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CASE REPORT

Mandibular manifestation of Langerhans cell histiocytosis in children

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KEYWORDS

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Summary Langerhans cell histiocytosis (LCH), previously known as histiocytosis X, is a rare, proliferative disorder in which the accumulation of pathologic Langerhans cells leads to local tissue infiltration and destruction. In this article, we report a case with LCH. The history, radiological appearance, histopathology and treatment options of the patient were discussed.

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Introduction

Langerhans cell histiocytosis (LCH), previously known as histiocytosis X, is a rare, proliferative disorder in which the accumulation of pathologic Langerhans cells leads to local tissue infiltration and destruction. Clinical presentation differs from single or multifocal bone lesions to disseminated bone disease with multiorgan involvement such as bone, liver, spleen, lung, central nervous system, skin,

bone marrow or gastrointestinal tract.¹ The term “Langerhans cell histiocytosis” comprises three morphologically similar lesions: Eosinophilic granuloma, Hand–Schueller–Christian syndrome and Abt–Letterer–Siwe syndrome. The localized LCH (monostatic or multifocal eosinophilic granuloma) refers to a form of the disease typified by solitary or multiple skeletal lesions without extra skeletal involvement; it commonly affects children and young adults. The disseminated, chronic form named Hand–Schueller–Christian syndrome, consists of skeletal and extra skeletal lesions with a progressive chronic course and usually affects children older than 3 years. The disseminated, acute or subacute form named Abt–Letterer–Siwe

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syndrome, refers to the form of the disease that is most often fatal because of the extensive skeletal and extra skeletal lesions; this form usually affects infants and children younger than 3 years.

In this article, we report a case with LCH, which is still very rare in head and neck region. The history, radiological appearance, histopathology and treatment options of the patient were discussed.

Case report

A 9-year-old girl with a history of 20 days swelling on the left lower jaw applied to our ENT Clinic at a community based hospital. She had been treated for left parotitis 20 days ago at another hospital. Her IgM antibody for mumps was positive at that time. The patient was treated with sulbactam ampiciline and ornidazol; however, the swelling persisted. She denied any history of fever, rash, allergy and feeding difficulties. Ultrasonography obtained to confirm the parotitis demonstrated a solid mass on left lower jaw.

On physical examination, the patient was well developed, well nourished, and in no acute distress. She was afebrile, and her vital signs were within normal limits. The general physical exam was normal, with the exception of head and neck area, where a very painful mild left mandibular swelling was noted. Other ENT exam was within normal limits including normal oral and gingival mucosas.

Her laboratory findings were within normal limits including complete blood count, blood biochemistry, and urine analysis, VMA in the urine. Meanwhile she was consulted with a dentist. There was no relation of this swelling with dental disease. Panoramic mandible showed a lytic lesion with discrete border and no sclerosis (Fig. 1). Computerized tomography (CT) of the jaws showed a destructive, solid, lytic lesion of the lower jaw (Fig. 2). With all these radiological investigations, the possible differential diagnoses were Langerhans cell histiocytosis, Ewing sarcoma, lymphoma and osteomyelitis. She was evaluated for distant similar lesions with bone survey and vertebral Magnetic Resonance Imaging (MRI). All these investigations showed negative clues. Oral biopsy obtained under general anesthesia was reported as Langerhans cell histiocytosis (LCH) (Fig. 3). Curettage was performed to treat the lesion.

She had twin sister. Her sister was also evaluated for similar lesion with bone survey. Interestingly, she had 8 mm lytic lesion on the same place (left lower jaw) on bone survey. But CT did not confirm any lesion on the mandible.



Figure 1 Panoramic mandible showing lytic lesion on the left mandibular ramus. Arrow: the lytic lesion.



Figure 2 CT of the patient. Arrow showing the lesion.

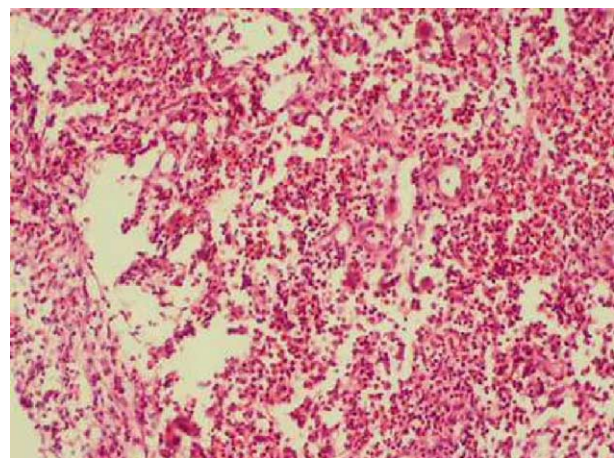


Figure 3 Histiocytes with eosinophils, H&E, $\times 100$.

Discussion

The aim of this paper is to give a short introductory overview on current diagnostic and treatment strategies of LCH in the oral and maxillofacial region and to present a case with LCH and discuss the differential diagnosis and evaluation of these patients.

