CASE REPORT

Langerhans' Cell Histiocytosis Diagnosed through Periodontal Lesion in a 15-year-old Child: A Case Report

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Abstract

Langerhans' cell histiocytosis (LCH) is a rare disease of the reticuloendothelial system in which there are abnormal proliferation and accumulation of histiocytes, abnormal cells deriving from bone marrow that can migrate from the skin to the lymph nodes. Langerhans' cell histiocytosis has three variants: unifocal (eosinophilic granuloma), multifocal unisystem (Hand–Schuller–Christian triad), and multifocal multisystem (Letterer–Siwe disease). We present a case of oral lesions associated with LCH in a young male aged 15 years. The history, radiological appearance, histopathology, and treatment options of the patient are discussed.

Keywords: Histiocytosis, Langerhans' cell, Reticuloendothelial system.

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Introduction

Langerhans' cell histiocytosis (LCH) forms a part of a group of a clinical syndrome called histiocytoses, which involves abnormal proliferation of histiocytes (démodé term for activated dendritic cells and macrophages). Historically known by various terms including Hand–Schüller–Christian disease, Abt–Letterer–Siwe disease, and histiocytosis X, eventually renamed in 1985 by the Histiocyte Society.[1]

Langerhans' cell histiocytosis can be categorized into three groups: unifocal (eosinophilic granuloma), multifocal unisystem (Hand–Schuller–Christian triad), and multifocal multisystem (Abt–Letterer–Siwe disease).[2]

Unifocal also called eosinophilic granuloma mainly involves the abnormal proliferation of the Langerhans cells, especially in the bones. Further can be divided into two varieties: monostotic (single bone involved) and polyostotic (multiple bones involved). Extraskeletal involvement is rare but in a few incidences skin, lungs, and stomach may show similar lesions. Primary bone involvement helps in differentiating from other variants like the Hand–Schuller–Christian triad and Abt–Letterer–Siwe disease.[3] And if it is pulmonary it has to be differentiated from pulmonary LCH — a variety is seen in chronic smokers.[4]

Multifocal unisystem (Hand–Schuller–Christian triad): the triad involves diabetes insipidus exophthalmos and lytic bone lesions. Commonly present in children characterized by fever, bone lesions, and diffuse eruptions (mostly on scalp and ear canal) due to the involvement of pituitary stalk in 50% of the cases it leads to diabetes insipidus.

Multifocal multisystem (Abt–Letterer–Siwe disease): rapidly progressing disease in which Langerhans cells proliferate and accumulate in many tissues. Mostly seen in children <2 years of age, has poor prognosis even with aggressive chemotherapy, the 5-year survival rate is nearly 50% only.[5]

Langerhans' cell histiocytosis may involve different tissues or systems like the skeletal system, respiratory system, integumentary (especially skin), mucous membrane, hypothalamus, lymph nodes, liver, and other soft tissues. It may involve either a single system or multiple systems at times but mostly the skeletal system is involved mainly involving the bones of the skull, long bones, and flat bones.

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Langerhans' cell histiocytosis is rare in children (about 3–5 cases per million children aged 0–14 years).[5] Langerhans' cell histiocytosis is also rare in adults but the prevalence and incidence are uncertain because of the lack of population-based studies.[6]

The purpose of this study is to present a case of a child patient with LCH of a variety of eosinophilic granuloma who presented oral lesions.

Case Description

A 15-year-old male reported to the OPD of dept. of periodontology with the chief complaint of pain, burning sensation, swelling, and bleeding from the gums. Medical, dental, and family history were not found to be significant. The patient was poorly built and undernourished. On clinical examination, submental and submandibular lymph nodes were palpable but non-tender.

At the time of oral examination, the patient had entire dentition but the oral hygiene was poor (Fig. 1). The periodontal examination showed fragile and erythematous gingivae along with swelling and sloughing in both jaws. On further examination, deep pockets were

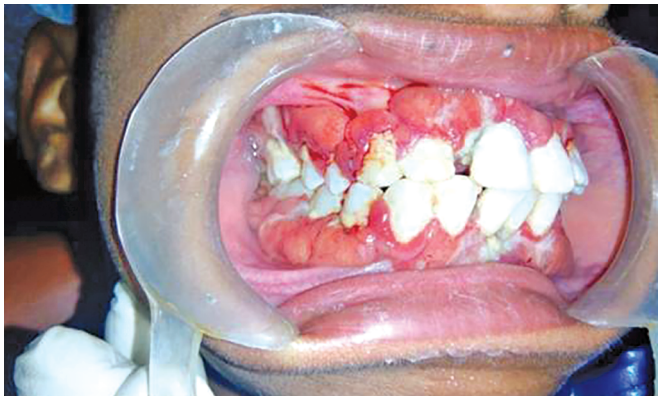

Fig. 1: Preoperative (before debridement)

