

# A rare and unusual case report of Langerhans cell histiocytosis

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## Abstract

Langerhans cell histiocytosis (LCH), previously known as histiocytosis X, is an uncommon hematological disorder affecting infants and young children. It is the condition characterized by uncontrolled stimulation and proliferation of normal antigen presenting cells, Langerhans cells. Because of its relatively low incidence, limited data are available regarding the epidemiology of LCH, with estimation of 2–5 cases per million inhabitants per year. The purpose of this report is to describe the case of LCH in the 3-year-old male child with multiple focal involvements of bones and to discuss clinical, radiological and histopathological features of LCH and role of the dental surgeon in diagnosing and managing such lesions.

**Keywords:** Eosinophilic granuloma, gingival ulceration, Langerhans cell histiocytosis

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## INTRODUCTION

Langerhans cell histiocytosis (LCH), previously known as histiocytosis X, is an uncommon hematological disorder affecting infants and young children. It is the condition characterized by uncontrolled stimulation and proliferation of normal antigen presenting cells, Langerhans cells. Although because of its relatively low incidence, limited data are available regarding the epidemiology of LCH, with estimation of 2–5 cases per million inhabitants per year in the year 2009.<sup>[1]</sup> The diagnosis of LCH is mainly based on histopathological examination, and the disease is broadly categorized into three disorders based on the clinical presentations, each of which is staged clinically according to Greenberg *et al.* clinical staging system.<sup>[1]</sup> Oral involvements are commonly the first manifestation in LCH, but the initial symptoms are generally nonspecific,

causing misdiagnoses.<sup>[1]</sup> The purpose of reporting this case is to discuss clinical and radiological features of LCH and role of dentists in diagnosing and managing such lesions. Management and prognosis of LCH are based on the clinical presentation of the lesion.

## CASE REPORT

A 3-year-old boy [Figure 1] reported along with his mother to the Department of Pedodontics and Preventive Dentistry, AME's Dental College and Hospital Raichur, with the chief complaint of painful gingival growth in the upper and lower, right and left regions of jaw since 1 month. Pain was sudden in onset, intermittent in nature, nonradiating and aggravates on mastication and relieves on its own. Past dental history revealed that they visited to private dental clinic 1 month back with the similar chief

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complaint and routine analgesics and antibiotics were given. However, there was no improvement in patient's condition and was referred to AME's Dental College for treatment. There was no relevant history of trauma and medical history and family history were insignificant.

On general examination, patient was healthy and moderately built except the complaint. Extraoral examination revealed a diffuse swelling in relation to the left side of lower jaw, 4 cm × 2 cm in size extending from lower border of the body of mandible to the superior border of ramus of mandible. The swelling was firm in consistency and tender. There were palpable left submandibular lymph nodes 0.5 cm × 2 cm sized, firm and nontender. All inspectory findings were confirmed on palpation.

Intraoral examination exhibited a diffused, erythematous swelling over attached gingiva with respect to 55, 65, 75 and 85 over buccal aspect and 55 and 65 with a palatal aspect. Mucosa over the swelling was ulcerated covered with necrotic slough with tiny bleeding spots with 55, 65, 75 and 85 [Figure 2a-d]. Grade II mobility was recorded with 55, 65, 75 and 85. Intraoral periapical radiograph of 55, 74 and 75 revealed a mild radiolucent lesion surrounding the root of 55, 74 and 75 [Figure 3a and b].

Based on the case history, a provisional diagnosis was made as localized chronic periodontitis with 55, 65, 75 and 85. The differential diagnoses were made as Papillon-Lefevre syndrome, Eosinophilic granuloma and cyclic neutropenia. Blood investigations revealed anemia (10.5 g%), and the peripheral blood smear revealed microcytic hypochromic anemia. The findings of complete urine and liver function tests were normal; creatine (0.3 mg/dl, normal = 0.4–1.4 mg/dl) and C-reactive protein (2.5 mg/dl normal ≤2.8 mg/dl) levels were in normal range. Patient was negative with HIV and hepatitis B surface antigen.

Orthopantomogram [Figure 4] revealed multiple areas of bone loss in the left mandibular region. Axial and coronal computed tomography [CT] [Figure 5a and b] revealed multiple soft tissue density lesions with irregular and punched out bony destruction noted involving left mandibular, left side of occiput, right maxillary and right temporal bone. Three-dimensional CT [Figure 6] revealed multiple osteolytic lesions in relation to maxillary alveolar process, body and ramus of the left side of the mandible.

