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Langerhans cell histiocytosis: oral and orbital manifestations

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Abstract

Background: Langerhans cell histiocytosis (LCH) is a rare disorder of the reticuloendothelial system associated with proliferation of Langerhans cells and mature eosinophils with unknown etiology. This report aims to present a case of LCH with diffuse involvement of the oral cavity and to raise awareness of the distinguishing features of this diagnostically challenging entity.

Case Report: A 5-year-old male patient presented with complaints of teeth mobility, intense pain, and difficulty in chewing. Radiological examinations revealed widespread alveolar bone loss with erosion of wall of orbit. Biopsy revealed Langerhans cells and positive reaction to S-100 and CD1, and the patient was diagnosed with LCH. The patient underwent systemic chemotherapy.

Conclusion: The rarity and variable system involvement of LCH necessitate a multidisciplinary approach be carried out for accurate diagnosis, effective treatment, and an uneventful follow-up. Awareness of oral manifestations of LCH may aid clinicians greatly in reducing morbidity and mortality associated with this debilitating condition.

Keywords: Langerhans cell histiocytosis, pedo patient, oral cavity, orbit

Introduction

Langerhans cell histiocytosis (LCH) is a rare disorder of the reticuloendothelial system characterized by intense and abnormal proliferation of bone marrow-derived immature myeloid dendritic cells-Langerhans cells in the skin, bone, lymph nodes, and other organs with unknown etiology.[1, 2] It mainly affect children. The incidence of the disease is reported to be 8.9 per million in children and 1-2 cases per million in adult populations.[1- 4] LCH is a reactive disease that may result from environmental or other triggering factors, which leads to the aberrant reaction between Langerhans cell and T-lymphocytes.[2]

It was previously classified into three different clinical entities including eosinophilic granuloma, Hand–Schuller–Christian disease and Letterer–Siwe disease.

Eosinophilic granuloma of the monostatic and multifocal form which affects children and young adults and manifests as solitary or multiple skeletal lesions without extra skeletal involvement. The chronic and disseminated form of LCH termed as the Hand–Schuller–Christian syndrome consists of skeletal and extra skeletal lesions usually affecting children below 3 years of age. The Letterer–Siwe syndrome is a disseminated acute or subacute form of LCH, that is, most often fatal because of extensive skeletal and extra skeletal lesions; this form usually affects infants and children below 3 years of age.[2]

The relative incidence of organ system involvement in LCH is as follows: bone in 80% of the cases; skin 60% of the cases; liver, spleen, and lymph nodes 33%; lungs and orbit in around 25% of the cases; and maxillofacial in around 25% of the cases. Mandible is more commonly involved when compared to the maxilla. [2]

Orbital involvement by LCH accounts for 1-2% of all orbital tumors and commonly manifests as eosinophilic granuloma.[4] Gingiva and hard palate are the most commonly affected sites in maxillomandibular involvement. The symptoms of LCH may occur first in oral cavity before elsewhere in the body. Therefore, a thorough examination as well as establishing and ruling out differential diagnoses has significant importance in reaching the diagnosis of LCH at an earlier stage.[1, 3, 4]

The diagnosis of LCH is reached by evaluating clinical and radiographic findings and confirmed by histopathological and immunohistochemical studies. Other imaging methods used include somatostin receptor scintigraphy using 111In-DTPA-D-Phe1-octreotide, which depicts the active sites of disease and thus can help in monitoring the response to treatment. Whole-body magnetic resonance imaging is a diagnostic alternative for assessing the extent of skeletal and extra skeletal lesions of LCH in patients with multisystem involvement (except for pulmonary lesions). Positron emission tomography with fluorodeoxyglucose can detect metabolically active lesions with uptake values greater than 2. It is currently used for monitoring the response to treatment.[4]

Treatment modalities available for LCH depend on the site of the lesion, its extent, and the number of lesions present. Depending on this either surgical curettage, radiotherapy or chemotherapy can be used alone or in combination.[2, 4]

Here we are presenting a case of Langerhans cell histiocytosis in a 5 yrs. old boy presented with typical oral and orbital manifestations.

