Langerhans Cell Histiocytosis: Impact on the Permanent Dentition After an 8-year Follow-up

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ABSTRACT

Langerhans cell histiocytosis (LCH) is a rare disorder which mainly affects children. Oral changes, such as gingival ulceration, halitosis, osseous lesions associated with tooth mobility, and early loss of primary teeth, comprise the disease's first manifestations for most patients. In the long term, dental changes may occur as a result of dental and systemic treatment. Therefore, this study's purpose is to report Langerhans cell histiocytosis' effects on the permanent dentition 8 years after diagnosis, which had been established by performing a biopsy of gingival tissue on a 3-year-old patient. (J Dent Child 2008;75:64-8) Received August 29, 2006 | Last Revision October 29, 2006 | Revision Accepted November 17, 2006.

KEYWORDS: LANGERHANS CELL HISTIOCYTOSIS, ORAL MANIFESTATIONS, CHILD, PERMANENT DENTITION

Langerhans cell histiocytosis (**LCH**) is a group of clinicopathological disorders characterised by abnormal proliferation of Langerhans cells and whose aetiology is still unknown.[1-4] Such dendritic mononuclear cells are derived from the bone narrow and are usually present in both the epidermis and mucous membrane. They also have important immunologic functions, particularly in antigen developmment to the T-lymphocytes.[3,5,6]

LCH, also known as histiocytosis X, involves 3 distinctive entities (Table 1) presenting similar histopathological characteristics, but with varied clinical features.[1,7] Nevertheless, most authors consider LCH a single disorder, as its signals overlap considerably in its 3 clinical forms, which makes patient classification difficult for a single condition.[1,7-9]

LCH is a rare disease which can affect any age group, with an incidence of 5:1000000. More than 50% of all cases, however, involve children younger than 15 years old.[3] The disease has a peak incidence in 1- to 4-year-old children[3] and affects males more than females.[6,10] Additionally, it can affect different organs, resulting in osseous, skin lesions, diabetes insipidus, lymphadenopathy, anaemia, exophthalmos, hepatomegaly, pulmonary disease, otitis media, fever, leucocytosis, and mental retardation.[3,8] LCH commonly involves the head and neck, particularly skull bones, maxilla and mandible.[3] Among the oral manifestations, intraoral mass, pain, gingivitis, loose teeth, impaired healing, halitosis, oral mucosal ulcer, and paresthesia are commonly seen.[3,8,10]

Through histological examination, a definitive diagnosis can be established.[3,8] Treatment options vary according to LCH's presentation and extension, but they usually include surgical intervention, chemotherapy, radiotherapy, and corticotherapy (both systemic and intralesional).[3,11-13] Some cases of histiocytosis require only periodic management because of the possibility of spontaneous resolution of the lesions.[9] As LCH presents an unpredictable course, recurrence may occur a few months or even one year after the treatment, which emphasises the importance of long-term follow-up.[8,13]

A dental literature review showed no report demonstrating LCH's long-term effects on the developing dentition or on the dentofacial development of patients who had been treated for the disease.[10,14]

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Table. Different clinical denominations and presentations for LCH [2,8,16]	
Letterer-Siwe disease	Acute, fulminant, proliferative form Mostly new-born babies and children younger than 3 years old Disseminated osseous, visceral, and skin involvement
Hand-Schüler-Christian disease	Disseminated, chronic form Clasic triad: Multiple bone lesions of the skull Exophthalmos Diabetes insipidus Mostly children older than 3 years old and young adults
Eosinophilic granuloma	Chronic, localised form Solitary or multiple skeletal lesions No visceral or skin involvement More frequent in children and young adults

Therefore, this study's purpose was to report the effects of Langerhans cell histiocytosis on the permanent dentition of a pediatric patient who had been treated with chemotherapy and followed-up for 8 years.

CASE REPORT

A 3-year, 10-month-old male child of African descent was brought by his mother to the Department of Pediatric Dentistry of the Federal University of Rio de Janeiro, Brazil, with the chief complaint of a loose tooth and gum inflammation. During consultation, the mother reported that she noted swollen gums at 1½ years of age and loose teeth 1 year later. The child was under medical treatment for seborrheic dermatitis at another public institution and he was also being followed-up by a dentist who instructed him on oral hygiene. As no accurate diagnosis was given, the dentist referred the patient to our institution at Federal University of Rio de Janeiro, Brazil.

The patient's medical history revealed frequent episodes of otitis media as well as the use of antibiotics and shampoos for both skin and scalp lesions. Despite the inflammation and tooth mobility, the mother did not note any painful symptoms or eating difficulties. Gingival bleeding, however, occurred during mastication, tooth brushing and spontaneously when the child cried.

