

Langerhans Histiocytosis in a Child – Diagnosed by Oral Manifestations

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ABSTRACT

Langerhans Histiocytosis (LCH) is a rare reactive and proliferative disease of histiocytes with unknown etiology, characterized by excessive proliferation of histiocytes called Langerhans cells. It occurs mainly in children but occurrence in adults has also been reported. It manifests as punched out lesions in the skull, maxilla, mandible, sternum and other flat bones and causes rapid resorption of the alveolar bone leading to floating teeth appearance in the radiographs. This disease manifests initially in the oral cavity in most of the cases and can be diagnosed by careful clinical and radiological examination. Here, we present a case of LCH in a child which was diagnosed by a swelling in the mandibular region.

Keywords: Chemotherapy, Dendritic langerhans, Gingival hyperplasia, Histopathology, MRI, Proliferative disorder

CASE REPORT

A 4-year-old female child reported to the Department of Pedodontics and Preventive Dentistry with the chief complaint of pain and swelling in the lower left back region of the mouth since two weeks. Patient's father gave history that she had been complaining of pain and burning sensation in mouth and increased thirst. The family history revealed that the parents had consanguineous marriage. Her medical history was not significant. On physical examination the patient was moderately built, moderately nourished and well oriented to the surrounding. Child was very irritable and unco-operative for clinical examination. On extra oral examination facial asymmetry was obvious, a swelling measuring 5cm x 4cm in the left mandibular region which was diffuse and soft to palpate [Table/Fig-1]. It was not tender and the temperature of the skin over the swelling was normal. An erythematous macule measuring 1cm X 1cm was seen on the upper lip on the right side near the angle of mouth. Patient's right and left submandibular lymph nodes were palpable. Intra oral examination showed gingival recession with 65 and missing 74, 75 with a nodular swelling in the region of 74, 75 [Table/Fig-2].

Patient was sent for radiographic investigation. Orthopantomograph revealed multiple radiolucent lesions in the mandible on the left side

extending from the canine region to the ramus of the mandible. There was marked alveolar bone loss showing floating teeth in 74, 75 region. The permanent teeth buds were seen to be embedded in the radiolucent area of the mandible [Table/Fig-3]. Based on the clinical examination and radiographic findings a provisional diagnosis of Langerhan's Histiocytosis was made. Differential diagnosis included Ewing's sarcoma, Osteomyelitis and Tuberculosis which also produce lytic bone lesions.

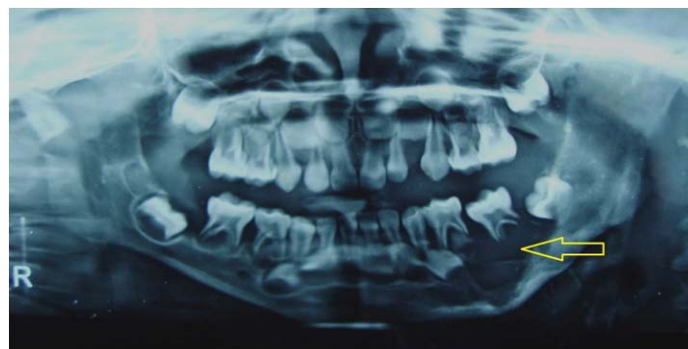
To arrive at a definitive diagnosis fine needle aspiration cytology-(FNAC) of lesion in the mandible was planned under conscious sedation as the patient was very unco-operative. A 21 gauge needle was used to obtain sample from the left mandibular lesion by puncturing the mucosa in the buccal vestibule. The sample was sent for histopathological examination and patient was sent for



