CASE REPORT

Premature loss of primary teeth with gingival erythema: An alert to dentist

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ABSTRACT

Premature exfoliation of primary teeth is an important diagnostic event warranting urgent investigation. The majority of conditions presenting with early loss of teeth are serious and in some cases could be fatal. The most common causes of premature tooth loss are Papillion-Lefevre syndrome, Chediak-Higashi syndrome, hypophosphatasia, neutropenia, leukemia and in some cases Langerhans cell histiocytosis (LCH). LCH is a disorder of unknown cause, characterized by abnormal proliferation of histiocytes. The disease has a predilection for children, although LCH may occur in adults. Owing to the relative rarity of the condition, it remains a disease in which the diagnosis is often delayed or missed and in which many questions remain unanswered, ranging from etiology and pathogenesis to therapy. The purpose of the review is, therefore, to raise awareness of the disease and to highlight the clinical findings that should make the odontologist or primary caregiver suspect the diagnosis.

Key words: Diabetes insipidus, gingival erythema, histiocytes

INTRODUCTION

Premature exfoliation of the primary teeth in children is attributed to multisystemic diseases. Langerhans cell histiocytosis (LCH) is included in the differential diagnosis for children presenting with gingival inflammation and bone loss in primary dentition. LCH commonly involves the oral and maxillofacial region and comes to the attention of dental practitioners when a patient presents with hard and soft tissue involvement.

Histiocytosis is the general term used to indicate some reticuloendothelial system diseases. These conditions are the result of accumulation or primary proliferation of the mononuclear phagocytic system. Histiocytosis encompasses two types of immune cells:

- Macrophages
- Dendritic cells.[1]

LCH, formerly known as histiocytosis X, is one of a group of poorly understood diseases of histiocytes.[2] LCH is characterized by intense and abnormal proliferation of bone marrow-derived histiocytes (Langerhans cells), along leucocytes, eosinophils, neutrophils, lymphocytes, plasma cells and giant multinucleated cells causing tissue destruction. This tissue destruction is because of the cellular infiltration that replaces bone and invades the skin, mucosa and internal organs.[3]

The clinical presentation of disease ranges from the chronic, localized form to acute leukemia - like disease with a fatal outcome. Alfred Hand was the first to report a case of histiocytosis in 1893. Later, in 1941, Farber described this condition when reporting the overlap among diseases that would later be termed histiocytosis X. Since that time, numerous case reports have been reported in the dental literature, each having a diverse focus and using inconsistent terminology.[2] Here we present a case of LCH, which highlights the disease aggressiveness and emphasizes the importance of a dentist in its early diagnosis.

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CASE REPORT

A 4-year-old, female patient was brought by her father to the Department of Oral Surgery with chief complaints of pain while chewing food, mobility of teeth and increased water uptake since 3 months. Her father also denied any history of fever, rash and allergy. The medical history revealed that diabetes insipidus was diagnosed 3 months back at All India Institute of Medical Sciences, New Delhi for which the patient had not taken any medication. The family history was unremarkable.

On examination, there were no extraoral findings. Intraoral examination revealed generalized gingival erythema. The gingiva was tender and bled on palpation. Generalized tooth mobility was evident. Some of the teeth appeared to be supported by the soft tissue only. Many deciduous teeth were already exfoliated and the remaining teeth showed abundant calculus deposits causing severe halitosis [Figure 1].