Bilateral maxillary swelling, mainly involving the mandible, poor labial sealing, sialorrhea, and cervical lymphoadenopathy, were found during the extraoral examination, which suggested an inflammatory picture. In addition, cutaneous alterations in the scalp were also observed. Poor oral hygiene resulted in excessive accumulation of biofilm and halitosis. The gingiva was severely inflamed with areas of ulceration and necrosis (Figure 1). All the primary teeth had mobility, and some of the permanent teeth (permanent mandibular first molars) had erupted, but without changes. A radiographic examination revealed severe bone loss and poor osseous implantation of both primary and permanent tooth roots, thus configuring the "floating teeth."

LCH diagnosis was established by incisional biopsy of the affected gingiva and histopathological exam, after which the patient was referred to the hematology service of Federal University of Rio de Janeiro, Brazil. The LCH diagnosis was confirmed by biopsies of bone narrow and skin lesions performed by his physician. After further exams to rule out organ lesions, chemotherapy treatment with vinblastine, 6-mercaptopurine, and prednisone was initiated, lasting approximately one year. During this time, the treatment selected was the extraction of all primary with great mobility, and the mother received instructions regarding her child's oral hygiene.

Following chemotherapy, the patient's clinical picture was stabilized as symptoms decreased and his osseous condition improved. The permanent mandibular incisors and maxillary first molars had erupted with no change, despite slight root formation due to early eruption. Also, a

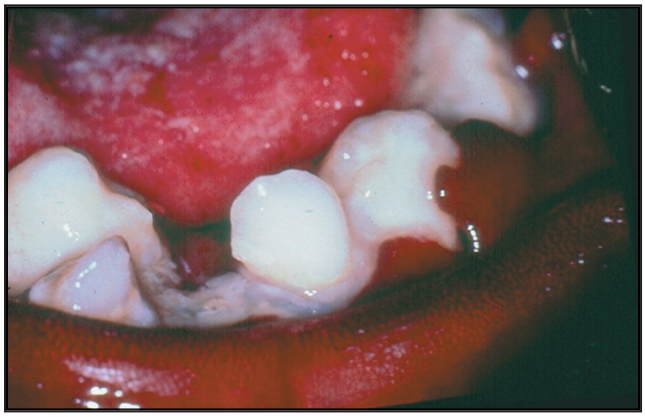


Figure 1. Initial clinical aspect showing severe inflammatory process with areas of ulceration and necrosis.

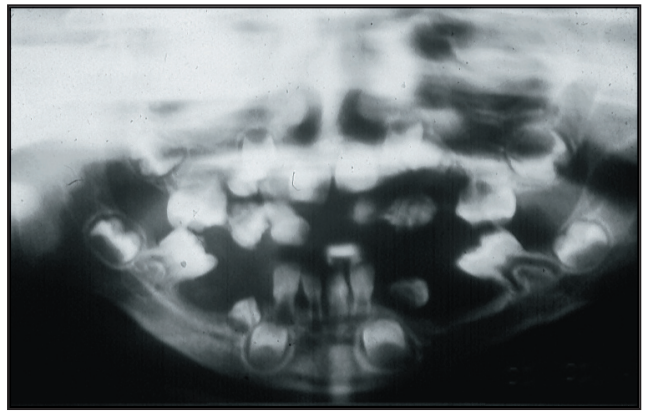


Figure 2. Radiographic examination 1 year after diagnosis. Note abcense of elements 14, 12, 22, 24, 35, and 45.

radiographic exam showed that some permanent teeth were absent, including the maxillary first premolars, maxillary lateral incisors, and mandibular second premolars (Figure 2). The mother was asked about the family's history of missing teeth, but she denied any previous family case.

The patient could not be contacted for 4 years. Then, he returned at 9 years of age. The mother reported that the child had been under medical observation during the past 4 years and that panoramic radiographs were periodically taken for follow-up by his physician. Also, the child was taken to another public dental service institution where tooth restorations were performed whenever necessary.

Following this time, the patient presented white spots and poor oral hygiene. Consequently, follow-up visits were scheduled. Periodontal intervention and endodontic treatment for tooth no. 16 were also done (Figure 3).

Eight years after the LCH diagnosis, the 11-year-old patient presented gingival recession on the buccal and lingual surfaces of his permanent mandibular first molars and permanent mandibular right canine. He had no complaint of sensibility and no furcation exposition, but hypoplasia was present in the permanent mandibular right first premolar, and also dental inclination involving those teeth adjacent to the missing ones (Figures 4 and 5). Also observed were a concave facial profile (Figure 6) with a Class III malocclusion and anterior and posterior crossbites (Figure 7), therefore the patient was referred for orthodontic evaluation.