LCH is a disorder in which the lesions contain cells with features similar to the Langerhans cells of the epidermis. It is used to be called "histiocytosis X". The etiology of such a disease is unclear. Studies suggest that Langerhans cell is an immunocompetent cell that originates in the bone marrow and is related to the mononuclear phagocyte system. The cytoplasm of the histiocytosis X cell contains characteristic inclusions called histiocytosis X bodies, which resembles the Birbeck granules found in Langerhans cell. Thus histiocytosis X is viewed currently as a proliferative disorder of Langerhans cell or their marrow precursors.² Besides the observation that patients with LCH do have a certain immune compromise not being the cause of the disease, there is no evidence why such a proliferation of Langerhans cells leading to tissue infiltration and destruction occurs. In studies, various possible etiological mechanisms were accused. On the one hand, a basic immune defect may lead to proliferation of Langerhans cells; on the other hand, the Langerhans cell itself may carry a genetic defect leading to abnormal cellular proliferation. Besides, an increased incidence of the disease was reported in conjunction with neonatal infections, exposition to chemical solvents, positive family history of thyroid disease, which our patient did not have any of them. Cytogenetic abnormalities were accused as well.³ Our patient had parotitis during the course of the disease. She also had dysentery with *E. histolytica*, which responded well to the treatment. All these comorbid diseases reminded us of the possible immunologic nature of the disease. We do not have genetic research facilities in our institution. However, interestingly her twin sister had similar lytic lesion in the same place on bone survey, which we could not be able to confirm with CT findings. But we planned to follow up her sister for the possibility of genetic nature of the disease.

LCH is a very rare pathology with an incidence of 1 in 560,000. It seems to be more frequent in males than in females, with a reported ratio ranging from 1.1:1 to 4:1. Skeletal involvement is one of the most common features presented in LCH.⁴ Skeletal lesions of LCH can occur in any bone. However, they are most common in the pelvis, ribs, skull, long bones, vertebra and facial bones. It has been

reported that the incidence in the jaws is 7.9%. In the mandible, the body and angle are the most commonly affected sites.⁵

The most common oral findings are local pain and swelling as in our case, mucosal ulceration, gingival necrosis and destruction of alveolar bone with tooth mobility and exfoliation. These patients rarely have systemic symptoms, with many lesions asymptomatic and diagnosed accidentally during radiological investigation for unrelated problems. As a matter of fact, the lesion in our patient was detected accidentally during radiological evaluation for her left parotitis. Radiologically, LCH presents as localized, punched-out radiolucencies with no calcification and no sign of sclerosis or reactions at the borders. There may be severe alveolar bone resorption producing the appearance of teeth "floating in space" (Fig. 1).^{2,6} Unlike many other infiltrative processes of bone there are no characteristic laboratory findings. But these laboratory investigations are needed for differential diagnosis of LCH with other lesions. With the absence of pathognomonic signs and specific laboratory abnormalities, the diagnosis of LCH can only be established by biopsy. For this patient, the differential diagnosis included LCH, Ewing sarcoma, lymphoma and osteomyelitis. Eosinophilic granuloma was the first possible diagnosis. Because the Letterer–Siwe syndrome is very acute and lethal and it usually affects children younger than 3 years. Hand–Schuller–Christian disease is mainly seen in children older than 3 years and it is a more chronic form and it is characterized by multiorgan and multifocal involvement such as pituitary gland and orbita. But our case had only left mandibular involvement and no other systemic or skeletal involvement. So, eosinophilic granuloma was the first possible diagnosis. The second differential diagnosis was Ewing sarcoma related to the CT findings. Both LCH and Ewing sarcoma cause similar lesions radiologically when flat bones are involved. But Ewing sarcoma usually attacks the long bones and it rarely affects mandible. So it was rather a far possibility. Burkitt lymphoma affects children, too. But it usually attacks maxilla instead of mandible. The fourth-possible diagnosis was osteomyelitis. But this patient had no history of trauma to the jaws and no history of tooth infection, which could have caused osteomyelitis. Moreover, a dentist had seen her and this lesion had no relation to tooth infection. For final diagnosis and start of the treatment, transoral biopsy was obtained by curettage of the lesion. Histopathological characteristic of the lesion comprised proliferation of Langerhans cells, which was immunohistochemically identified by the presence of the antigens S100 and CD1a. This

predominant cell population was admixed with variable numbers of eosinophils and neutrophils.

As LCH can be a multifocal disease, radiographic skeletal surveys to be a reasonable procedure for a complete evaluation of the bone condition. In addition, extra skeletal involvement is more likely in patients with multiple bony lesions.⁷ A bone scintigraphy can also be useful to exclude or to detect additional bone lesions and to follow up patients.^{2,3} According to most authors, LCH is basically not a malignant disease, although the etiology of Langerhans cell proliferation-neoplasia or immune defect—still remains controversial. Clinical prognosis of patients will become worse with the growing number of involved organs, with growing number of organ dysfunctions, with rapid disease progression, with limited treatment response and decreasing age of first disease manifestation. Probably the most relevant prognostic parameter is the number of involved organs, since a solitary lesion in children does not have a worse prognosis compared to adults.²

Treatment modalities for LCH are variable according to location, extension and number of lesions. Surgical curettage, radiotherapy and chemotherapy can be used alone or in combination.^{1–7} In our patient we performed only curettage because

of the unifocal involvement. However, if there are multifocal involvement and systemic disease, chemotherapy should be considered in these patients. 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.⁷

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