Histopathology revealed hypercellular discohesive singly scattered Langerhans cells which are having abundant eosinophilic cytoplasm with characteristic retiform,



Figure 1: Extraoral photograph of patient

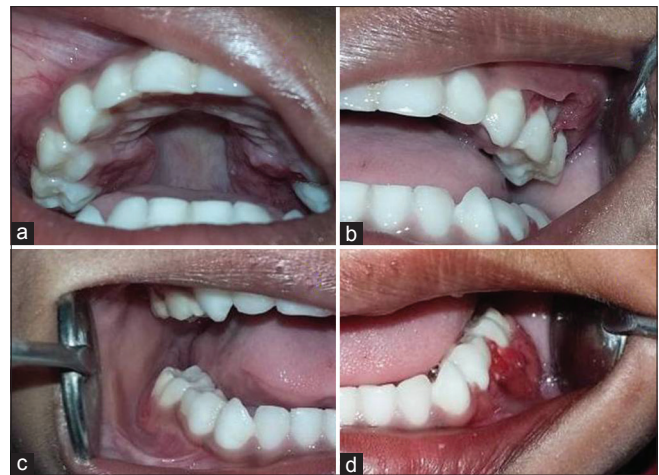


Figure 2: Clinical photograph showing (a) gingival swelling on palatal aspect of 54.55 and 64.65 (b) diffused, erythematous ulcerated gingival swelling covered with necrotic slough over buccal aspect of 64.65 (c) and (d) gingival swelling with tiny bleeding spots over buccal aspect of 75 and 85

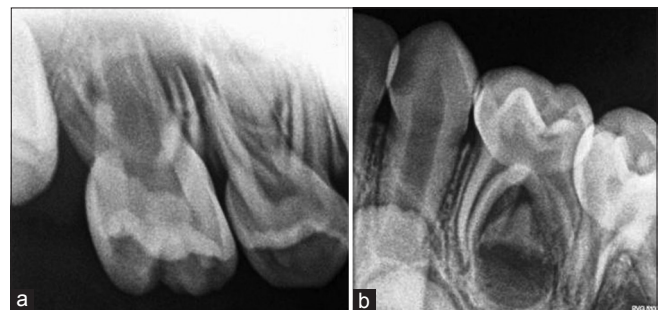


Figure 3: (a and b) Intraoral radiograph showing radiolucent lesion surrounding root of 55, 74 and 75

convoluted nuclei with distinct longitudinal grooves. Also seen are binucleated and multinucleated cells with similar nuclear features. Background is showing a variable number of lymphocyte, eosinophils and plasma cells and occasional mitosis [Figure 7].

The definitive diagnosis of LCH involving multiple bones was considered. It was correlated on the basis of clinical, radiographical and histopathological findings. The patient was referred to the nearby cancer institute for further treatment.

## DISCUSSION

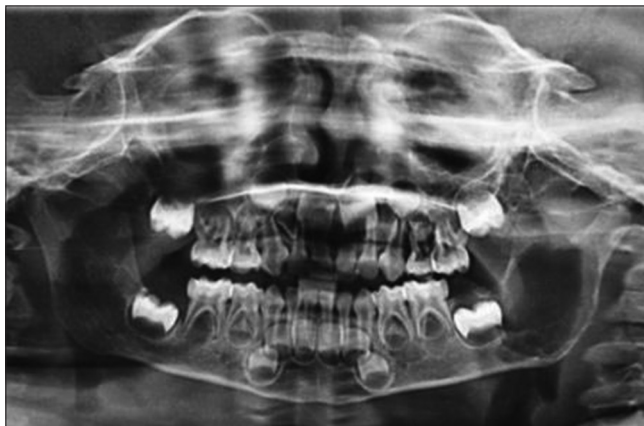
LCH, formerly called histiocytosis X, was introduced as a collective term to represent a spectrum of clinicopathological conditions that are characterized histologically by a monoclonal proliferation of histiocyte-like cells accompanied by varying numbers of eosinophils, lymphocytes, plasma cells and multinucleate giant cells.<sup>[1]</sup> The histiocytes present in this lesion have been identified as Langerhans cells. Langerhans cells are dendritic mononuclear cells normally found in the epidermis, mucosa, lymph nodes and bone marrow. Their normal function is to process and present antigens to T-lymphocytes; however, in LCH, literature review suggests a monoclonal proliferation of Langerhans cells leading to destruction of hard and soft tissues.<sup>[2]</sup> For many years, it has been considered as a reactive disorder of immune regulation and

not true neoplasm. However, recent evidence has shown monoclonal proliferation of lesional cells, findings that is indicative of neoplastic lesion.<sup>[3-5]</sup>

