CASE REPORT

# Langerhans Cell Histiocytosis of the Oral Cavity: A Rare Case Report and Diagnostic Dilemma

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## Abstract

Langerhans cell histiocytosis (LCH) is a peculiar derangement regulated by cells of the reticuloendothelial system that may sometimes involve the oral cavity. The purpose of the present report is to suggest a case of LCH manifesting in the cavities of the mouth and how it may present as a diagnostic challenge. A female patient aged 33 reported having complaints of loose teeth, bleeding gums and foul smell from the mouth. Clinical and radiographic examination revealed multiple areas of gingival necrosis, ulcerations and aggressive bone loss. Initially diagnosed as aggressive periodontitis, when the lesions did not resolve, an incisional biopsy along with immunohistochemistry found Langerhans cells, affirmative reciprocation to langerin as well as CD1a, subsequently the female patient was clinically diagnosed as positive for LCH. The patient was given chemotherapy supplemented with Vinca alkaloids coupled with corticosteroids through a systemic route. The patient had multiorgan involvement, but successive retrogradation of lesions lying in the gingival area, along with a marked reduction in overall tooth mobility and harshness of pain perception, observed on the 6-month follow-up.

**Conclusion:** Langerhans cell histiocytosis is a uniquely rare malady that may sometimes manifest in the oral cavity, so precise detection using appropriate clinical diagnostic methods, treatment and none-relapse follow-up are essential for adequate management. Awareness regarding oral manifestations of LCH is indispensable in clinical practice, as it not only aids in timely diagnosis but also encourages early intervention, thereby providing a better prognosis for the affected subject cases.

**Keywords:** Case report, Langerhans cell histiocytosis, Mobile teeth, Rare disease, Systemic involvement.

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## Introduction

Langerhans cell histiocytosis (LCH) is a peculiar disease manifested through the proliferation and clonally expansion of precursors myeloid lineages that evolve in $CD1a^{+}$/$CD\ 207^{+}$ cells in oral cavity lesions that result in a myriad of organ engagement and dysfunction. The disease is evidenced to occur in 0.2–0.5 patient cases over a total count of 100,000 patients per year. The ailment is usually diagnosed in the early stages of life, making it more common in children. Most often, there is a preoccupation with the mandibles, skull, ribs, long bones and vertebra. Anatomically, there is an occurrence of giant cells with multiple nuclei inhabiting necrosis at focal points.[1]

Since it is difficult to classify between Langerhans cells and routine histiocytes by employing basic histological staining techniques. Consequently, immunohistochemistry for the mononuclear histiocytes is required, measuring CD1a, S-100 and langerin (CD207).[2]

The primary clinical signatures of LCH were alterations in the oral cavity, and at certain places, the only afflicted component of the body is the mouth. The most commonly reported complaints were of pain, swelling and tenderness.

There is ulceration and inflammation in the gingival tissue, leading to bone destruction. As the lesions progress, they cause peculiar punched-out erosions on the gingiva with floating teeth.[3] Once the diagnosis is confirmed by histo-chemistry, full body tests involving serum and urine analysis along with radiographs to check the extent of other bone or organ involvement are required.

When examined in histological sections, LCH is represented by the progression of sizable cells with enormous cytoplasmic material, vague cellular perimeters and characteristically shaped reinforms to ovate nuclei. They are extremely prevalent and stacked in the form of sheets, amalgamed with distinct scores of inflammatory cells and eosinophils.

In children, the disease presents as a trilogy of clinical manifestations, including osteo-lytic lesions found in the cranium, exophthalmos and diabetes insipidus.[4]

## Case Description

A female patient subject, having 33 years of age, consulted the department of oral and maxillofacial surgery with the primary

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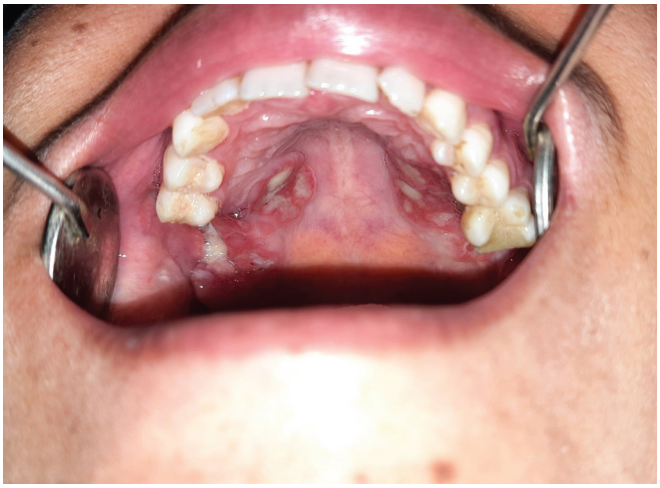

