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ORAL MANIFESTATIONS OF LANGERHANS CELL HISTIOCYTOSIS - A CASE REPORT

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ABSTRACT Langerhans cell Histiocytosis (LCH) is a group of rare disorders histologically characterized by the proliferation of Langerhans cells. It may involve a single system or may have generalized systemic involvement. Most commonly there is bone involvement and, less frequently, lesions may be found in the lungs, liver, lymph nodes, skin, and mucosa. The diagnosis is tricky in such cases as it may mimic a lot of other conditions. We report a case of a 5 year old child presenting with oral manifestations of this disease who was managed with curettage followed by systemic therapy.

KEYWORDS : Langerhans Cell Histiocytosis, Oral Manifestation, Case Report

INTRODUCTION

Histiocytes/macrophages are derived from monocytes and these play an important role in the regulation of immune functions. Langerhans cell histiocytosis (LCH), which was previously known as histiocytosis X, is a rare proliferative disease of histiocytes. These have variable grades of tissue infiltration and it may present as a single or a multisystem disease (1). The main feature of LCH is the abnormal proliferation of the antigen-presenting Langerhans cells (LC) (2). This condition is usually seen in childhood with an incidence of one case per 200,000 children per year however it has also been observed to occur in adults as well (2). It can present in three different forms – acute and chronic (disseminated form) and eosinophilic granuloma (localized form) (1).

Different organs and systems may be affected in LCH. Some of these include bones, lungs, liver, skin, lymph nodes, spleen, endocrine organs, haematopoietic tissue and muco-cutaneous tissues. However, skin and bone are most frequently affected (3). Most patients present with solitary or multiple bony lesions and involvement of the jaws (particularly the mandible) is not unusual.

Aetiology is unknown and various authors have suggested a combination of factors like environmental, infectious, immunologic and genetic (4). With the discovery of mutations in the mitogen activated protein kinase (MAPK) pathway (i.e. BRAF and MAP2K1 mutations), LCH is also considered to be a part of a neoplastic process (5). The highlight of LCH is the abnormal proliferation of the antigen-presenting Langerhans cells (LC) (1). Immunological abnormalities resulting from a suppressor cell deficiency have has also been implicated as one of the causative factors (6). Some even implicate role of viral infection in its aetiology (7). The clinical features usually are a result of underlying organ involvement for example skin lesions may present as papules or eczematous lesions and bone LCH most often present with localized pain and swelling of the affected area sometimes associated with concurrent fever.

Oral involvement presents as mucosal ulceration and is associated with lesions of the underlying bone (8). LCH can mimic many other conditions. Its diagnosis is especially difficult due to its wide clinical spectrum (9).

Herein we report a case report of a young boy who presented with oral manifestation of the disease.

CASE REPORT

A 5 year old boy initially presented to the dental department with the complaints of loose teeth in the lower jaw since the three years. Initial clinical examination showed presence of swelling on anterior region with marked expansion, loosening of all teeth with respect to mandible and upper region appears normal. Orthopantomogram (OPG) showed loss of bone support on all the teeth in the lower jaw. All teeth were virtually floating in air with only soft tissue support. The vertical height of mandible was considerably reduced because of the destruction of bone. Following periodontal treatment, no improvement was observed.

His Chest X Ray and Ultrasound abdomen were normal. Blood Counts were Hb: 9.91g/dL TLC: 12,660 cells per mm^3 N 41% L 46% E 09% M 04%. ESR was 33. Peripheral Blood Smear showed moderate anaemia – microcytic hypochromic type. Other blood investigations like Liver Function Tests, Kidney Function Tests and urine analysis were within normal limits. Mycobacterium tuberculosis-PCR was negative and HIV antibody test was nonreactive. Immunofluorescence assay was done to rule out autoimmune diseases. His skeletal survey was normal. Bone Marrow Aspiration and Imprint smears showed no evidence of infiltration or hemato lymphoid malignancy.

Biopsy was done which showed Ulcerated stratified squamous mucosa with submucosa showing extensive granulation tissue and intense inflammatory infiltrate comprising of eosinophils, plasma cells, neutrophils and lymphocytes. With diffuse infiltration of atypical cells which are large and ovoid with indented bland nuclei and pale eosinophilic cytoplasm and mitotic activity was readily seen (Figure 1)

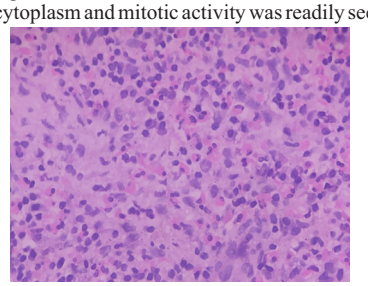

Figure 1 shows the representative H&E section 40 x showing Langerhans cells with cleaved nuclei and abundant eosinophils in the background

On Immunohistochemistry, the atypical cells were strongly positive for Langerin (Figure 2) and S-100 (Figure 3) – with the diagnosis consistent with Langerhans Cell Histiocytosis.