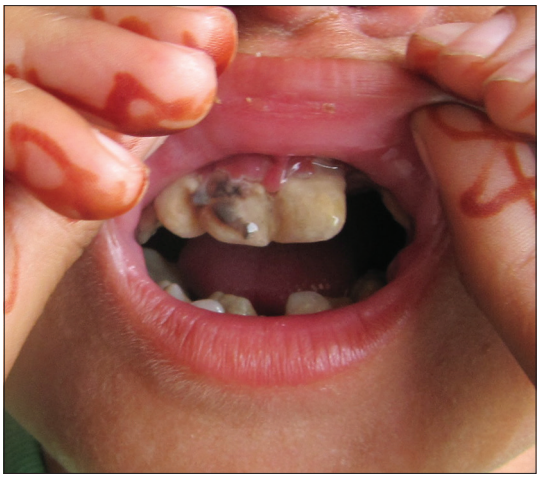

Figure 1: Gingival erythema with calculus deposits on the crowns

Radiological examination

Orthopantomogram revealed mixed dentition in all the four quadrants with few exfoliated deciduous teeth present. Generalized bone loss extending up to the apical third of roots is also evident [Figure 2].

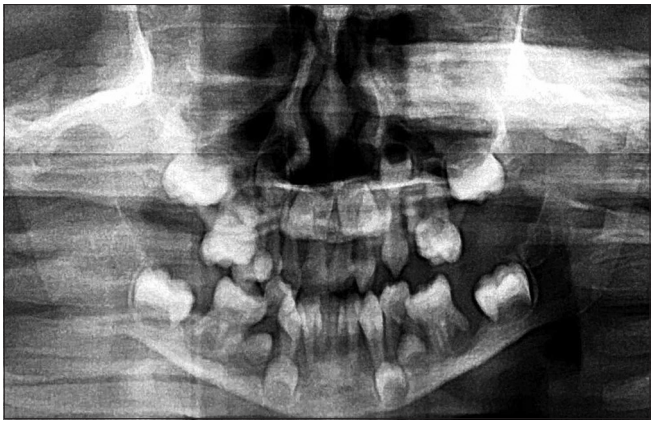

Figure 2: Orthopantomogram showing generalized horizontal bone loss extending up to the apical third of roots

Anterior and posterior projections of bone scan using technetium-99m labeled methylene diphosphate showed multiple foci of intense activity on the right parietal bone of cranium, mandiblec and right femur.

Histopathological features

An incisional biopsy was performed under local anesthesia. The gross specimen consisted of three small bits of soft tissue from the lower anterior region. All the soft tissue bits were creamish white in color and soft in consistency. Histopathological examination revealed an admixture of inflammatory cells including many eosinophils with Langerhans cells. These large mononuclear histiocytic cells are round or oval in shape, with a vesicular nucleus and moderate quantity of eosinophilic cytoplasm. Lymphocytes and mononuclear phagocytes were also found accompanying these cells. Areas of hemorrhage were also evident [Figure 3]. Mononuclear histiocytes were immunohistochemically identified as Langerhans cells by the presence of antigens S-100 and CD1a [Figures 4 and 5]. A final diagnosis of LCH was made based on the clinical, medical, radiological and histopathological examination.

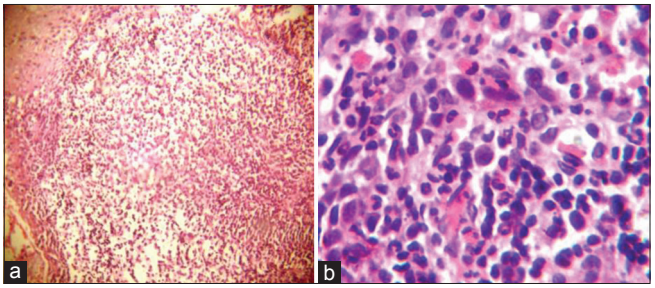

Figure 3: (a) Superficial surface epithelium with underlying connective tissue showing chronic inflammatory cells (H & E stain, x40). (b) Infiltrates of histiocytes, lymphocytes and presence of eosinophilic granuloma are observed in the connective tissue (H & E stain, x400)

Treatment plan

Since the child was young and her erythematous gingiva was painful. She received gingival and periodontal care including regular scaling, a short course of metronidazole, preventative advice, and continued monitoring by the Department of Pedodontics. She was also sequentially referred to the Department of Pediatric Medicine for the better management of diabetes insipidus. The patient is on regular follow-up since last 6 months and is on multidisciplinary inputs.