**Fig. 1:** Granulomatous erosions on the posterior hard palate

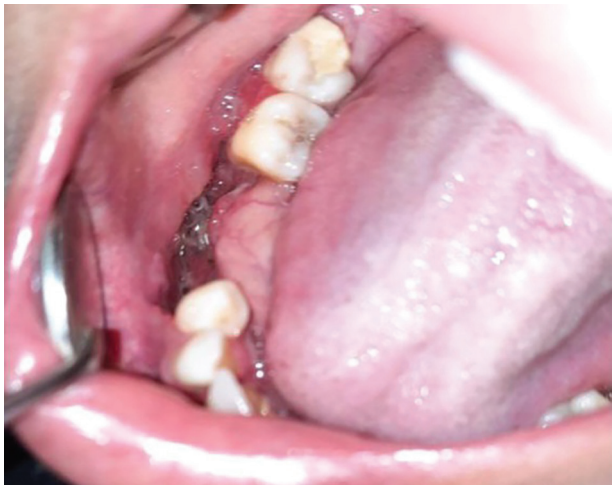

**Fig. 2:** Impaired healing of post-extraction socket of right mandibular first molar

complaint of loose teeth in upper and lower back regions of the jaws. History dates back to 2 years, when the patient first noticed loosening of teeth and bleeding from gums. The patient had undergone extraction of mandibular molars a month ago due to mobility and developed poorly healed ulcerated sockets. The patient had a history of polycystic ovarian syndrome (PCOS) and had been on treatment for infertility for 3 years. During this period, only the patient developed gingival inflammation and noticed frequent episodes of bleeding from the mouth. There was no history of any other medical/dental treatment.

On intraoral examination, crater-like ulcerative lesions were seen on the attached gingiva in the mandible and on the palate (Figs 1 and 2). There was clinical attachment loss in multiple teeth and most aggressive in mandibular posteriors. Generalized periodontal inflammation and bleeding on probing were evident. The patient also developed halitosis over time. There were multiple areas of aggressive bony necrosis, especially in the interdental area. The comprehensive radiograph demonstrated acute loss of bony tissue at the mandibular posterior region, with no signs of any

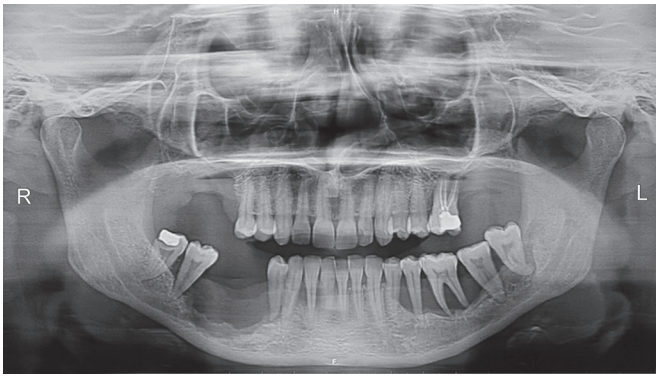


**Fig. 3:** Orthopantomogram (OPG) showing aggressive alveolar destruction

periapical lesion or pathology (Fig. 3). Multiple mobile teeth with extensive difficulty in mastication, and a constant burning sensation were experienced by the patient.

Upon serological investigations, there were normal levels of thyroid and parathyroid hormones, and normal hematocrit was seen. Serum calcium was marginally low, and the patient was already on medication for the same. Normal renal function tests were seen, but liver function tests were deranged. The patient had raised levels of SGOT and SGPT along with very high levels of GGT indicating liver distress. Also, raised GGT levels were indicating an aggressive periodontal disease. The patient was referred to a specialist for a deranged liver function test, and ultrasonography of the abdomen demonstrated two nodules in the liver of sizes 6- and 8-mm diameter. No surgical intervention was planned, and it was put on regular follow-up for the same. The patient was also tested for tuberculosis and other granulomatous diseases, which came out to be negative.