Case report

A 5-year-old boy reported to the department of oral medicine and radiology with a chief complaint of swelling and pain in the right & left lower back teeth region for 9 months. Patient was relatively asymptomatic before 9 months then he noticed pain over lower back teeth region along with mobility of teeth. Then patient noticed self-exfoliation of teeth. They visited private clinic where analgesics were prescribed but pain was not reduced. So, patient's parents came to GDCH for needful treatment. Family history and past medical history were noncontributory. On physical examination, the patient was healthy, moderately built and had a markedly uncooperative behavior.

On extraoral examination, a solitary diffuse swelling was noticed on the right side of the face measuring around 2 cm × 1 cm in size extending superoinferiorly from the corner of mouth to the inferior border of the mandible, mediolaterally from the right corner of mouth to the angle of mandible which was not much remarkable. Extraoral swelling was soft to firm in consistency, tender on palpation with intact and slightly erythematous overlying surface. Bilateral Submandibular and preauricular lymph nodes were not enlarged and not palpable.

Patient didn't had any complaint relation with the orbit. But on examination, level of orbital floor was changed on right side. Patient didn't had any blurring or loss of vision (Figure 1) On intraoral examination, missing of all quadrants 2nd deciduous molar were seen with mesially drifted 1st permanent molar. Local factors along with grade 3 mobility were present irt 5D, 16, 6D, 26, 7D, 36, 8D and 46. (Figure 2) Based on age, duration of the complaint, generalized mobility of deciduous dentition, malignancy, mostly sarcomatous, metastatic lesion, blood cancer was suspected clinically. Various investigations were done to rule out the same.

OPG showed ill-defined mixed radiolucent and radiopaque lesion present over body of mandible extending A/P from right side mid ramus to distal to left side tooth bud of 2nd molar and S/I from alveolar ridge to lower border of mandible. Arc shaped bone loss with floating teeth appearance present irt both permanent and deciduous teeth of mandible & maxilla supporting our clinical suspicion. (Figure 3) Advanced imaging technique such as CT and MRI was carried out.

CT scan of the patient showed sclerosis involving roof of right orbit with erosion at roof and lateral wall of right orbit and right squamous temporal bone. Expansile lytic lesions involving body and ramus of mandible and maxillary alveolar arch on either side with mild involvement of floor of maxillary sinus and hard palate on right side. Mild mucosal thickening was seen in right maxillary and sphenoidal sinus. (Figure 4) MRI brain of the patient showed presence of altered marrow signal density lesion is noted in right temporal, right greater wing of sphenoid bone and roof of orbit. Lesion appears hypointense on T1w, hyperintense on T2w. CT and MRI findings were favoring malignant lesion and also suspected metastatic tumor.

Bone marrow aspiration was to done to rule out blood related malignancy. Bone marrow aspiration shows normocellular marrow with microcytic hypochromic anemia, mild leukocytosis and thrombocytosis uninvolved by primary or secondary malignancy with features suggestive of iron deficiency anemia. Biopsy shows histiocytic along with many eosinophils, neutrophils and plasma cells infiltrating underlying bone. Occasional giant cells present. Many histiocytes show longitudinal grooves. Overall features suggest P/O Langerhancell histiocytosis – Histiocytosis X into final diagnosis.

Immunohistochemistry shows positive result for S100, CD1a & LCA markers and negative result for CD 20 (figure 5).

The patient was referred to Gujarat cancer hospital and treated with surgical excision followed by chemotherapy (vinblastin and prednisalone). The patient is currently under periodic follow-up.

Discussion

LCH is more frequent in males than in females with a ratio ranging from 1.1:1 to 4:1. It predominantly affects children and young adults, recently reported cases described LCH in a five-month-old infant and patients aged between 17 and 63 years old. [2, 8] The reported case was 5 yrs. old child which is a rare occurrence.

At present, LCH is classified into three distinct forms: single-system single site (SS-s), single-system multi-site (SS-m), and a multisystem type (MS).[11] The present case will be under MS type with involvement of jaw bones and orbit. In the skull, frontal and parietal bones are commonly involved followed by the jaws. Mandible is more commonly involved when compared to the maxilla.[2] In the present case, temporal, sphenoid, orbit, maxilla, mandible and palatal bones were involved according to CT scan.

LCH involving the orbit is generally regarded as infrequent, although estimates range from 1%–37.5%.[13] The most common site of involvement in the orbit is the part of frontal bone forming the superior orbital rim and roof. It can present as an isolated osteolytic lesion or with associated soft tissue mass in the orbit and surrounding tissue.[9] Similar findings were reported in our case.