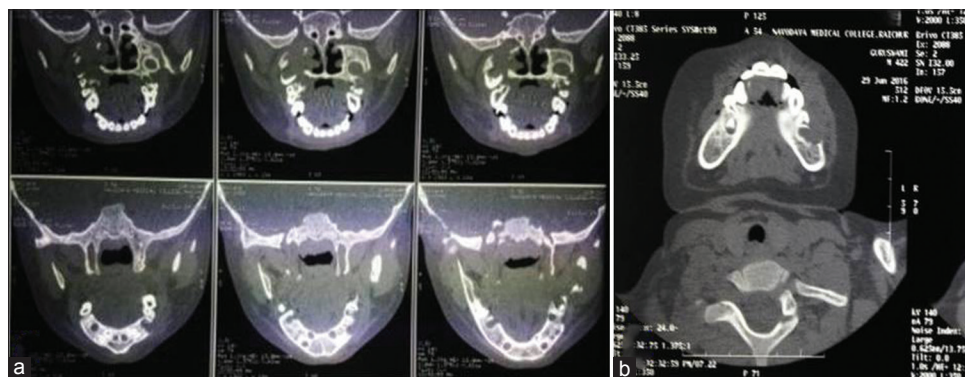
LCH usually encountered in children between 1- and 15 years old with a peak incidence between 2 and 4 years of age, with male predilection twice that of female.<sup>[6]</sup> Among children under the age of 10 years, yearly incidence is thought to be 1 in 200,000.<sup>[7]</sup> The present case was reported in a 3-year-old male child. Solitary or multiple bone lesions are the most common clinical presentations seen in the majority of cases, involving skull, jaws, ribs and vertebrae. Among jaws in particular, posterior aspect of the mandible is more commonly involved, especially the region distal to canine.<sup>[8]</sup> In the present case, skull and posterior aspect of mandible was involved.

LCH is classified into three categories based on the age and clinical presentation. These variants include (1) acute disseminated form with multiple system involvement often occurring mainly in infants known as Letterer–Siwe disease. (2) Chronic localized form with solitary or multiple skeletal lesions and occasionally extraskeletal involvement mainly seen in adult known as eosinophilic granuloma. (3) Chronic disseminated form with osseous lesions which are frequently multiple and with extraskeletal lesions known as Hand–Schuller–Christian disease. Hashimoto–Pritzker syndrome is a congenital form of LCH presenting with deep subcutaneous skin lesions.<sup>[9-10]</sup> In the present case, the patient exhibited a multiple skeletal lesion with no extraskeletal involvement; hence, it was considered as eosinophilic granuloma.

LCH has a broad clinical spectrum, wherein clinical course varies considerably upon the age of the patient and extent and a number of pathological infiltration of Langerhans cells in various organ systems of body such as bone, skin, lymph nodes, bone marrow, liver, spleen, lung, endocrine



**Figure 4:** Orthopantomogram revealed multiple areas of bone loss in the left mandibular region



**Figure 5:** (a and b) Axial and coronal computed tomography revealed multiple soft tissue density lesions with irregular and punched out bony destruction noted involving left mandibular, left side of occiput, right maxillary and right temporal bone

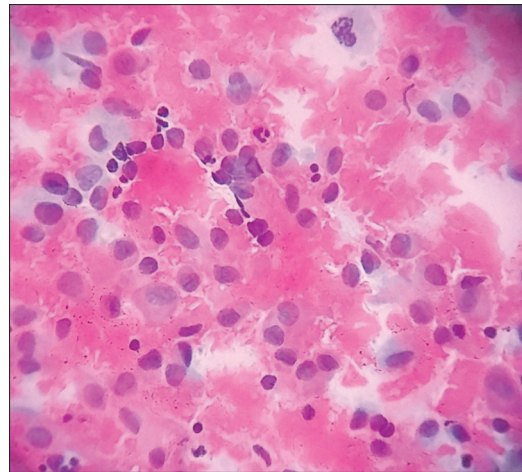


**Figure 6:** Three-dimensional computed tomography revealed multiple osteolytic lesions in relation to maxillary alveolar process, body and ramus of left side of mandible

system, ear and brain. Bones of the skull bones commonly involved are orbital and temporal bones, the sella turcica and mandible, as well as the ribs and pelvis. 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%.<sup>[11]</sup>

Oral manifestations are the earliest manifestations seen in around 5%–75% of patients. In some occasion, it is the only manifestation of LCH, as seen in the present case, hence, leading the patient to visit a dentist. Oral signs include sore mouth, halitosis, gingivitis, gingival hypertrophy and unpleasant taste, mobility of teeth with alveolar expansion, jaw pain, facial swelling, mental nerve anesthesia and failure of extracted tooth sockets to heal. Loss of supporting alveolar bone mimics advanced periodontal disease.<sup>[12]</sup> In the present case, gingival swelling associated with bleeding, ulceration and necrosis was present along with Grade II mobility of primary second molars and pain and swelling in the left posterior region of mandible.