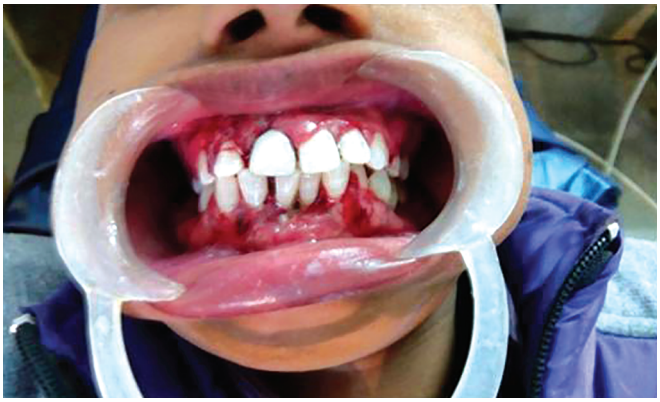

Fig. 2: Immediate postoperative after debridement

Table 1: Clinical observation of the teeth involved

Tooth number	*Probing depth (mm) Mesial | Distal*	*Bleeding on probing (mm) Mesial | Distal*	*Recession Mesial | Distal*	*Mobility (1–3)*	*Furcation involved (0–3)*
11	3 | 3	Y | Y	N | N	1	N
12	3 | 3	Y | Y	N | N	1	N
12	3 | 3	Y | Y	N | N	1	N
13	3 | 2	Y | Y	N | N	1	N
21	3 | 3	Y | Y	N | N	1	N
35	8 | 9	Y | Y	N | N	2	N
36	8 | 10	Y | Y	N | N	3	Y
46	3 | 10	Y | Y	N | N	3	Y
47	8 | 4	Y | Y	N | N	2	Y

present in wrt posterior teeth (Fig. 2). Periodontal measurement of the involved teeth is shown in Table 1. Radiographic examination (orthopantogram) revealed an osteolytic lesion in the mandible along with generalized bone loss, especially in the mandibular molar region.

Oral prophylaxis was performed to remove the local factors, debridement was done to remove sloughing and inflammatory exudates (Fig. 2). Medications including antibiotics and analgesics along with betadine mouthwash were given for oral rinsing. Oral hygiene instructions were given and the recall was made after 7 days. No clinical signs of improvement were seen.

Routine investigations included (CBC, BT-CT, ESR, RBS, HBsAg, HIV, etc.) and biochemical reports revealed that most of the blood and urine parameters were abnormal [Hb-11.7 g/dL, hematocrit-37%, MCV-72.6 fl, MCH-23 pg, RDW-14.5%, PLATELETS-526 thousand/µL, ESR-36 mm at 1 hour, SERUM alkaline phosphatase level-203 µ/L (kinetic method)].

In urine analysis: Protein, blood, RBC, and WBC were detected in large numbers.

In peripheral blood smear, RBCs were predominantly microcytic hypochromic with moderate anisopoikilocytosis. Few teardrop cells were present, pencil cells were also seen. Nucleated RBCs were not detected. WBCs were in the normal range, no immature cells were detected. Thrombocytosis was seen. Taking consideration of the above reports, it was decided to take the biopsy from both the jaws and were sent to the department of oral pathology for histopathological examination. Three samples were taken — single soft tissue from the left palatal mucosa, two soft tissues from the right gingival wrt 46 region, and two soft tissues from the intrabony area wrt 46 region.

Histopathologic Examination

Report

Sample 1—(Single soft tissue from the left palatal mucosa) H&E stained section shows epithelium overlying connective tissue stroma showing sheets of round to oval cells with vesicular nuclei. Abundant inflammatory cells like lymphocytes eosinophils and plasma cells present accompanying these cells. Areas of hemorrhage and necrosis were seen. Submucosa shows mature adipocytes infiltrated by chronic inflammatory cells (Fig. 3).

Sample 2—(Two soft tissues from the right gingival wrt 46 region) section shows gingival epithelium with highly fibrocellular connective tissue stroma showing sheets of round to oval cells with vesicular nuclei. Abundant chronic inflammatory cells were seen. Areas of hemorrhage were seen.

Sample 3—(Two soft tissues from the intrabony area wrt 46 region) section shows fibrocellular connective tissue with round to oval cells with vesicular nuclei. Abundant chronic inflammatory cells and areas of hemorrhage were present. The periphery of the section shows bony trabeculae.

