

Case Report

Langerhans Cell Histiocytosis of the Oral Mucosa: A Rare Case Report

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ABSTRACT

Langerhans cell histiocytosis (LCH) is a rare idiopathic disease characterized by the clonal proliferation of bone marrow derived Langerhans cells. It usually occurs in children. Their clinical features simulate common oral findings such as gingival enlargement, oral ulcers, and mobility of teeth, along with nonspecific radiographic features, thus easily leading to the misdiagnosis and therefore, it could be overlooked by dentists. We report a rare case of LCH in 38-year-old adult male, characterized by oral mucosal ulcerations with no involvement of the underlying bone. The lesion was histologically proven to be LCH and was confirmed with immunohistochemical staining of S100 protein and CD1a antigen.

Keywords: Langerhans cell histiocytosis-oral cavity-oral ulcer-immunohistochemistry.

INTRODUCTION

Langerhans cell histiocytosis (LCH) is a rare idiopathic disease characterized by the clonal proliferation of Langerhans cells, which are freely mobile cells that originate from bone marrow myeloid precursors. [1] The nomenclature-histiocytosis X-was coined by Lichtenstein in 1953 to account for three clinical varieties which showed some histological characteristics in common eosinophilic granuloma, Letterer-Siwe syndrome and Hand-Schüller-Christian syndrome. The recent adoption of the terminology 'Langerhans cell histiocytosis' is due to the fact that the histiocytes involved in the disease present a phenotype which is similar to that of Langerhans cells found in normal mucosa and skin. [2] The disease usually occurs during childhood and the incidence is one case per 200000 children per year, but it may also occur later in life. [3] Though the etiopathogenesis is not clear, various theories have suggested

contribution of environment, infections, immunology, genetics, and neoplastic process. [4]

Different organs and systems may be affected in LCH, such as the lungs, liver, lymph nodes, spleen, haematopoietic tissue and mucocutaneous tissues. [5] However, isolated oral mucosa lesions without bone involvement are rare. Oral manifestations may be the first sign of LCH, and on some occasions the oral cavity may be the only area affected. The incidence of oral lesions in LCH is 77%, therefore the initial diagnosis in many cases is made by the odontologist. [6] The severity and prognosis of the disease is in turn dependent on the type and extent of organ involvement. [7]

The purpose of reporting this paper is to present a rare case of LCH characterized by oral mucosal ulcerations with no involvement of the underlying bone and to discuss the clinical features and the

role of dentists in diagnosing and managing such lesions.

CASE REPORT

A 38-year-old male patient with an uneventful medical history was referred to our department of oral surgery with a complaint of ulcerations on the palatal mucosa and maxillary and mandibular gingiva of three weeks duration. There was

no pain or bleeding, but he occasionally experienced a burning sensation on the ulcerated areas.

Intraoral examination revealed poor oral hygiene with erythematous gingiva and ulcerations on the palatal mucosa without induration on palpation (Figure 1). Panoramic radiograph showed no bone lesions (Figure 2).



Figure 1: Intraoral findings showing ulcerations of hard palate (a), gingiva (b) and alveolar ridge (c) with non-defined margins, non-painful and non-bleeding.

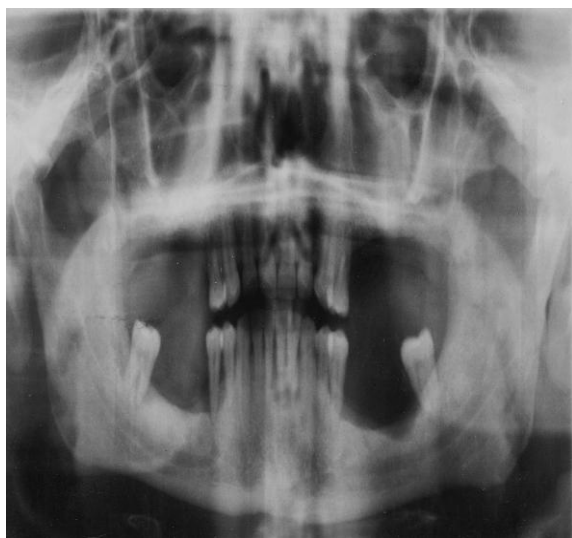


Figure 2: Panoramic radiograph showing there is no pathosis of the related bone.

Blood investigations showed increased sedimentation rate (67mm for the

first hour and 92 mm for the second one). However, white cell count, haemoglobin level and random blood glucose value were within normal range. Moreover, Mantoux test was negative and human immunodeficiency virus (HIV) antibody tests and hepatitis B virus serology were negative.

A biopsy of the palatal lesion revealed histologically in the haematoxylin-eosin stain a mixed inflammatory infiltrate with localized and nodular accumulations of large atypical histiocytic cells with kidney-shaped nuclei that in immunohistochemistry stained positively for CD1a (Figure 3a) as well as for S100 (Figure 3b). Histology and immunohistochemistry were diagnostic for LCH.

