# Langerhans Cell Histiocytosis Involving Maxilla and Mandible

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#### Abstract:

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occurrence of Langerhans cell histiocytosis in both the jaws of a four-year-old boy.

Langerhans cell histiocytosis is a relatively rare unique disease process characterized by an abnormal proliferation of immature dendritic cells usually affecting children and young

adults. Jaws are involved in less than 10% of children with the disease while mandibular

involvement in young children is uncommon and bilateral affection is very rare. The pur-

pose of this report is to describe a unique and very rare case of simultaneous and bilateral

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# INTRODUCTION

Langerhans cell histiocytosis (LCH) is a rare unique disorder of the reticuloendothelial system characterized by an abnormal proliferation of histiocytes and eosinophilic leukocytes [1]. Lichtenstein gave the term histiocytosis X in 1953 to include three clinical varieties including eosinophilic granuloma, Hand-Schüller-Christian, and Letterer-Siwe disease, which shared some common histologic features and clinical findings [2]. In 1973, the term LCH was introduced as an alternative to histiocytosis X [3].

The etiopathogenesis of this disease remains unclear. Some studies suggested that the etiology may be related to immunological abnormalities resulting from a suppressor cell deficiency [1,4]. The proliferation of dendritic cells, similar to langerhans cells of epidermis, in addition to eosinophils, histiocytes, neutrophils and plasma cells is the histological hallmark of LCH which is a very rare pathology

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with reported annual incidence rate of around 5.4 million children per year with a peak incidence between 1 and 4 years of age and affects males more frequently than females [1,5-10]. Clinical Manifestations may range from single or multifocal bone lesions to disseminated oral disease with multi organ involvement [11]. Diagnosis is based on biopsy and clinical prognosis of patients becomes worse with the number of involved organs and organ dysfunctions growing, rapid disease progression and the age of first disease manifestations decreasing [12]. Oral lesions may be the earliest and only manifestations of the disease in majority of the cases [8,10]. Pain and bony swelling are the most commonly presenting complaints. Intraoral findings include gingival necrosis, mucosal ulceration, loosening and premature exfoliation of the teeth, precocious eruption of permanent dentition, ectopic eruption of permanent molars and halitosis [1,7,8]. Radiographic features in jaw lesions include either a



**Fig 1.** Clinical picture showing proliferative gingival growth & precocious eruption of lower right first permanent molar.

unilocular radiolucent appearance with welldemarcated borders in two-third of the cases or poorly defined borders in the remaining cases. Affected teeth present with a "floating in air" appearance due to the destruction of lamina dura [8].

Studies have reported an incidence of 7.9% in the jaws with angle and body of the mandible being the most commonly affected sites [13]. The purpose of this report is to present a rare case of LCH in a four-year-old male child patient simultaneously affecting both the maxilla and the mandible.

# **CASE REPORT**

A four-year-old boy reported to the Department of Pediatric Dentistry, Sri Ramachandra Medical College and Research Institute, with the chief complaint of mobile teeth and painful growth on the right side of both upper and lower jaws over a period of approximately six months. The child appeared generally healthy and moderately built.

Past medical and family history were unremarkable, while Intra oral examinations revealed a proliferative growth in the posterior region of all quadrants, more severe on the right side with Precocious eruption of the first permanent molar in the lower right quadrant (Fig 1). There was generalized mobility of



**Fig 2.** Red inflamed gingiva and exposed apical third of roots evident in right upper first and second primary molars.

teeth and marked gingival recession on the buccal aspect of the right upper and lower first and second primary molars exposing almost the apical third of the roots. Hyperplastic gingiva was evident on both buccal and lingual aspects of these teeth and appeared fiery red (Fig 2). Marked involvement of soft and hard tissues was noticed on right maxillary and mandibular quadrants, whereas left quadrants were less severely involved and no evidence of significant calculus deposits was seen in them. Intra oral periapical radiographs showed a well-defined radiolucent area due to excessive destruction of the alveolar bone producing the appearance of teeth "floating in air" (Fig 3).

Accordingly, possible differential diagnosis consisted of aggressive periodontitis, LCH, and osteomyelitis and the child was referred to the department of pediatric medicine for systemic evaluations, which turned in unremarkable. Oral biopsy was obtained under local anesthesia and sent for histopathological examination.

Sections stained with hematoxylin and eosin showed proliferation of histiocytes with large indented or coffee bean shaped nuclei and abundant indistinct cytoplasm admixed with numerous lymphocytes, plasma cells and focal collection of eosinophils, suggestive of LCH (Fig 4). Facility for electron microscopy and



**Fig 3.** Intraoral periapical radiographs with well defined radiolucent area indicating excessive destruction of alveolar bone in primary molar region.

immunohistochemical staining with S-100 protein was not available.

