Langerhans Cell Histocytosis of the Mandible in a Pediatric Patient

Ahmed Alshadwi, BDS *Mohammed Nadershah, BDS*
Saleh AlBazie, BDS, DScD

ABSTRACT

Langerhans cell histiocytosis (LCH) is a rare, proliferative disorder in which the accumulation of pathologic Langerhans cells leads to local tissue infiltration and destruction. In this article, a review of LCH is presented and a case of a single LCH lesion affecting the mandible of healthy infant is discussed. The history, radiological appearance, histopathology and treatment options are discussed.
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KEYWORDS: LANGERHANS CELL HISTIOCYTOSIS, PEDIATRIC TUMORS, ORAL PATHOLOGY

Langerhans cell histiocytosis (**LCH**), previously known as histiocytosis X, is a rare disease of unknown etiology. Controversy continues as to whether it is a malignant process or an immune-mediated inflammatory condition.[1,2] LCH is characterized by proliferation of pathological Langerhans cells within different organs in the human body.[3-5] In 1953, Lichtenstein observed cytoplasmic bodies, known as X bodies, within histiocytes from tissues of patients suffering from what were previously considered 3 distinct clinical disorders: (1) eosinophilic granuloma; (2) Hand-Schüller-Christian disease; and (3) Abt-Letterer-Siwe disease.[3] Later, Lichtenstein proposed that these three disorders represented manifestations of a single pathologic process involving the reticuloendothelial system, characterized by focal proliferation of abnormal histiocyte-like cells.[3,5-9]

LCH has a predilection for males over females by a 4:1 ratio.[4] It predominantly affects children, although it may appear at any age.[4,7,9] The incidence of this disease is estimated to be 3 to 5 cases per million in children (1-2 cases per million in adults).[10] Although lesions may appear in tissues of different origins, such as skin, hypothalamus, liver, lung, or lymphoid tissue,[4,7,9,11] bone is the most common site of the disease.[3,12] The head and neck region is involved in nearly 90 percent of cases and may be the only affected area.[5] Oral mucosal involvement tends to manifest as a gingival swelling or ulceration, usually resulting from an underlying bone lesion. Maxillary and mandibular bones are affected in 5 percent to 10 percent of the cases, with mandibular bones being more commonly involved in adults.[5]

The purpose of this paper is to report a rare case of monostotic LCH affecting the mandible of a 13-month-old boy whose lesion was completely resolved following surgical intervention.

CASE REPORT

A 13-month-old healthy boy presented to Asir Central Hospital, Southern Providence, Saudi Arabia, with tender swelling of his chin that had been present for the past 2 months. His parents initially sought help from a pediatric dentist who referred them to an oral and maxillofacial surgeon at their local hospital. At the time of presentation, the patient was afebrile, and his parents did not give any history of trauma, past surgeries or recent hospitalization. He was not taking any medications nor did he have any environmental or drug allergies. An examination revealed that the patient had a tender, indurated swelling measuring 1 x 1 cm on the chin area and no lymphadenopathy. Intraorally, the patient had mild swelling in the anterior mandible with

Dr. Alshadwi is a resident and Dr.Nadershah is an oral and maxillofacial oncology and a reconstruction fellow, Department of Oral and Maxillofacial Surgery, Boston University, Boston Medical Center, Boston, Mass., USA; and Dr. AlBazie is a consultant in oral maxillofacial surgery, College of Dentistry, King Saud University, Riyadh, Saudi Arabia.
Correspond with Dr. Alshadwi at alshadwi@bu.edu

normal overlying oral mucosa, mild mobility of the mandibular incisors, and no discharge.

The surgeon performed an incision and drainage under general anesthesia (GA), believing that an infection was present, given the acute onset of symptoms. No purulence was drained, although some bloody drainage was encountered. He also obtained an incisional biopsy of the lesion. A histopathological examination indicated LCH of the mandible (Figures 1 and 2). The patient was admitted to King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia, for hydration and diagnostic workup. A computed tomography (**CT**) scan showed a large cystic lesion in the anterior mandible measuring approximately 2 x 3 cm, causing a cortical expansion and displacement of the primary and unerupted permanent teeth (Figure 3). No other lesions were found. The patient was treated by surgical enucleation via a transoral approach under GA. No lingual cortical perforation was noted intraoperatively. The roots of the anterior primary mandibular teeth were visualized and protected during the lesion excision (Figure 4).

The procedure was uneventful, and the patient was discharged the following day. The surgical site healed without any complications. A 1-year follow-up CT scan showed complete resolution of the bony lesion with normal tooth eruption (Figure 5). He was followed up for 5 years and no radiographic or clinical signs of recurrence were observed.