Oral manifestations are the earliest manifestations seen in around 5% to 75% of patients suffering from LCH.[6] In our case also oral manifestations (tooth mobility) are the earliest manifestation reported by the patient. The most common presenting symptom is local bone pain (41%). Oral mucosal lesions although infrequent, are characterized by gingival hypertrophy and ulcers of the buccal mucosa, hard and soft palates, and tongue.[5] Gingivitis with hyperplasia, bleeding, recession and necrosis, mucosal ulcerations and destruction of the alveolar bone and periodontal support, impaired healing, abnormal primary dentition mobility ('floating teeth'), intraoral mass, halitosis, and odontalgia are common findings in pediatric patients.[10] In our case bone pain, early exfoliation and mobility of teeth were present without any soft tissue involvement. Langerhans cell histiocytosis should be looked for in children presenting with severe bone loss in primary dentition.[5]

The conventional radiological findings observed in LCH are due to destruction of bone by Langerhans cells. Involvement of the alveolar bone leads to a "tooth floating in air" appearance, causing tooth mobility and displacement, thereby mimicking the appearance of periodontitis.[6] In our case similar findings were seen.

Histopathology reveals a sheet-like proliferation of pale-staining Langerhans cells, with abundant cytoplasm, indistinct cell borders, rounded or indented "coffee-bean-" shaped vesicular nuclei, and absence of mitotic activity.[6] Similar histopathological findings were present in our case. (Figure 5) On immunohistochemistry, LCH is positive for S-100 and anti-CD-1a, which was also seen in the present case.

After the diagnosis of LCH has been established, a complete physical and hematological examination along with liver function tests, urine osmolality, bone marrow examination, complete skeletal radiographic survey, and chest radiography is necessary to check for multiorgan involvement.[6] All these tests had been done in our patient was in normal range.

Differential diagnosis of Ewing's sarcoma, hyperparathyroidism, metastatic lesion, hypophosphatasia, papillon- lefever syndrome and leukemia were considered. 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. Acute myeloid leukemia may present with gingival hypertrophy and appear as LCH. Papillon-Lefevre syndrome is associated with marked destruction of alveolar bone with premature primary tooth loss. This condition is differentiated from LCH by the associated hyperkeratosis of the palms and soles. Hypophospatasia is characterized by low serum alkaline phosphatase levels and excessive excretion of phosphoethanolamine in the urine. The classic oral finding of hypophosphatasia is premature tooth loss generally involving the mandibular primary incisors, which often have abnormally large pulp spaces.

In general, available treatment options include combinations of surgical removal of localized bone lesions, chemotherapy and radiation. Diverse agents have been employed, such as corticosteroids, antibiotics, prednisone-vinblastine combination, vincristine sulphate, indomethacin, methotrexate, cyclophosphamide, indomethacin, adrenocorticotropic hormone (ACTH), etoposide, and 6-mercaptopurine; or therapeutic

procedures, such as interferon or cyclosporine-A, bone marrow transplant, monoclonal anti-CD 1a antibody therapy, and gene transfer into hemopoietic progenitor or stem cells.[10] In our case surgical removal of orbital bony lesions were done and patient was under prednisone-vinblastine combination therapy.

Conclusions

LCH is rare neoplasm of the immune system which is frequently misdiagnosed. Importance of reporting such cases lies in the fact that oral lesions may be the earliest manifestations of LCH and, in many cases, the only site that may be involved. It should be kept in mind that oral cavity is often the indicator of systemic diseases. A thorough history and oral examination by a dentist may aid in determining the underlying cause of oral manifestations and allow for earlier intervention by other medical subspecialties. Correctly timed diagnosis by a dentist saves time, expenses, and limits the extent of the disease. It reflects the role of a dentist in improving the quality of patients' lives and easing their families' sufferings by treating oral manifestations of serious systemic illnesses.