Immunohistochemical Analysis

On immunohistochemistry (IHC) evaluation, the tumor cells were positive for CD1a (Fig. 4) and S100 PROTEIN (Fig. 5).

Radiological Examination

For the extent of the lesion, non-contrast CT (NCCT) was performed—the presence of irregular destruction was noted involving the right angle of the mandible extending in the body of

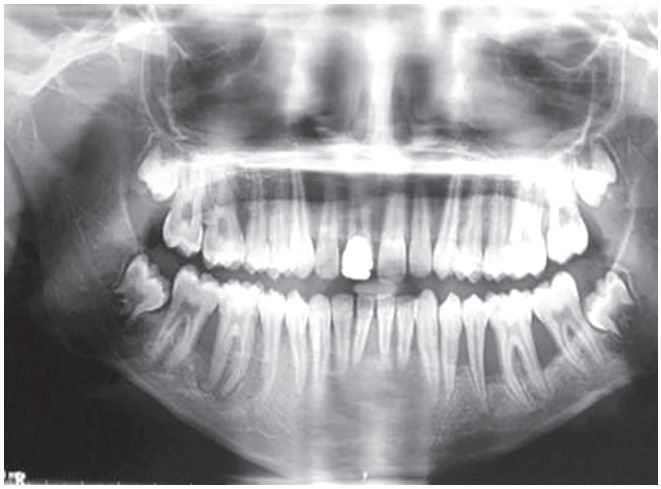

Fig. 3: Orthopantogram reveals osteolytic lesion wrt 36 46

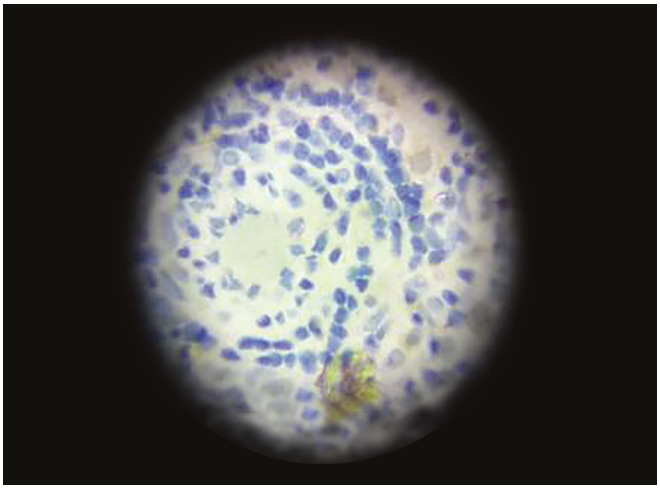

Fig. 4: CD1a

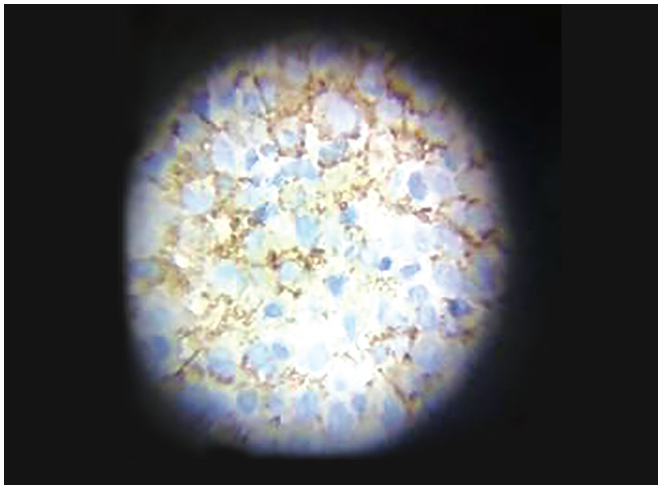

Fig. 5: S100

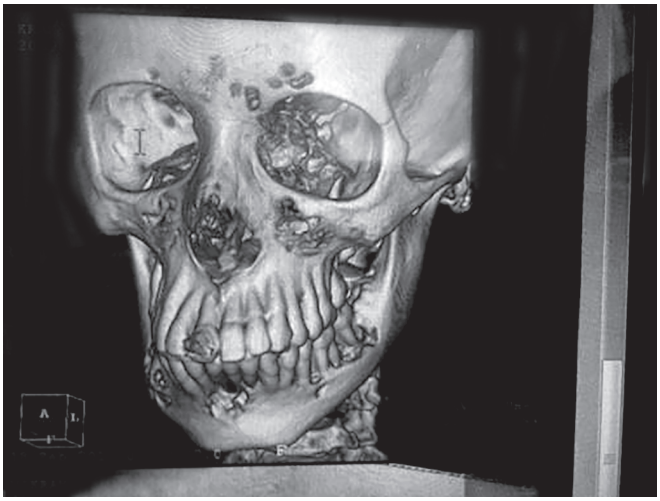

Fig. 6: NCCT face

the mandible on the right side. There is an associated presence of soft tissue components extending in the oral cavity (osteomyelitis?).