A provisional diagnosis of acute necrotizing ulcerative periodontitis was made, and the patient was treated with antibiotic therapy along with frequent follow-up visits wherein irrigation with chlorhexidine and betadine was done. During the follow-up visits, in spite of aggressive periodontal therapy, there was no sign of improvement, rather the condition worsened over time as there were new ulcerative lesions formed in the anterior region as well. The decision was made to take the patient for a biopsy.

## Histopathological Examination

Upon progression of disease after failed antibiotic therapy, a biopsy of incisional tissue at the ulcerative gingiva carried out with locally administered anesthesia in a clinical set-up. Upon routine staining of the sections from both the mandibular and maxillary posterior regions, including the ulcerated, punched out areas and microscopic examination, stratified squamous epithelium was seen with ulcerations. There was abundant granulation tissue infiltrated with lymphocytes, plasma cells, neutrophils, histiocytes and histiocytic giant cells. There were sections at places showing lymphoid tissue forming follicles. There were no well-formed epithelioid cell granulomas or malignant cells seen in the sections. These sections were further subjected to immunohistochemistry and found to be positive for CD1a, and CD207 (langerin) antigens. The samples were also tested for BRAF (V600E) gene expression, and it turned out to be negative.

Based on the histopathological findings, the clinical prognosis of the Langerhans cell phenomenon of histiocytosis was positively affirmed, and a full body analysis of the patient was done to see if any other organ or bone was involved. On full-body PET scan, metabolically active bone erosions associated with adjacent soft tissue involvement in both the maxillary and mandibular regions were seen, consistent with clinical findings. Also, multiple metabolically active hypodense lesions were seen in both lobes of the liver, suggesting liver involvement. There were multiple bilateral inguinal lymphadenopathies, indicating lymphoid infiltrations.

## Treatment

Primarily, the patient subject received surgical curettage and exteriorly given steroid therapy, but after the final prognosis with LCH, the subject started on chemotherapy for the same. Since the condition of the patient was multifocal, the therapy included Vinca alkaloids, i.e., Vinblastine with a dose of 6 mg/m$^2$ per week, and corticosteroids, i.e. Prednisolone, with a dose of 40 mg/m$^2$ per day. Also, intralesional injections of triamcinolone acetonide (40 mg) were also administered on a weekly basis with mouthwash benzydamine (0.15%) on a regular basis for 4 weeks. There was evident regression in gingival lesions, with great improvement in pain after 6 months follow-up. There was also no progression of bone loss, and mobility of teeth in both the arches. The patient is presently stable and no new lesions seem to have developed. The prognosis seems good as the patient was diagnosed timely and no new bone or visceral organ involvement has been seen so far.

## Discussion

A rare disorder exacerbated by reticuloendothelial cells and their physiological system, previously known as Histiocytosis X, LCH has mostly been characterized in children, and very few studies have been recorded in adults. From the present literature, it has been found to be more frequent in the first and third decades of a child's life.[5] Initially LCH is retained to serve as a proliferative disease as a counter repercussion to a particular antigen-mediated incitation. Although due to perils in histological diagnosis the exact etiologies still to be elucidated. Some authors believe that the reactive disease process of LCH with accumulation of histiocytes occurs in retort to unidentified antigen, relatively a bonafide neoplastic anomaly.[6] However, some authors consider it to be a similar to a neoplasm especially in cases of multifocal and multi organ disease. There is also evidence of inflammatory origin of the disease due to microscopic and clinical characters.[7]

The disease was previously classified clinically into granuloma of eosinophils, and Letterer-Siwe disease and Hand Schüller-Christian disease, but the present classification is categorized as a single system/multisystem parallel to the dissemination of the disease. The prognostic appearances of LCH are multivariate, ranging from unilocular (present at one site) or multilocular (vivid presence at multiple sites), it could be a one-organ or multi-organ disorder and could be disseminated or life-threatening as well.[1] Although the most familiar counter indication incorporates a singular or multifaceted lesion in the skull, ribs, vertebrae and jaws, young patients have common involvement of skull or femoral bones, while adults have common involvement in the girdle, shoulder, ribs and mandible. Grown-up patients may also have lymphadenopathy along with seborrheic dermatitis or eruption-mediated eczematous of the scalp tissue and trunk.[8]

Among these, oral features, are comparably early to occur, and dental practitioners must be keen on early diagnosis of the disease. Common oral signs are gingivitis, mobile teeth, ulcerations or growth intraorally, impaired healing, halitosis and bone destruction.[1] Once involving the jaw bones, the lesion may mimic giant cell granuloma, osteomyelitis or granulomatous diseases. In severe cases, it may mimic neoplasias like lymphomas, leukemia, multiple myeloma and metastatic diseases.[9]