Abbreviations:

LCH- Langerhan Cell Histiocytosis

GDCH- Government Dental College and Hospital, Ahmedabad

CT- Computed tomography

OPG- Orthopantomogram

MRI- Magnetic Resonance Imaging

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Legend of figures

Figure 1: Diffuse swelling present at the right lower third of face with change in the level of right eye

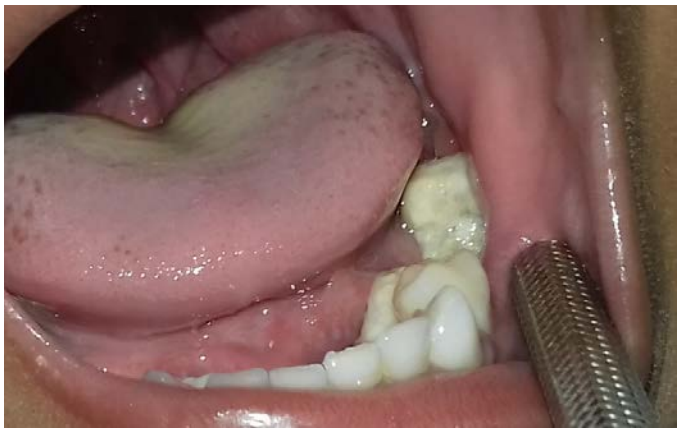

Figure 2: Shows missing 2nd deciduous molar with drifted 1st permanent molar with local factors.

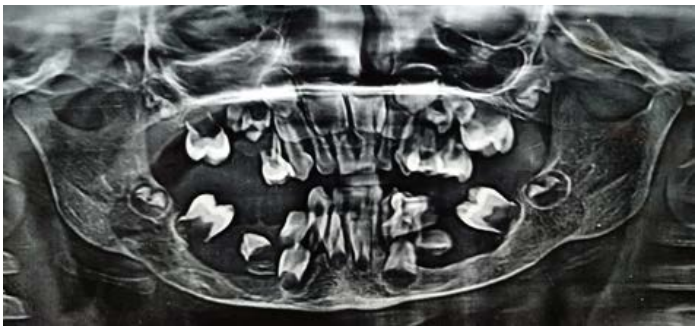

Figure 3: OPG showed ill-defined mixed radiolucent and radiopaque lesion present over body of mandible extending. Arc shaped bone loss with floating teeth appearance present irt both permanent and deciduous teeth of mandible & maxilla.

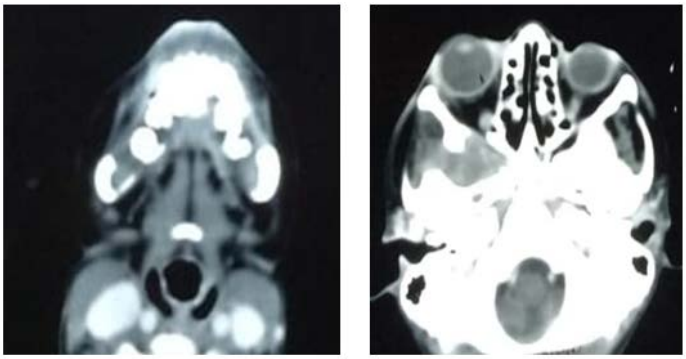

Figure 4: CT scan showed sclerosis involving roof of right orbit with erosion at roof and lateral wall of right orbit and right squamous temporal bone. Expansile lytic lesions involving body and ramus of mandible

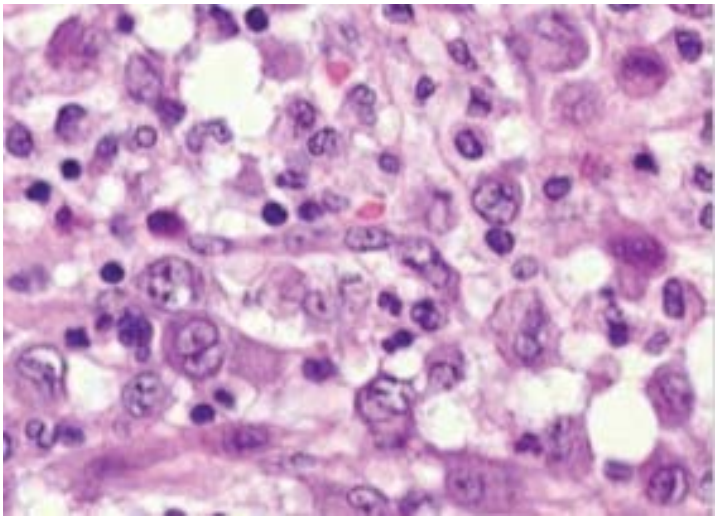

Figure 5: microphotography (10x) showing excess proliferation of histiocyes