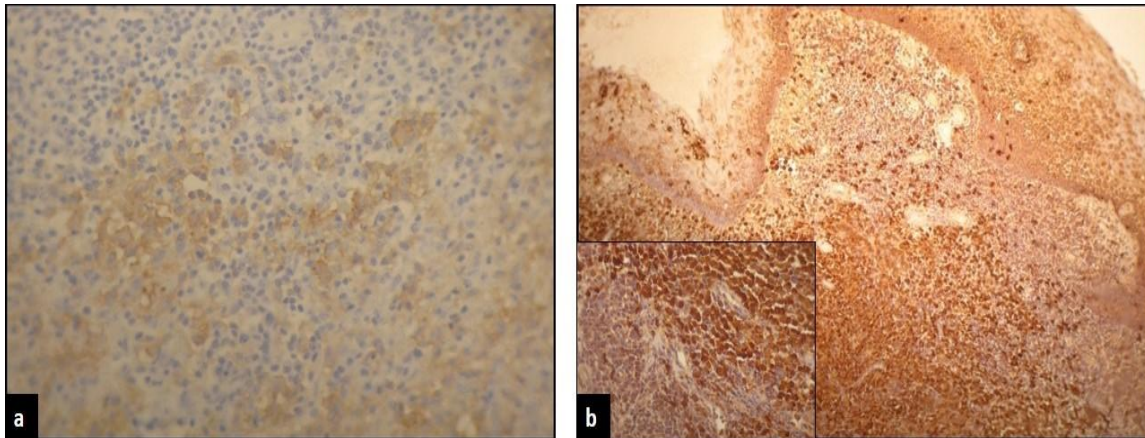


Figure 3: Microscopic examination showing inflammatory cells with diffuse and nodular infiltration of large histiocytic cells with kidney-shaped nuclei; a: Immunohistochemistry showing positivity for CD1a antigen; b: Immunohistochemistry showing presence of Langerhans cell S100 protein.

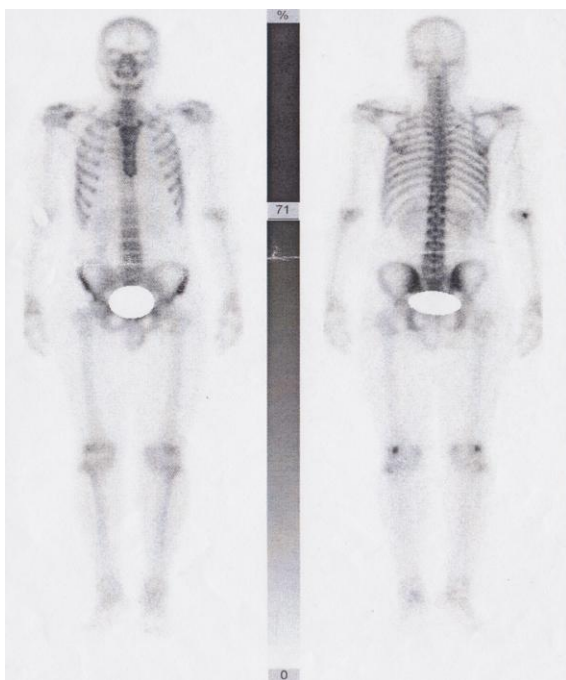


Figure 4: Bone scintigraphy showing no lesion.

Multifocal LCH was ruled out because chest radiographs, abdominal sonography, liver function studies showed normal results, and a whole-body skeletal scintigraphy showed no evidence of bone lesions (Figure 4).

In view of the above findings, a final diagnosis of LCH exclusively limited to the oral mucosa was established. Thus, prednisone 20 mg in mouthwash twice daily was prescribed. After two weeks the lesions did not show any improvement. Therefore, we have prescribed a corticotherapy systemically (prednisone 20 mg twice daily for 10 days then once per day for the last 10 days). After three weeks the lesions resolved completely. No new lesions have been observed after 1 year of follow-up (Figure 5).



Figure 5: Uneventful healing of the hard palate ulcerations (a, b and c) and gingival lesions (d, e and f) after 1 year of follow-up.

DISCUSSION

Proposed by Lichtenstein in 1953 as histiocytosis X, the term LCH was introduced as a collective designation for a spectrum of clinicopathologic disorders (eosinophilic granuloma, Hand-Schüller-Christian disease, and Letterer-Siwe disease) characterized by proliferation of histiocyte such as cells accompanied by eosinophils, lymphocytes, plasma cells, and multinucleated giant cells. [4,8] The aetiology and pathogenesis are still unknown. Most studies suggest that it is a reactive disease caused by abnormal immune regulation. [4,5,8] Whereas studies examining the clonality of the lesional cells of this condition have shown it to be a monoclonal proliferation, a finding more consistent with a neoplastic process. [8]

LCH may be encountered over a wide age range with a peak incidence from 1 to 4 years with a male predilection, twice that of the females. [1,2,4] They are rarely seen in adults with incidence around 1–2 cases/million persons per year. The present case was reported in adult male of 38-year-old. [2,4]