DISCUSSION

LCH is a rare disease that primarily affects children. Its natural history is interesting, because it has the potential for spontaneous resolution as the patient approaches adulthood. Although primary adult cases are less common than those involving children, LCH may occur in any age group.[13,14] The clinical spectrum of LCH ranges from limited and localized lesions to disseminated disease that, in some instances, may have a rapid and even fatal outcome.[15] Acute morbidity (eg, diabetes insipidus, anterior pituitary dysfunction, and neurodegenerative changes) may accompany LCH at any age group. Moreover, mortality is a concern in the multisystem disseminated form (especially in children).[16]

The Writing Group of the Histiocyte Society[17] has identified 3 levels of confidence in the diagnosis of LCH:

1. A presumptive diagnosis can be made when light morphologic characteristics are consistent with the findings defined in the literature for LCH.
2. A designated diagnosis can be made when, besides consistent light morphologic features, 2 or more supplemental positive stains for adenosinetriphosphatase, S-100 protein, alpha-D-mannosidase, or peanut lectin are also present.
3. A definitive diagnosis can be made when, besides light morphologic characteristics, Birbeck granules are detected in the lesion's cells using electron microscopy and/or there is a positive staining for CD1a antigen (T6) on the surface of the cells.

In 1987, the Histiocyte Society was founded by the collaboration of multiple international scientific centers, which was a critical point in the history of studying this rare disease. It established uniform standards in terms of definition, clinical classification, criteria for response to treatment, and management, which led to multiple international multicenter prospective

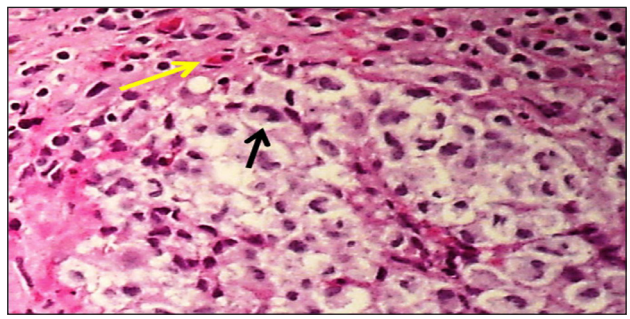

Figure 1. This low magnification hematoxylin and eosin–stained slide shows a Langerhans cell cluster (black arrow) in dense stroma with a prominent eosinophilic component (yellow arrow).

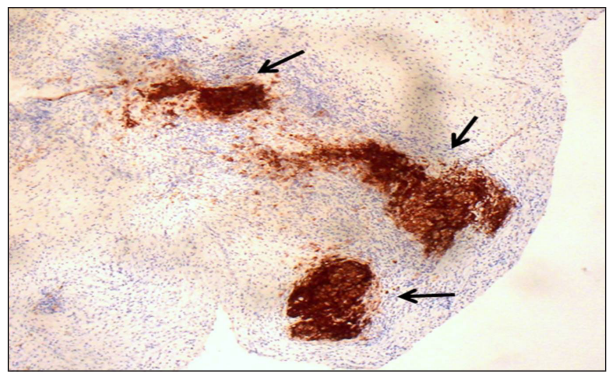

Figure 2. This low magnification CD 1 stained slide shows Langerhans cell clusters (black arrows).

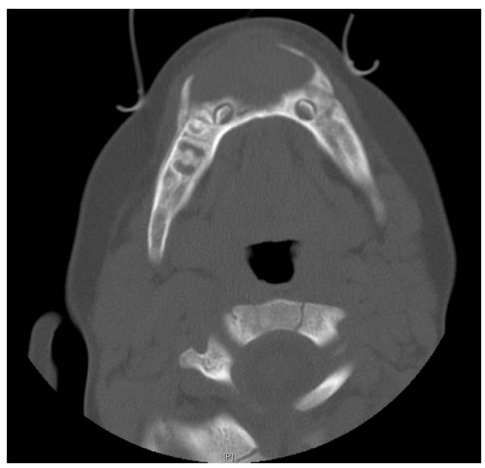

Figure 3. Computerized tomography at the level of the mandibular symphysis showing a large expansile radiolucent mass causing displacement of the mandibular teeth.

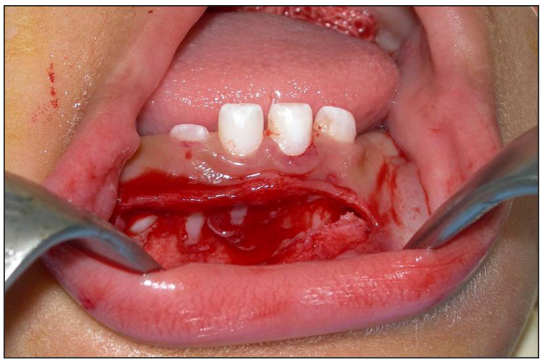

Figure 4. Intraoperative view showing the roots of primary mandibular incisors.