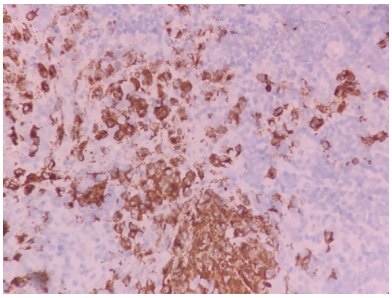

Figure 2 shows representative section of immunohistochemistry showing Langerin positivity

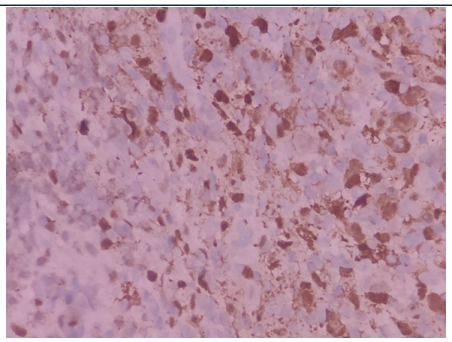

Figure 3 shows representative section of immunohistochemistry showing S-100 positivity

The child underwent curettage under paediatric surgery team followed by chemotherapy for LCH (Vinca Alkaloids and corticosteroids). The child has been on follow up for 5 years now and is doing well.

DISCUSSION

Alveolar bone loss in young children is clearly a serious finding. Gingival lesions could be one of the first manifestations of LCH. LCH can manifest itself in multiple ways which can lead to incorrect diagnosis. Clinically, it is difficult to distinguish oral LCH lesions from juvenile periodontitis, ulceration by HIV infection, vasculitis, bone metastases and lymphoma (10).

Various case reports are published in literature. Juyol et al reported a case of fourteen month old boy who developed lytic lesions in the jaw which led to loosening of temporary molars (2). Minguez et al described 10 children with oral manifestations of LCH. In their study, oral manifestations presented as tooth mobility and loss, gingival bleeding and ulcerations. However more than 50% of cases who presented with oral manifestations were part of generalized disease. Few patients presented with nonspecific pain, candidiasis, orofacial swelling as well as osteolytic areas on X-ray finding were also seen (11).

Several authors have noted that oral lesions are common early findings and these may predate other evidence of the disease by as much as 10 years. Therefore, in children who present with features of prepubertal periodontitis, the differential diagnosis should always include LCH (12). Rockman described three cases of oral LCH presenting with loose molars, periodontal disease and precocious eruption of the primary dentition with gingival bleeding (13).

Pathophysiology of LCH involves histiocytes and these cells derived from monocytes of granulocyte/macrophage series after extravascular diapedesis. Pathologic LC are characterized by the presence of antigenic surface markers that react with specific monoclonal antibody and by histologic presence of granules called Birbeck's granules (14). For this patient, definitive diagnosis was based on immunohistochemical analysis. S-100 and Langerin positivity are hallmarks of LCH, which were evident in our case (15).

Oral lesions can be a sign of systemic disease. Clinicians dealing with the maxillofacial area should be aware of the oral symptoms of systemic disease and the clinical findings, and verify the diagnosis by biopsy if necessary. A definitive diagnosis was achieved with an open biopsy from the oral mucosa.

A wide spectrum of treatment modalities has been adopted to deal with LCH, including wide surgical excision, chemotherapy or radiotherapy. Some authors suggest using topical corticosteroids – clobetasol propionate – 0.05% for the oral lesion followed by chemotherapy (16).

Risk stratifications and tailored treatment is done in case of multisystem LCH. The risk for mortality can be predicted based on the organ system involved (for example hematopoietic system, liver and/ or spleen). The patients in low risk group still do require systemic therapy so as to control the disease and avoid recurrence in the future (17).

The International Registry of the Histiocyte Society on Adult LCH (IRHSA) has reviewed the clinical presentations of 274 cases from 13 nations. The reported 5 year Overall Survival (OS) was 92.3% with 100% for patients with single-system disease. It was 87.8% for isolated pulmonary disease. The number of organs affected is related with the prognosis of the disease. In case of multisystem involvement, reactivation in adults may occur in about 25%–38% of cases (18). The present case report is an example of single system involvement of LCH treated with both local and systemic treatments.

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