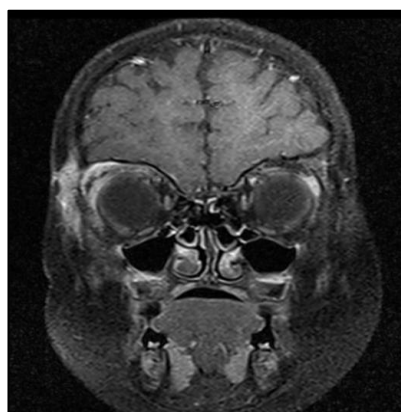


Fig-6B

Figure 6A (Axial view T1 weighted) and 6B (Coronal view): MRI images showing marked reduction of previous mass at superotemporal aspect of right orbit with residual lesion.

Following MRI findings, she was then planned for a further 7 cycles of chemotherapy, which she had completed recently.

DISCUSSION

Patient with Orbital LCH typically presented with painful, tender, and erythematous swelling in the upper eyelid with eyelid edema and ptosis [11]. The swelling is frequently found extending to the superolateral anterior part of the orbit [11]. Although our patient was painless on presentation, the location of swelling, with the aid of radiological imaging made

Orbital LCH as one of the possible differential diagnosis along with other orbital childhood malignancies. Apart from proptosis, they can also present with ocular motility disturbances, cranial nerve palsies, and papilledema due to posterior orbital involvement if the lesion extends to lateral orbital wall or sphenoid bone[12-14]. Subconjunctival hemorrhage is an unusual presentation of Orbital LCH. Its presence in our discussed child upon presentation could be due to the intratumoural hemorrhage as evidence in the radiological imaging and HPE, which showed presence of Langerhans cells admixed with red blood cells. Based on the history and clinical presentation, other childhood malignancies particularly rhabdomyosarcoma and neuroblastoma, have to be excluded as these malignant diseases can also present with painless, non-inflammatory proptosis, occurring over a short period of time, with average age of affected children is less than 10 years [10,15].

Radiological imaging aids in the diagnosis of Orbital LCH. A well-defined bony lesion with classic 'punched-out' lytic appearance that is often accompanied by soft tissue involvement in the orbit [16] was frequently described in CT scan imaging. In our discussed child, bony erosion was seen affecting the lateral orbital wall. Having said that, bony destruction and involvement is also a common radiological feature in rhabdomyosarcoma [17] and neuroblastoma with orbital involvement [18].

Diagnosis of Orbital LCH is mainly based on histological and immunophenotypic examination of biopsied tissue. The main feature is the morphologic identification of the characteristic LCH cells [19], which is moderate eosinophilic cytoplasm and bland nuclei, and eosinophils [20]. Additionally, positive staining of the lesional cells with CD1a and/or Langerin (CD207) is required for definitive diagnosis [21-23]. Since HPE of the tissues taken during incision biopsy of this unfortunate child showed presence of Langerhans cells with positive CD1a staining, the diagnosis of Orbital LCH was confirmed.

Once the diagnosis of LCH is confirmed, further evaluation of general condition of patient is needed in order to determine the therapeutic approach. Pre-treatment clinical evaluation needed to identify organ involvement, risk organs involvement and Central Nervous System (CNS) risk lesions based on the clinical, biological, and radiological criteria as listed in Histiocyte Society Evaluation And Treatment Guidelines, April 2009 [19].

After the pretreatment clinical evaluation had been made on this child, she was classified as 'Special Site – CNS-risk lesions', characterized by involvement of the facial bones or anterior or middle cranial fossa (temporal, sphenoidal, ethmoidal, cygomatic bone, orbital bones). As it carries about three-folds risk for

involvement of central nervous system [19], she was indicated for systemic therapy. A combination of Prednisone and Vinblastine has been proven to be effective treatment with minimal toxicity and is therefore the standard initial therapy for all patients in whom systemic therapy is indicated. Six weeks course of therapy with Vinblastine and Prednisone is suggested for initial treatment for systemic therapy and clinical evaluation at the end of the initial therapy is necessary to determine further treatment course [19] as in this case.

Patients with 'multifocal bone disease' as well as 'special site' and 'CNS-risk' lesions are known to have an excellent prognosis (survival of 100%), but have a high tendency for disease reactivation (30-50%) with permanent consequences [19]. Patients should be followed up after completed treatment to monitor recurrence or systemic involvement based on the LCH treatment guidelines.

CONCLUSION

This report is aimed to share our experience in dealing with a 3 year old child presented with sudden progressive right upper eyelid mechanical ptosis with superotemporal orbital swelling. Eventhough Orbital LCH is a rare disease, several cases have been reported with almost similar presentation [2, 3]. However, in these cases, diagnosis of more sinister conditions such as orbital childhood tumours should be ruled out first before considering Orbital LCH as one of the differential diagnosis and it should be confirmed with early tissue biopsy.

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