DISCUSSION AND LITERATURE REVIEW

The term histiocytosis X was a generic term developed as a result of similarities in the pathophysiology among the

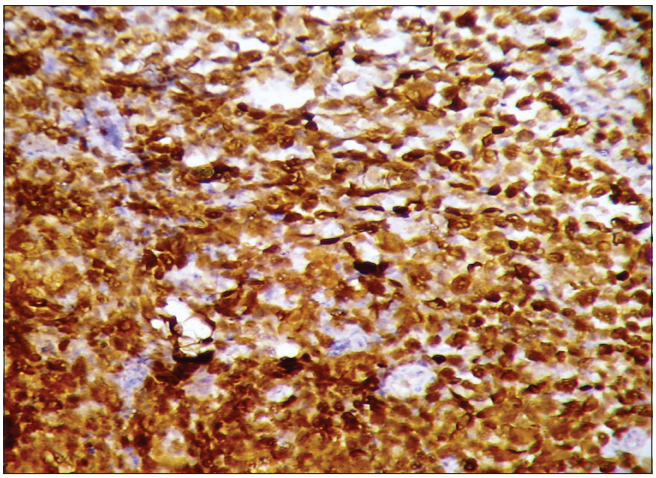

Figure 4: S-100 immunopositivity in nucleus and cytoplasm of Langerhans (IHC stain, x400)

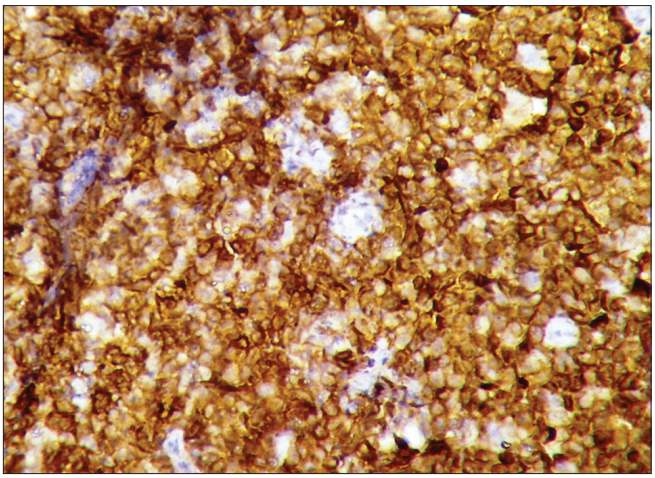

Figure 5: Uniform membrane staining of Langerhans cells with CD1a (IHC stain, x400)

diseases of histiocytes, as well as the shared clinical and histological features.[2]

Classification of histiocytosis

Histiocytosis, according to histiocyte society, is traditionally classified into three main groups:

- Class I: (LCH), formerly called X histiocytosis
- Class II: Histiocytosis of other mononuclear phagocytes different from Langerhans cells
- Class III: Histiocytic malignancies.[1]

Classification of Langerhans cell histiocytosis

Lichenstein classified LCH into three clinical forms depending on the age of the patient when the lesions first appear and their distribution. Although other classifications have been proposed, this remains the most commonly used term in the literature, adding congenital reticulohistiocytosis described some years later.

