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# Langerhan Cell Histiocytosis –Review Of Literature

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## ABSTRACT

**Background:** 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.

**Discussion:** Histiocytosis are rare diseases of great biological variability and a wide range of clinical manifestations. The first manifestations of LCH may occur in the oral cavity may vary from a continuous gingival infection or a dental abscess to necrotizing ulcerating defects or a painful jaw swelling. The criteria for diagnosis of LCH includes identification of the characteristic clinical features histopathological, Immunohistochemical findings. Various treatment modalities has been adopted including wide surgical excision along with radiotherapy, chemotherapy, isolated radiotherapy and use of alkalinizing agents.

**Keywords:** Langerhans Cell Histiocytosis; HistiocytosisX; Osteolysis of Skull.

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## 1. Background

Langerhans cells are an important part of the immune system. They originate in bone marrow, derived from CD 34 $\beta$  stem cells and are transported by blood into the skin, lungs, thymus, lymph nodes and the gastrointestinal tract mucosa(Kilborn *et al.*, 2003). Histiocytic diseases originate from mononuclear histiocyte cells of the macrophage system(Huang and Arceci, 1999). Under normal conditions, histiocytes are a part of the reticuloendothelium system, proliferation of their precursors in bone marrow causes monocyticleukaemia, proliferation of immature histiocytes in tissues is typical for histiocytic medullary reticulosis, and proliferation of mature histiocytes is called as histiocytosis X<sup>[1]</sup>. Langerhans cell histiocytosis (LCH) also known as histiocytosis X, a rare disease characterized by monoclonal proliferation of dendritic-cell related histiocytes (Langerhans cells). These histiocytes have destructive behaviour for the surrounding tissue, which they infiltrate. Among the organs often involved are the skeletal system, skin, thyroid gland and risk organs like liver, lung, and spleen. 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<sup>[2]</sup>. In 1973, the term Langerhans cell histiocytosis was introduced as an alternative to histiocytosis X<sup>[3]</sup>. The etiology of the disease is unknown, although there are some evidences that the disorder is a manifestation of an immunological aberration<sup>[4]</sup>. It is a rare pathology with an incidence of 1 in 560,000, more frequent affecting males than females, with a reported ratio ranging from 1.1:1 to 4:1<sup>[5]</sup>. 75% of the cases occurs in children and young adults under 25 years<sup>[6,7]</sup>.

The disease may involve multiple tissues or remain localized to a single organ, especially lung and bone. Incidence in the jaws is 7.9%, in mandible, the body and angle are the most commonly affected sites<sup>[5]</sup>. Oral lesions may be the earliest and only manifestations of the disease in majority of the cases<sup>[8,9]</sup>. Pain and bony swelling are the most commonly presenting complaints. Intraoral finding includes gingival necrosis, mucosal ulceration, loosening and premature exfoliation of the teeth, precocious eruption of permanent dentition, ectopic eruption of permanent molars and halitosis<sup>[8,10,11]</sup>. Langerhans cell histiocytosis presents a diagnostic challenge because it may manifest with a heterogeneous

spectrum of lesions, ranging from a single bone lesion to multisystem disease. The clinical course and outcome vary, depending on the patient's age, its distribution and extension of the lesions, and also the degree of organ dysfunction present at the time of initial diagnosis.

## 2. Discussion

The aim of this paper is to present an overview on current diagnostic and treatment strategies of LCH in the oral and maxillofacial region. Histiocytoses are rare diseases of great biological variability and a wide range of clinical manifestations. According to the working group of the Histiocyte Society, they are presently divided into dendritic cell disorders, macrophage-related disorders, and malignant histiocytic disorders<sup>[12]</sup>. Current classification of the histiocytic disorders (Table-1).