The radiological features are present due to the destruction of bone by Langerhans cells that are similar in all three forms of LCH. This process of bone destruction may involve any part of any bone; however, in head and neck region, it is commonly involved in the posterior region of mandible. In the disseminated form of the disease, multiple areas of bone destructions are involved, of varying size leading to perforation of the cortical plate which leads to pathological fracture. At the base of mandible, lesions are often present as multiple punched out radiolucencies without a corticated rimming suggestive of active disease, occasionally giving an ill-defined pattern, probably due to the confluence of many smaller lesions<sup>[14]</sup> which was



**Figure 7:** Histopathological picture showing diffuse infiltrate of Langerhans cell with eosinophils (H&E stain, x40)

observed in this case also. In the present case also, multiple soft tissue density lesions with irregular and punched out bony destruction noted involving left mandibular, right maxillary, right temporal bone and left side of occiput were present. Involvement of superficial alveolar bone shows characteristic “scooped out” appearance with floating of teeth, displacement, periodontitis and often loss of teeth at a very early age. The mucosal lesion may develop as gingival mass if lesion has broken out of the bone.<sup>[15]</sup> In the present case, similar features were present.

As there are no pathognomonic clinical and radiographic features of LCH are there, the diagnosis of LCH is based on histopathological examination. The histopathological pattern demonstrates a diffuse infiltration of pale staining mononuclear cells that resemble histiocytes with indistinct cytoplasmic borders and rounded or indented vesicular nuclei. The number of eosinophils vary and are typically interspersed among the histiocytes along with the presence of plasma cells, lymphocytes and multinucleated giant cells. The histopathology is similar in all LCH variants except in acute disseminated form as they also demonstrate acute form of lymphomas.<sup>[13]</sup> In the present case, similar histopathological features were seen.

Based on clinical and radiological findings of the present case, LCH was included in the differential diagnosis for children presenting with advanced periodontal disease and/or bone loss in the primary dentition. Other differential diagnoses were multiple myeloma and metastatic carcinoma; they were also ruled out as there were no general systemic manifestations or any other skeletal abnormalities.

Treatment of LCH remains controversial due to high variation in clinical features and absence of standard

diagnostic and evaluation criteria. The treatment of LCH depends on the pathogenesis of disease, age of the patient and dissemination of the lesion. The dental surgeon is limited to the treatment of the oral manifestation of this group of diseases. The systemic treatment should be carried out by a specialist. Localized oral lesions which are accessible as those in maxilla and mandible may be treated by surgical curettage or excision. Low doses of radiation may be used for less accessible lesions although the chance of malignancy secondary to this treatment is a concern in younger patients. Intralesional corticosteroid agents may be effective in some patients with localized lesions (e.g., prednisolone 20–30 mg/day for 2–4 weeks and then followed by tapering of the dose). Multisystemic disease needs systemic chemotherapy. The most common agents used in different combination regimens and several cycles are corticosteroids, vinblastine, etoposide, cytarabine, 6-mercaptopurine, methotrexate, 2-chlorodeoxyadenosine, cyclosporine, thalidomide and others. A combination of vincristine and prednisone seems to reduce the risk of recurrence.<sup>[13]</sup>

Prognostic criteria for LCH include (1) age – children <2 years generally have disseminated disease and a poorer prognosis; (2) number of sites involved - multisystem disease carries a poorer prognosis and (3) organ dysfunction, which, if present, also results in poor prognosis.<sup>[11]</sup>

The purpose of reporting this case report in a 3-year-old child is that it is rare and unusual. Oral manifestations of LCH mainly help in diagnosis. These oral manifestations may easily be mistaken for common dental disorders such as periodontal and periapical diseases. Hence, common oral findings have to be carefully observed, diagnosed and investigated by the dental surgeon to rule out systemic involvement as oral cavity is the indicator of systemic diseases.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will

not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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