[Table/Fig-1]: Extra oral photograph showing mandibular swelling



[Table/Fig-2]: Nodular gingival swelling in relation to unerupted primary molars

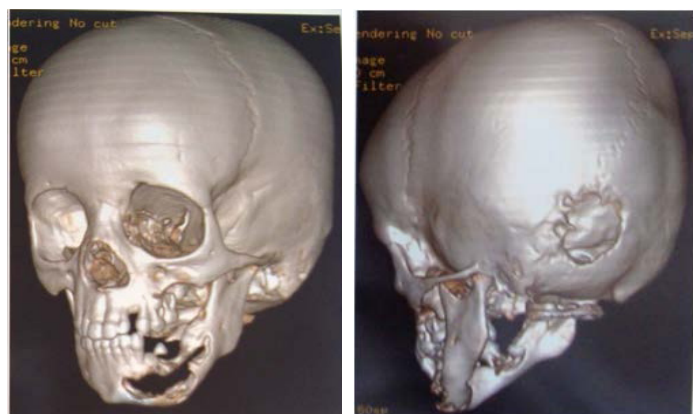


[Table/Fig-3]: OPG showing marked alveolar bone loss with floating teeth appearance in 74, 75 region

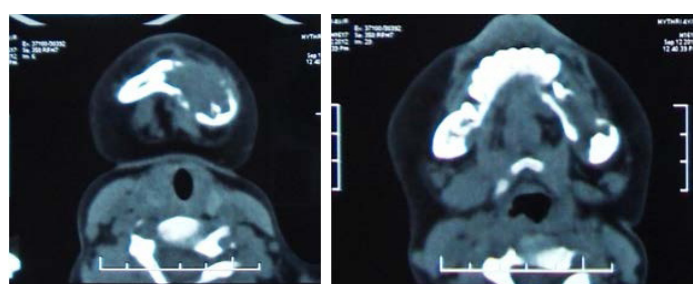
computed tomography (CT) scan for further investigation. Helical – plain and contrast enhanced CT study of craniofacial region revealed an irregular lytic expansile lesion involving the body of the mandible with cortical expansion [Table/Fig-4] and defect in the occipital bone on the left side [Table/Fig-5]. The axial sections of CT showed the lesion measuring about 5cm along in its larger dimension and extending anteriorly from the midline to the ramus of mandible posteriorly [Table/Fig-6,7]. Another similar lytic lesion seen involving the occipital bone on the left side. The bony defect measured about 35mm X 35mm in size.

The histopathological investigation showed a large number of histiocytes with abundant, pale eosinophilic cytoplasm, irregular and elongated nuclei with prominent nuclear grooves and folds, fine chromatin and indistinct nucleoli [Table/Fig-8]. Occasionally multinucleated cells were found. Patient was examined for other lytic lesions in the skeleton apart from the skull but none was found.

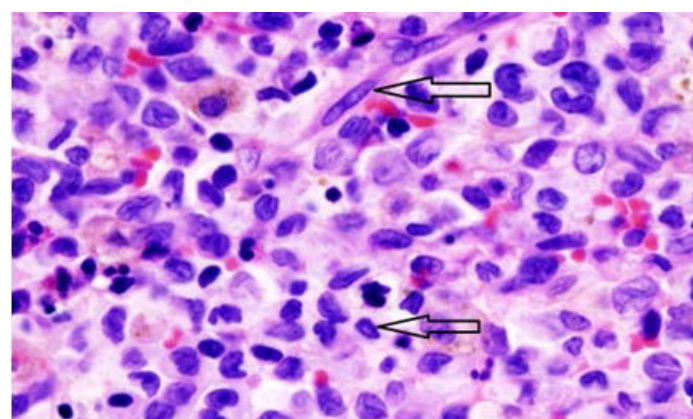
Confirmatory diagnosis of LCH was made based on histopathological report. The patient was referred to Kidwai Memorial Institute of Oncology, Bengaluru for chemotherapy and radiotherapy. Patient was put on chemotherapy with CHOP regime (Cyclophosphamide, Adriamycin, Vincristine and Prednesolone) for three weeks. The



[Table/Fig-4]: CT scan revealing irregular lytic expansile lesion involving the body of the mandible **[Table/Fig-5]:** CT scan showing defect in the occipital bone on the left side



[Table/Fig-6]: Axial section of CT showing cortical expansion in the mandible **[Table/Fig-7]:** Axial section of CT showing lesion extending to the ramus of mandible



[Table/Fig-8]: The histopathological examination showing large number of histiocytes

patient had a complete clinical remission after completion of chemotherapy.