- Chronic focal LCH (eosinophilic granuloma): Is considered the most frequent and benign of the clinical forms. It appears as a uni- or multi- focal lesion in a single, or occasionally various bones, with or without soft tissue involvement, without systemic involvement and presenting at any age[3]
- Chronic diffuse LCH (Hand–Schüller–Christian disease): Usually seen in children or young adults, with lesions that arise desynchronously over the years.[3] It consists of skeletal and extraskeletal lesions.[4] It manifests with the characteristic triad of exophthalmos, osteolytic lesions of the cranium and diabetes insipidus. Other manifestations, petechiae, purpura, ulcerations, lesions mimicking seborrheic dermatitis, pulmonary dysfunction, tachypnea, dyspnea and cyanosis, may appear. This clinical form may mimic cystic lesions, leukemia, lymphoma, metastasis, meningioma and congenital processes such as encephalocele[3]
- Acute disseminated LCH (Letterer–Siwe disease): The patients are generally children under 3 years of age, who, due to the aggressive behavior of the disease follow a fatal course in a short time.[3] The characteristic features are fever, rash, lymphadenopathy, hepatomegaly and splenomegaly, osteolytic lesions and general skin eruptions (petechiae, scaly papules, nodules and vesicles)[1]
- Congenital reticulohistiocytosis (Hashimoto–Pritzker syndrome): Believed to be a purely cutaneous form, which appears in the form of dark nodules on the trunk, face and scalp. The mucosae are always involved, without implication of other organs.[3]

Epidemiology

LCH is an infrequent disease.[3] The National Pediatric Institute (Instituto Nacional de Pediatria) reports a total of 224 patients treated in the period 1970–1999. Out of this number, gingival lesions were identified in 21 patients.[1]

The annual incidence of LCH is reported to be between 2.6 and 5.4 cases per million children in the general population. The highest incidence of initial diagnosis is from 1 to 3 years, but the disease may manifest at any age.[5] It is more common in males. Aggressive forms occur mainly in young children.[1]

Etiopathogenesis

The pathogenesis of LCH is unknown and various hypotheses have been postulated about its possible etiology.[3]

Pathologic Langerhans' cells are thought to be derived from precursor cells or through alteration of normal histiocytes. The mechanism by which this proliferation and accumulation takes place remains unknown.[2] Deficiency of suppressor lymphocytes (T8), altered immunoglobins, autoantibodies, anomalous lymphocytic response to various mitogens and

structural changes in the thymus in all the advanced forms have been found in LCH patients.[3]

Viruses have been found to play a role in LCH, but their involvement remains theoretical.[2] An inflammatory origin is also suspected due to the microscopic characteristics and clinical evolution; or a bacteriological origin, although no specific causal microorganisms have been identified.[3] In adults, cigarette smoking is a clear risk factor for pulmonary LCH. The exact relationship of this sometimes polyclonal lung disease to the monoclonal forms of the disease remains to be explained, particularly in view of a Swedish study which raised the possibility of an increased risk for the development of lung LCH in adult survivors of pediatric LCH who smoke.[6]

The systemic alterations in these patients result from the accumulation of Langerhans cell infiltrate that produces different clinical manifestations depending on the location.[3]

Clinical picture

The clinical course of LCH varies considerably depending on the extent and number of organs involved, as well as the age of the patient at the time of diagnosis.[2] In disseminated disease instances, many organs are compromised and several general expressions of the disease can be present, such as fever, anorexia, weight loss, anemia, hemorrhagic manifestations (petechiae on the trunk) asthenia and irritability.[1]

The relative frequency of organ system involvement is as follows: Bone, 80%; skin, 60%; liver, spleen, lymph nodes, 33%; lungs, 25%; orbit, 25% and maxillofacial, 20%.[2]

Diabetes insipidus is the most common endocrine problem with multisystem disease ranging from 22% to 50%.[7] Involvement of endocrine system with established diagnosis of diabetes insipidus was observed in the present case by the department of oral medicine.