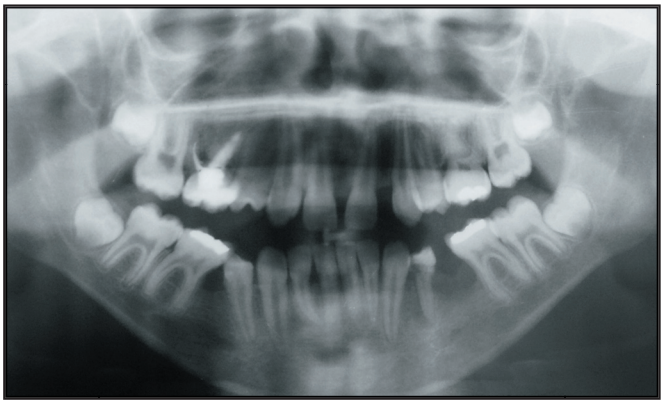


Figure 3. Radiographic examination 8 years after diagnosis.

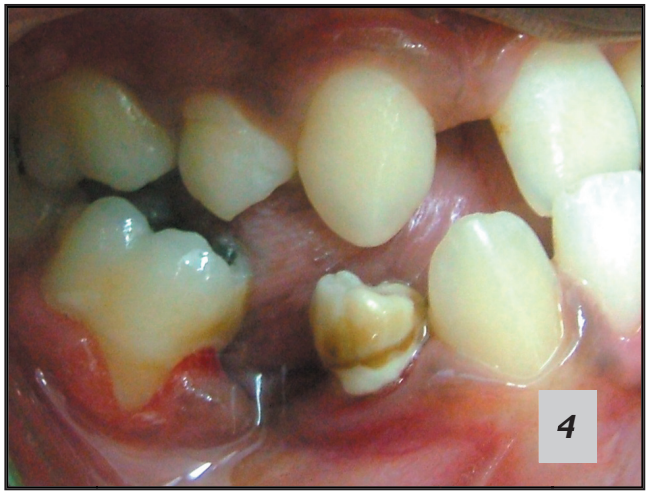
DISCUSSION

Although LCH's pathogenesis and aetiology are unknown,[8,10,15] its clinical characteristics are often reported in the dental literature.[3,12,14] The resulting oral changes are of special interest because they are usually the first, unique manifestations of the disease.[6,10,15] Therefore, dentists play an important role in diagnosing LCH. In the present case, a dentist performed a biopsy of the gingival tissue, which led to an accurate diagnosis. As LCH is a disease predominantly affecting children,[3] pediatric dentists should monitor signals and symptoms because, in general, they are the first professionals to inspect the patient's oral cavity.

In a 1972 study of 50 histiocytosis cases, Sigala et al[16] found that oral development had occurred in 36% of all individuals, only 16% of whom had initially been examined by a dentist. Since, an incidence of 77% of oral manifestations involving such patients has been reported[17] performing an early diagnosis is also important, since LCH may be fatal in more severe cases.[1,8]

This case report's patient presented common oral manifestations, such as gingival ulceration, halitosis, osseous lesions associated with mobility, and early loss of primary molars.[3,16] In addition to these signs, anterior teeth were also involved, which some authors believe is a rare result of the disease's advanced stage.[8,10,14,16]

LCH's prognosis varies, according to some factors, namely by age (it is more severe for children younger than 2 years old), number of sites involved and degree of dysfunction in the affected organs.[14] Although LCH was not diagnosed for this patient at the moment of symptom emergence, his prognosis was favourable because he patient had no changes involving other organ systems, except for skin lesions and advanced oral involvement.



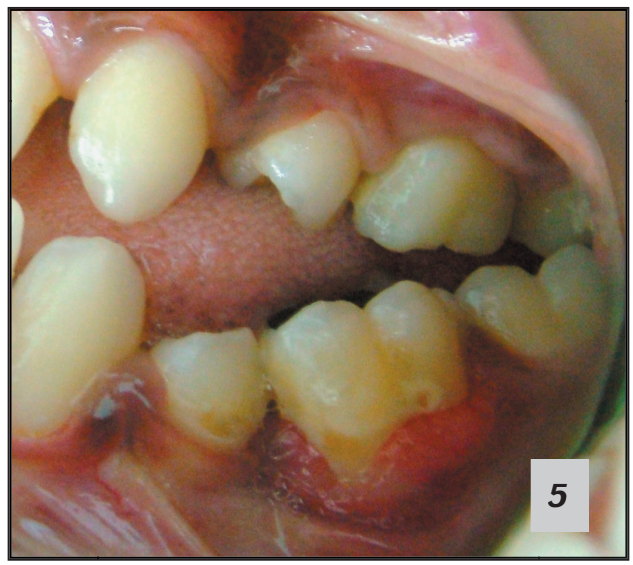


Figure 4 and 5. Lateral view. Note gingival recession on the permanent mandibular first molars.