Langerhans cell histiocytosis predominantly starts in the posterior mandible, as was seen in this case. The patient also had aggressive periodontitis, ulcerations, severe bone loss and halitosis, all signs indicating the disease. In the present case report, the authors have presented a very rare characterization of oral Langhans cell histiocytosis involving both the maxilla and mandible in a 33-year-old female subject. The mentioned subject also developed granulomatous growth and ulcerations on the palate and impaired healing of extraction sockets as the disease manifested. The conformational diagnosis was made from immunohistochemistry alone. The key factor in the prognosis of the disease is its early detection based on age of onset, degree of functional lesion, and number of organs involved.

## Conclusion

The prognosis for LCH is good if multi-organ or multisystem involvement is not present. The survival rate ranges from 70 to 100%, but the subjective well-being is notablely impaired by the disease and it's therapy.[10] Oral and maxillofacial clinicians play a pivotal part in early prognosis and timely intervention, as oral manifestations are the earliest or sometimes, as in this case, the only sign of LCH. Timely diagnosis with the aid of histopathological examination, especially immunohistochemistry, is necessary for subsequent diagnosis and subsequent management of the disease. Treatment mainly comprises radiotherapy/ablation, surgical removal, chemotherapy or an optimum amalgamation of these modalities. In the aforesaid case, the subject had multiple orally-located lesions in both the maxilla and mandible that showed improvement with chemotherapy. Kind attention by the oral health practitioner, proper treatment protocol, timely follow-up and patient determination are key to a better prognosis for the disease.

## References


1. Hicks J, Flaitz CM. Langerhans cell histiocytosis: Current insights in a molecular age with emphasis on clinical oral and maxillofacial pathology practice. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2005;100(2 Suppl):S42–S66. DOI: 10.1016/j.tripleo.2005.06.016.
2. Takahashi K, Harada M, Kimoto M, et al. Diagnostic confirmation of Langerhans cell histiocytosis of the jaws with CD1a immunostaining: A case report. J Oral Maxillofac Surg 2003;61(1):118–122. DOI: 10.1053/joms.2003.50019.
3. Pekiner FN, Borahan MO, Ozbayrak S, et al. Oral manifestations of chronic disseminated Langerhans cell histiocytosis: A case report. Clinical and Experimental Health Sciences 2012;2(3):138–142. Available from: http://musbed.marmara.edu.tr.
4. Mínguez I, Mínguez JM, Bonet J, et al. Oral manifestations of chronic disseminated histiocytosis. A report of 10 cases. Med Oral 2004;9(2):152–154, 149–152. PMID: 14990881.

5. Madrigal-Martínez-Pereda C, Guerrero-Rodríguez V, Guisado-Moya B, et al. Langerhans cell histiocytosis: Literature review and descriptive analysis of oral manifestations. Med Oral Patol Oral Cir Bucal 2009;14(5):E222–E228. PMID: 19218906.
6. Hartman KS. Histiocytosis X: A review of 114 cases with oral involvement. Oral Surg Oral Med Oral Pathol 1980;49(1):38–54. DOI: 10.1016/0030-4220(80)90030-4.
7. Neves-Silva R, Fernandes DT, Fonseca FP, et al. Oral manifestations of Langerhans cell histiocytosis: A case series. Spec Care Dentist 2018;38(6):426–433. DOI: 10.1111/scd.12330.
8. Kilpatrick SE, Wenger DE, Gilchrist GS, et al. Langerhans' cell histiocytosis (histiocytosis X) of bone. A clinicopathologic analysis of 263 pediatric and adult cases. Cancer 1995;76(12):2471–2484. DOI: 10.1002/1097-0142(19951215)76:12<2471::aid-cncr2820761211>3.0.co;2-z.
9. Putters TF, de Visscher JG, van Veen A, et al. Intralesional infiltration of corticosteroids in the treatment of localized Langerhans' cell histiocytosis of the mandible report of known cases and three new cases. Int J Oral Maxillofac Surg 2005;34(5):571–575. DOI: 10.1016/j.ijom.2004.10.020.
10. Quraishi MS, Blayney AW, Breatnach F. Aural symptoms as primary presentation of Langerhan's cell histiocytosis. Clin Otolaryngol Allied Sci 1993;18(4):317–323. DOI: 10.1111/j.1365-2273.1993.tb00856.x.