The histopathological report along with clinical and radiographic findings confirmed the diagnosis of LCH, eosinophilic granuloma variant, involving all the four quadrants. The treatment included extraction of the teeth involved followed by surgical curettage of the lesion.

The patient returned for a follow up visit at the age of 5.7 years. Clinical examinations disclosed completely healed oral lesions indicating a favorable response to therapy and radiological investigations yielded negative results; whilst, alveolar ridges were markedly resorbed and only a few teeth were present in the left quadrants including 21, 62, 63, 31, 73, 32 and 36 (FDI Notation) (Fig 5). Importance of good oral hygiene and regular follow-up visits was explained to the patient and the parents.

#### DISCUSSION

LCH is still a very rare disease in head & neck region, the etiology, and pathogenesis of which remain unclear. Varieties of etiological factors have been proposed including immunologic reactions, viruses, bacteria, and genetic influences [1,4,7,12]. Possible development of LCH under the influence of colony



**Fig 4.** Diffuse infiltration of large pale-staining mononuclear cells, resembling histiocytes. Eosinophils are seen interspersed among histiocytes.

stimulating factor (GM-CSF), interleukin-3, and tumor necrosis factor-alpha have also been suggested and recently, cytogenic studies have proposed the role of tumor suppressor genes (p53), oncogenes (c-myc, h-ras), growth factors, cell surface immunologic markers and apoptotic factors in LCH as well [14].

Unifocal disease involves a single disease system with a single site of involvement and has a good prognosis. Multifocal lesions are less common and skin lesions are quite rare [15]. Eosinophilic granuloma is considered the most common and benign form of LCH and is typically a localized unifocal osteolytic lesion. Severe destruction of the alveolar bone is characteristic of eosinophilic granuloma, which may be easily mistaken for either severe localized periodontitis or periapical infection. These osseous lesions may be wrongly diagnosed as prepubertal periodontitis in children [16].

The case reported here presented signs similar to those of severe periodontal disease, namely gingival bleeding, severe tooth mobility, and alveolar bone loss, both in the maxilla and the mandible.

Osteomyelitis, one of the possible diagnoses, was ruled out in the present case as the history regarding trauma to the jaws and tooth infection was negative.



**Fig 5.** High power view showing histiocytes with deep indented, grooved vesicular nuclei and indictinct cytoplasm & eosinophils.

Gnathic involvement in children with LCH is uncommon and forms less than 10% of the cases [15]. Majority of the cases with mandibular involvement are over 20 years of age while in the present case, the child is a four year old with simultaneous and bilateral involvement of both jaws, which can be considered as a unique and rare occurrence [17,18].

The lesions in LCH may consist of either pure histiocytic infiltrates or mixed histiocytic /eosinophilic lesions. The hallmark is the presence of Langerhans cells through light microscopy. With the absence of pathognomonic signs and specific laboratory findings, the diagnosis of LCH can only be established by biopsy. Histopathological findings in our case included proliferation of histiocytes with characteristic large indented or convoluted nuclei admixed with focal collection of eosinophils and the definitive diagnosis entered by correlation of clinical findings with histological features.

A wide spectrum of treatment modalities have so far been adopted, ranging from surgical curettage to radio and/or chemotherapy [12]. Accessible lesions are best managed by surgical excision or curettage since it promotes healing in most of the cases. In multifocal disease variants associated with dysfunction of vital organs, immunosuppressive treatments have been suggested with recently introduced 2chloro-2-deoxyadenosine (2-CdA) (Cladribine). However, the type and extent of the disease responding to this therapy needs further clarification [19].

Unfortunately, there has been no significant progress in the treatment of LCH for many decades. Monoclonal antibodies directed against CD1a or CD207 (Langerin) may evolve as one of the treatment modality in the future [15]. In our case, only surgical curettage and extraction of involved teeth was performed because of the unifocal involvement. There was neither recurrence nor progression of the initial lesions at the time of follow up after 18 months, which indicates a favourable response to the treatment.

Advances in immune-histochemistry, molecular biology, and radio diagnostic techniques may help in proper understanding of this variable group of disorders [20]. Nevertheless, the potential for the unifocal disease to become multifocal should not be underestimated as the disease can be unpredictable [19] and thereby long-term follow up in such cases becomes mandatory. There is a need for an interdisciplinary approach to treatment in patients with LCH so that an accurate diagnosis can be established and adequate treatment can be provided.

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