Oral manifestations

The oral changes are the first clinical signs in all forms of LCH and on some occasions the oral cavity may be the only affected area.[8] The incidence of oral lesions in LCH is 77%. Therefore the initial diagnosis in many cases is made by the odontologist.[1]

Mucosal lesions

There is pain and gingival inflammation (swelling). Upon palpation, it is found tumor like, which corresponds to Langerhans cell accumulation. This evokes oral ulceration with the possibility of tooth loss. Premature loss of deciduous teeth associated with bone loss is a clear sign of histiocytosis. Anterior teeth involvement is infrequent and indicative of a negative prognosis.[1]

Bone lesions

Bone is the most common single organ of involvement in childhood LCH and the majority present with a single bone lesion.[6] Solitary LCH may occur in any bone, although there is a predilection for the flat bones, with more than half of skeletal lesions occurring in the skull, mandible, ribs and pelvis. Lesions in the mandible and maxilla begin around the tooth roots, so that the teeth, which are never affected, remain dense and appear to float in the air.[5]

Multiple alveolar lesions: Normally present with well-defined though not corticated margins. However, 37.7% of alveolar lesions may have poorly-defined or invasive margins. "Scooped-out" alveolar lesions: Formed by bone destruction beginning below the alveolar crest, either at furcation level or at half the tooth root height and normally a part of the coronal portion of the bone crest remains intact on the mesial and/or distal margin of the damaged bone. This form of intrabony destruction is not seen in periodontal disease and may, therefore, be useful for a differential diagnosis.[3]

Periodontal lesions

Alveolar bone lesions form the basis for all the associated periodontal involvement in these patients. As new osteolytic areas develop, gingival ulceration and inflammation are observed, such that all the quadrants of the oral cavity are affected to a greater or lesser degree, even though the process begins initially in only one quadrant.[3]

As a result of the alveolar bone loss, these patients manifest gingival inflammation, ulceration, destruction of the keratinized gingiva, gingival recession, periodontal pockets and bleeding of the oral soft tissues, associated with pain and even swelling. As a consequence of this bone loss, the teeth begin to progressively move giving rise to the characteristic "floating teeth," completely surrounded by a radiolucent defect accompanied by dental displacement, odontalgia and on occasions, cervical adenopathies. This excessive mobility gives rise to the inevitable premature loss of these teeth.[3] This premature loss of deciduous teeth was present in our case also.

Diagnosis

The diagnosis is confirmed by histopathological examination supported by clinical and radiographic examination.[8] Histopathological characteristic of the lesion consists of a proliferation of Langerhans cells, which is immunohistochemically identified by the presence of the antigens S100 and CD1a.[4] Langerhans cells are round or oval in shape, with a vesicular nucleus, a moderate quantity

of eosinophilic cytoplasm and laminated or dispersed distribution. Abundant eosinophils and other inflammatory cells such as lymphocytes and mononuclear phagocytes may be found accompanying these cells.[3,4]

Electron microscopy reveals Birbeck granules in the lesional cells, described as organelles with rod-shaped or tennis racket morphology that could represent structural changes of the membrane following contact with an antigen. The percentage of histiocytes with Birbeck granules is not related to prognosis.[3]

Treatment

The treatment depends on the extent and severity of the disease. When lesions are large or locally invasive, treatment by curettage, low dose radiation therapy, or steroid injection is effective. Disseminated and multifocal LCH can be successfully treated with chemotherapy and thymus extraction.[7] Although spontaneous regression of localized disease has also been reported in the literature.[9]

Therapy is often unnecessary for patients with cutaneous LCH, but very young children should be carefully monitored to determine the progression to an advanced disease. Local or systemic corticosteroids are the first line of therapy in mild forms of cutaneous LCH while the most severe forms may need mild chemotherapy.[10]

CONCLUSION

Thus, the diagnosis of LCH in a lesion simulating periodontal disease is a must to prevent unnecessary delay in the diagnosis and management of such lesions. This lesion should be differentiated from other diseases and tumors which can cause similar alveolar bone loss, keeping in mind the different treatment strategies to be applied in such diseases.[11] It is of paramount importance for the dentist to be more aware about LCH, since oral lesions can well be the first manifestation of the disease and in many cases, the oral cavity can be the only affected site.[1]

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Conflicts of interest

There are no conflicts of interest.

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