The incidence of oral lesions in LCH is 77%. [6] Hence, oral manifestations can be the first sign of LCH and in some occasion the only area affected (5% of cases) as seen in the present reported case. Thus, this can lead the patient to consult a dentist. [4,6,9]

As the adult cases are rare, clinical features are poorly described in literature with nonspecific multiple presentations such as gingival hypertrophy, oral ulceration of hard and soft palates, and tongue, mobility of teeth with alveolar expansion, jaw pain, facial swelling, and mental nerve anaesthesia. [1,4,7,10] In our case, the patient showed ulceration of the hard palate, followed by the development of a similar lesion in the gingival mucosa of the alveolar ridge and the mandibular gingiva.

The most common radiologic features of LCH seen in the majority of cases are solitary or multiple bone lesions with a most frequent site involving skull, ribs, vertebrae, and jaws. [8] However, in

rare cases, no underlying bone lesions are observed as seen in this case. Exclusive mucosal involvement without bone involvement by LCH, as in our case, is a rarity and often leads to delay in diagnosis.

Based on clinical and radiological findings of the present case, the differential diagnosis should be made with tuberculosis ulceration, sarcoidosis, leukaemia, neutropenia, prepubertal periodontitis, hypophosphatasia, and Papillon-Lefevre syndrome. [1,4,6]

As LCH lacks pathognomonic clinical and radiographic characteristics, a definitive diagnosis should be based on the histologic and immunohistochemical study of lesional biopsy specimens. [2,3] The histopathological pattern demonstrates a diffuse infiltration of large pale staining mononuclear cells that resemble histiocytes with indistinct cytoplasmic borders and rounded or indented vesicular nuclei. [4,10] Electron microscopic evaluation shows rod-shaped cytoplasmic structures or tennis-racket morphology known as Birbeck granules within Langerhans cells, differentiating them from other mononuclear phagocytes. [4,6] A definitive diagnosis of LCH requires that the lesional cells exhibit positive staining with S-100 and CD1a. [2-4,7-9] Langerin (CD207) is a new monoclonal antibody targeting a type II transmembrane C-type lectin of the Langerhans cell that induces the formation of Birbeck granules. [9,11] Langerin appears to be more sensitive and selective for Langerhans cells than CD1a. [9] In the present case, the biopsy specimen was positive for CD1a marker and S100 protein, thus, confirming the diagnosis.

After the diagnosis of LCH of oral mucosa is confirmed, the staging of disease should be assessed. The histiocyte society has established a set of guidelines to assist in the diagnosis and study of LCH. [12] The initial evaluation consists of a complete physical examination, hematologic panel, coagulation studies, liver function tests, urine osmolality, arginine vasopressin (to detect diabetes insipidus), radiographic skeletal survey, and chest radiograph. [11,12]

A bone scintigraphy can also be useful to exclude or to detect additional bone lesions and to follow up patients. [3] Full body bone scan in our case revealed no bone involvements. Patient with any abnormalities requires additional assessments such as pulmonary function tests, lung biopsy, small bowel series, liver biopsy, endocrine evaluation, and otolaryngoscopy. [4] In our reported case, it was unifocal LCH of oral mucosa.

Optimal treatment of LCH remains controversial due to high clinical variability and absence of standard diagnostic and evaluation criteria; also most of the treatment related data are confined to the juvenile. [4] The treatment of LCH depends upon lesion size, the degree of tissue involvement, age of the patient whether it is unifocal or multifocal. [3,4] Therapy includes surgery, radiation, and chemotherapy, either individually or in combination. [7] More recently, intralesional injections of corticosteroids such as prednisone have been found to offer good results. In our case, prednisone (20 mg) twice par day was prescribed. After 3 weeks all the oral ulcerations were healed.

The prognosis of LCH as with any other disease depends on early detection. When considering the fact that LCH can often present initially with an oral lesion, the knowledge about the oral manifestations can greatly reduce the morbidity and mortality of this disease. The course of the disease is unpredictable and can evolve with multiple reactivations. [6]

The most important factors that may worsen the prognosis are visceral involvement (liver, lung, bone marrow), age at first presentation is less than two years and when the disease spreads to various bones or soft tissues. [6,8]

Recurrence rates depend on the treatment method and location of the lesion and are reported to range from 1.6% to 25% and patients should be closely followed up for a long period of time to ensure remission. [3,4]

To conclude, localized ulcerations of oral mucosa should lead to include oral LCH in the differential diagnosis. The present case tells us that LCH can be reported in adults even it's rare. Although, as pathognomic clinical or radiographic criteria are lacking, a lesional biopsy with immunohistochemistry is mandatory to confirm the diagnosis of LCH. Then, multifocal organ involvement must be ruled out by staging as recommended by the Histiocyte Society. The prognosis in unifocal involvement is generally very good. However, there is still no consensus on therapeutic protocols so a long-term follow-up is recommended to prevent or detect any relapse.

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