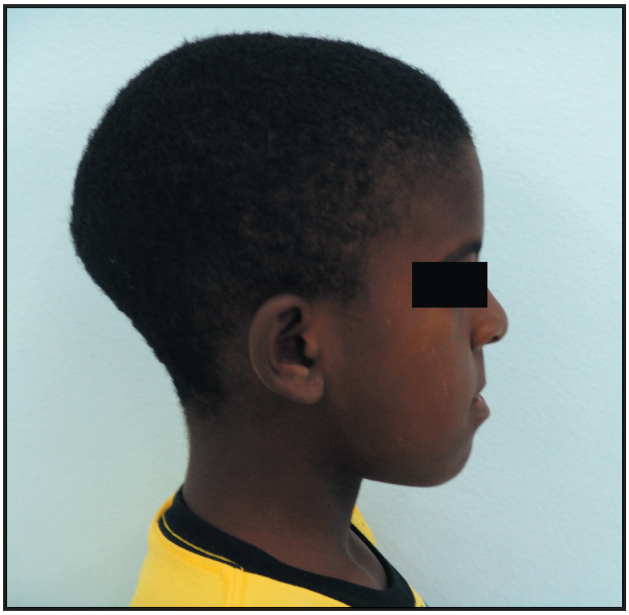


Figure 6. Patients profile showing concave facial profile.

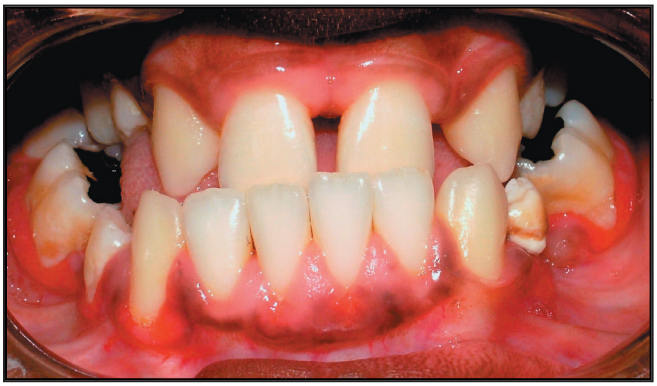


Figure 7. Frontal view showing anterior and posterior crossbites.

It should be emphasised that clinical and radiographic pathognomic manifestations do not exist in LCH.[8] Furthermore, oral symptoms can be confused with other disorders, such as diabetes-associated periodontitis, hypophosphatasia, leukaemia, cyclic neutropenia, fibrous dysplasia, Papillon-Lefèvre disease, agranulocytosis, and malignant neoplasms.[1,14,15] Thus, a definitive diagnosis is confirmed only by histopathological exam. In the present case, bone marrow and skin lesion biopsies were also performed and the results agreed with Hartmann,[8] who demonstrated in 1980 that histopathological characteristics of oral lesions match those found in other organs.

Because of the heterogeneity involving this pathology, there is no consensus about which is the best treatment.[14] Surgical removal is the treatment of choice for single osseous lesions, whereas lesions difficult to access or involving multiple organs are treated with radiotherapy or chemotherapy.[3,8,10] Dental intervention should not include extraction of all teeth involved, but only those having either severe mobility or lytic bone lesions associated with the root apex.[8,10] Therefore, extractions combined with chemotherapy provided intra- and extraoral regression of this patient's symptoms.

According to Jaffe et al,[18] chemotherapy may cause dental changes of varied degrees, depending on the dental developmental stage and the chemotherapy's type and duration. Enamel opacity, hypoplasia, periodontal problems, and high risk of caries are also described by Rosenberg,[19] corroborating some findings regarding this patient.

In addition to the chosen treatment's later outcomes, long-term consequences can be observed in LCH patients, according to Haupt et al.[20] In a retrospective study of 182 individuals, these authors found at least one sequelae in 52% of the sample—the most frequent ones being diabetes insipidus, orthopaedic anomalies, hearing loss, and neurological sequelae. In some cases, such sequelae appeared 10 years after the diagnosis.[20]

Nevertheless, recurrence and systemic outcomes were not found throughout the 8-year period, despite the patient presenting some dental problems. His family history was not indicative of any dental agenesis, and may be a result of the disease. The gingival recession's causes and mechanisms of development are considered very complex and difficult to establish,[21] as seen in this case. The findings regarding permanent dentition agree with Sigala et al,[16] who stated that LCH often affects dental development and residual outcomes may occur following disease interruption.

Therefore, in addition to adequate multidisciplinary care, long-term follow-up is needed for these patients to rule out any possibility of LCH's recurrence. Also, the permanent dentition's development should also be followed-up so that any change can be diagnosed and adequate treatment can be carried out.

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