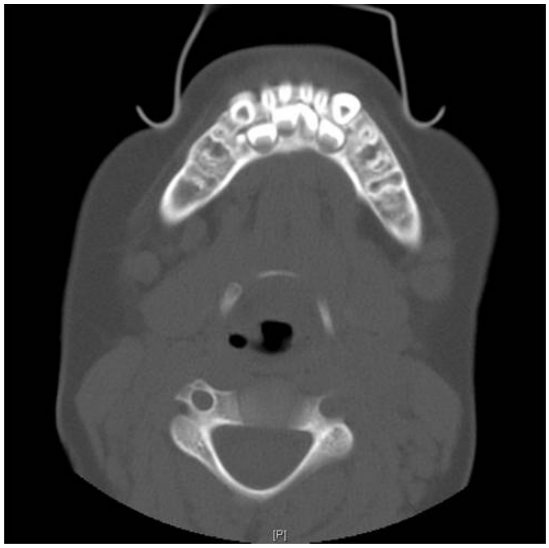

Figure 5. Computed tomography at the level of the mandibular symphysis 1 year after treatment showing complete resolution of the lesion with normal development of permanent teeth.

clinical studies. LCH was classified as either a single system or multisystem type. In addition to that, "risk organs" (hematopoietic system, liver and/or spleen) were associated with a poor prognosis.[18-20]

The most common oral findings of LCH are local pain, swelling, and ulceration. This can be easily confused with common dental infections like periodontitis and periapical disease.[21] Other clinical symptoms also include mobile teeth within the affected area, toothaches, facial asymmetries, and sensory disturbances.[3,7] Infrequently, LCH may be first noted as an asymptomatic radiographic finding during a routine dental examination.[22]

A radiographic evaluation of bony LCH lesions typically reveals noncalcified, lytic areas with or without peripheral sclerosis. This may lead to the typical description of "floating teeth" when the alveolar bone is involved.[23] In a retrospective study, Yu et al.[24] reported that LCH appears as an osteolytic lesion with uneven margins with either a continuous or discontinuous periosteal reaction. Holst et al.,[25] however, reviewed 24 cases of histiocytosis in the jaws and noted that each of these lesions had a round, oval, or irregular radiolucency, occasionally with a periosteal reaction. The radiographic finding in our case seems to be consistent with their findings. Scintigraphy was also found to be a useful aid for evaluating the extent of the disease and monitoring its evolution.[26]

The histological features of LCH lesions include, aside from Langerhans cells, a variable number of eosinophils, neutrophils, mononuclear and polynuclear histiocytes, and lymphocytes.[3,7,9,11] Initial stage lesions tend to be very cellular, whereas in more advanced stages a higher degree of fibrosis is present.[7] Histological appearance does not seem to correlate with the clinical behavior of the disease.[11] Langerhans cells are oval or rounded in shape, pale, and have a predominantly eosinophilic cytoplasm.[5,9] The nucleus is oval or lobulated, with a typical central sulcus, giving it a "coffee bean" appearance. Birbeck's granules, which can be seen inside the Langerhans cells using electron microscopy, are pathognomonic for LCH.[27] Takahashi et al.[28] reported the diagnostic superiority of immunohistochemical staining of CD1a to distinguish LCH from inflammatory changes secondary to periodontitis affecting the alveolar process of the maxilla and mandible on a microscopic level.

Multiple therapeutic modalities have been suggested for the treatment of LCH, such as curettage, resection, radiotherapy, chemotherapy, and intralesional and systemic corticosteroids.[29-31] For patients with single-system LCH, some authors recommend no therapeutic intervention, since spontaneous regression may occur. Others advocate surgical treatment, including curettage or an excisional biopsy.[7,32] Radiotherapy in doses of 6 to 15 Grays has been proposed for inaccessible lesions, those close to vital structures such as the optic nerve, and recurrences of previously resected lesions.[33,34] Oral mucosal lesions without underlying bone disease respond well to perilesional infiltration of triamcinolone acetonide.[12] For patients with multiple LCH lesions, there is no universally accepted single treatment strategy. While radiation alone or single-drug administration has been shown to be insufficient for treatment of multiple bony lesions, most of these patients respond to therapy with a combination of steroids and cytotoxic agents.[8]

In terms of prognosis, single-system LCH (unifocal and multifocal) lesions respond well to treatment, with cure rates up to 80 percent. The overall 5-year survival rate for LCH is approximately 92 percent.[35] In multisystem LCH, reactivation rates depend on the involvement of risk organs and the response to initial treatment.[36,37] It has been reported to range from 2 percent to 25 percent; hence, patients should be closely followed up for a long period of time.[38] The treatment of the multisystem LCH has been evaluated by 3 international prospective studies conducted by the Histiocyte Society.

Different combinations of systemic treatment, including chemotherapy and/or steroids, is available, but the details are beyond the scope of this review.[16]

In summary, LCH of the jaws is a rare disease which is encountered in children more often than adults. Most of the literature supports surgical intervention in isolated lesions. Conversely, multimodal combined therapy is used for more extensive disease that involves multiple systems. A yearly radiographic survey for isolated bony lesions in LCH patients is advocated by the Histiocyte Society, since disease reactivation is a possibility regardless of the treatment chosen.

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