DISCUSSION

Langerhans Histiocytosis (LCH) was previously known as Histiocytosis X where the term Histiocytosis refers to proliferation of histiocytes and X denotes its unknown etiology. Since the histiocytes involved in the disease are phenotypically similar to that of Langerhans' cells found in normal mucosa and skin the new term Langerhans cell Histiocytosis (LCH) is given [1,2]. Histiocytosis X is composed of three clinical variants, classified by Lichtenstein in 1953 depending on the patient's age, onset and distribution of the lesions into Eosinophilic granuloma, Hand- Schüller-Christian disease and Letterer-Siwe disease [3]. According to a recently proposed classification LCH is divided into 2 categories – non malignant disorder and malignant disorder. The non malignant disorders include unifocal and multifocal eosinophilic granuloma while the malignant disorders include Letterer Siwe disease and variants of histiocytic lymphoma. It has now been proposed that loss of heterozygosity on chromosomes 1, 4, 6, 7, 9, 16, 17 and 22, chromosomal instability and elevated expression of oncogene products, such as p53, H-ras and c-myc, causing disrupted cell-cycle regulation are considered to cause LCH [4].

LCH is a rare disease with a peak incidence of 0.5 to 5.4 cases per million persons per year [2]. The disease most commonly affects children from 1 to 15 y of age with the peak incidence from 2 to 4 y of age as in our case. Though a predilection for black patients has been reported, many cases have been reported in Asian population [5]. Then incidence is more common in males compared to females but in our case a girl child reported with the disease. The disease most frequently manifests as osseous lesions, characteristically involving the flat bones of the skull, ribs, pelvis and scapula but in our case lesions in any extra cranial bones were not found. The most common presentation of unifocal disease is a single lytic skull lesion [6] as seen in the occipital bone in the present case. It most commonly manifests in the head and neck region involving the oral cavity. If the underlying maxilla or mandible is destroyed in the course of disease, it manifests as gingival hyperplasia or ulceration. Bone lesions affect the skull and the mandible more than the maxilla. It is characterized by multiple punched out lesions in the skull and radiolucency mainly occurring in the central aspect of the mandible or maxilla. In alveolar lesions the lamina dura and surrounding bone along with the periodontium is destroyed which results in floating teeth appearance and tooth displacement occurs. Non infectious bone loss occurs [7] which is in accordance with our findings. In the present case the patient presented with nodular gingival hyperplasia. The underlying mandible was destroyed and even maxillary involvement could be seen on computerized tomography scan. The skull bones involved were the occipital bone where in a punched out lesion could be seen and a part of the parietal bone was also affected by the disease. These lesions involve the temporal bone most commonly [8]. When involving the mandible, severe alveolar bone resorption producing the appearance of teeth 'floating in space' can be seen as in our case. These clinical and radiographic features led to the diagnosis of Langerhans Cell Histiocytosis. Histological features of LCH include proliferation of large cells with indistinct cell borders. These cells have oval nuclei and abundant cytoplasm. The cells are oftenly arranged in sheets and are admixed with eosinophils, inflammatory cells and multinucleated giant cells [9].

Treatment of LCH usually consists of a tetrad of chemotherapy, radiotherapy, surgery and corticosteroid therapy. In the present case patient was put on chemotherapy with CHOP regime (Cyclophosphamide, Adriamycin, Vincristine and Prednesolone) for three weeks. The patient was under complete clinical

remission after completion of chemotherapy. The prognosis of the disease is unpredictable as it is a rare disease with lot of clinical variability.

CONCLUSION

The present case is unique where in the child was diagnosed to have a systemic problem- LCH by a pediatric dentist. Careful examination of the oral lesions is important to diagnose or to aid in the diagnosis of various systemic conditions. Pediatric dentists play an important role in educating the parents about the disease, the treatment and the possible outcome and also in referring the patients to specialty centers for appropriate treatment.

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