Dendritic cell disorders	Langerhans cell histiocytosis Secondary dendritic cell processes Juvenile xanthogranuloma Solitary histiocytomas with a dendritic phenotype
Macrophage-related disorder	Primary and secondary hemophagocytic syndromes RosaieDorfman disease Solitary histiocytoma with a macrophage phenotype
Malignant histiocytic disorders	Monocyte-related leukaemias Extramedullarymonocytic tumour Dendritic cell or macrophage-related histiocytic sarcoma

**Table 1.** Current classification of the histiocytic disorders

The first manifestations of LCH may occur in the oral cavity<sup>[13]</sup>. Symptoms that would cause a patient to consult a dentist vary from a continuous gingival infection or a dental abscess to necrotizing ulcerating defects or a painful jaw swelling. Loosening and early exfoliation of (deciduous) teeth should alert the dentist. Sometimes the lesions are asymptomatic. In a series of 50 patients with LCH, 36 per cent had oral involvement and the dentist was the first to see them in 16 per cent of the cases<sup>[14]</sup>. Radiographic features of LCH may be apparent about 6 weeks after the onset of the first symptoms<sup>[15]</sup>. The radiographic features are non-specific

and may resemble, amongst others, odontogenic cysts, periapical lesions, periodontal disease, osteomyelitis or even malignant neoplasms. Involvement of the skull and other flat bones in LCH appear as punched-out, osteolytic lesions. In the maxilla an mandible, the disease may appear as periapical lesions<sup>[15]</sup>, or as advanced periodontal disease with severe loss of alveolar bone<sup>[16]</sup>. In general, LCH in bone, manifests itself as a well-demarcated, round or oval cystic radiolucency with no peripheral bone condensation<sup>[15]</sup>. Tissue for histologic examination should be obtained of an oral lesion suggestive of LCH. If it is possible, some unfixed tissue should be sent rapidly to the pathologist. Such a procedure allows the appropriate processing of the tissue for ultrastructural examination, and the use of immunohistochemistry with monoclonal antibodies such as OKT6 and S-100 protein.

The criteria for diagnosis of LCH includes identification of the characteristic clinical features histopathological, Immunohistochemical findings<sup>[17]</sup>. Bartnick(Bartnick *et al.*, 2002) suggested the following staging for planning the therapy and stating the prognosis of LCH in the maxillofacial region: In case of a solitary lesion, it is characterized as stage I, in case of multiple lesions it is stage II. Stage III is characterized by lesions in the orofacial region with concurrent pathological changes of other organs. Along with this division, it is necessary to consider whether the lesions are found only in the bone, only in the soft tissues, or in the internal organs. Stages I and II when only the bone or only the soft tissues are involved carry the most favorable prognosis(Howarth *et al.*, 1999). In these cases, the treatment is solely surgical. In stage III or when the internal organs are afflicted, combined treatment by chemotherapy, radiotherapy and corticoids is necessary<sup>[11]</sup>. Conventional treatment of LCH is with surgery, radiotherapy, chemotherapy and steroid injections, alone or in combination as indicated by the extent of the disease<sup>[18]</sup>. The treatment of jaw lesions consists mainly of curettage. A recurrence rate of 16 per cent has been reported<sup>[19]</sup> and recurrences have been observed up to 11 years after first treatment<sup>[20]</sup>. Radiotherapy and/or chemotherapy should be reserved for lesions which are inaccessible to surgery and for disseminated visceral involvement. The latter may run an unpredictable course for which treatment is not always effective<sup>[21]</sup>.

### 3. Conclusion

Langerhans cell histiocytosis is a rare disease, There is no evidence that the disease originates in a malignant neoplastic process and no underlying viral or genetic cause has been identified, because of paucity of cases, multicenter, combined case series analysis can be a helping tool for extensive & thorough research to decide whether it is reactionary, inflammatory or malignant. To date, the most likely theory postulates a histopathologically benign, primarily reactive, and probably immunologically mediated process. Role of Maxillofacial surgeon is crucial as numerous reports stress that oral manifestation is among the earliest signs of the disease which draws the patients attention to seek treatment, careful clinical examination, extensive investigation and good diagnostic skill helps to reduce the mortality, thereby increasing survival rate. The progress of the disease, however, is difficult to predict, in some cases it get resolves without any treatment, sometimes it progresses up to a multi-organ failure with fatal consequence. Various treatment modalities has been adopted including wide surgical excision along with radiotherapy, chemotherapy, isolated radiotherapy and use of alkalizing agents.

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