Another small irregular destruction is noted in the body of the mandible in the midline with soft tissue components in the oral cavity and overlying subcutaneous tissue. There is polypoidal mucosal thickening noted involving the right maxillary sinus (sinusitis). The right osteomeatal complex is blocked.

The nasal septum slightly deviates toward the right. There is polypoidal mucosal thickening noted along the posterior-superior wall of the nasopharynx. Enlarged adenoids. The rest of the paranasal sinus is normal. Both orbits and eye globes are normal. The maxilla is normal (Fig. 6).

Clinical Diagnosis and Treatment

Based upon clinical examination, radiological findings, biopsy, and IHC report a definitive diagnosis of LCH was made.

Discussion

Langerhans' cell histiocytosis is a group of disorders histologically characterized by the proliferation of Langerhans cells. Langerhans are dendritic bone marrow-derived cells situated suprabasally in most st. squamous epithelium. They are believed to act as antigen-presenting cells (APCs) during the induction of immune responses. Besides having functions that are similar to other dendritic cells and macrophages. Langerhans cells are specialized and able to migrate, playing an important role in antigen presentation to the T-lymphocytes. It has been suggested that they play a key role in the induction of immune responses and also in immunopathological reactions taking place at cutaneous and/or mucosal levels. Langerhans cells may represent a "first line" of sensitization of the immune system, leading to clearance of the antigen or to pathological phenomena. It is not known, however, what leads to the proliferation of these cells in the histiocytosis lesions.[7]

There is a risk-stratification system based upon the degree of organ or system involvement and the number of organs or systems involved.

The etiopathogenesis of LCH is still uncertain, but there are two schools of thought: a disorder of immune regulation or a neoplastic process. The presence of aggregates of other immunologically active cells in lesions, the presence of thymic abnormalities, and a deficiency in the number of suppressor T-lymphocytes and increased cytokines suggest an exuberant reaction of Langerhans cells to an unknown antigen or neoantigen. However, the monoclonal proliferation of Langerhans cells infers the neoplastic

origin of the disease. Different organs and systems may be affected by LCH, particularly the skeletal system, most commonly the skull and maxillary bones. Soft tissue involvement may occur, whereas lymph nodes, lungs, and mucous membranes are mostly affected.[8,9]

Periodontal manifestations were observed in 28 cases of histiocytosis in young adults. The mandible is more frequently affected than the maxilla, with most of the lesions occurring in the molar area.[10] The case reported here came with the chief complaint of pain, swelling, bleeding gums, and burning sensation of the oral mucosa. After thorough clinical examination, lab investigations, biopsy, IHC, and radiological investigation, a definitive diagnosis of LCH was made.

When the periodontal tissues are involved, symptoms and clinical features are similar to advanced periodontitis, especially when osseous lesions are associated with an apical shifting of marginal tissues which is also seen in the present case.[11]

In addition, denudation of root surface with grade II furcation involvement was seen.

Clinically, it is difficult to differentiate oral LCH lesions from bone metastases, lymphoma, ulceration (HIV infection), vasculitis (especially, Wegener granulomatosis), and simple chronic periodontal inflammation.[8,9] Furthermore, LCH is a rare disease, with an incidence of one case in 560,000.[12] For this patient, the definitive diagnosis was based upon the histological and immune histochemical analysis of the lesional biopsy specimens. The strong positive result for both of the most significant markers of the disease, S-100 and CD1a, made the ultrastructural examination unnecessary. A provisional diagnosis of LCH may be made based upon light microscopic findings and a compatible clinical picture, but a definitive diagnosis requires that lesional cells sample exhibit positive staining with S-100 and CD1a proteins, and the subsequent identification of Birbeck granules upon electron microscopy. Although the "gold standard" for the identification of Langerhans' cells has been the detection of Birbeck granules by transmission electron microscopy, this technique is rarely performed today.[11]

Conclusion

From the above discussion, we can conclude that the clinicians' aim should not be just focused on the periodontal condition of the patient, rather than it should include the patient as a whole. In this case, despite following the standard protocol/regime for the treatment of periodontitis when the patient did not respond to the treatment, systemic involvement of the patient was suspected and with the help of clinical examination, radiological examination, and laboratory investigations a definitive diagnosis of LCH was reached. Therefore, suspicion of LCH should also be considered in the case of the recurrent periodontal lesion and bone loss.

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