CASE REPORT

A rare occurrence of Langerhans cell histiocytosis in an adult

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ABSTRACT
Langerhans Cell Histiocytosis (LCH) is a disease process characterized by accumulation and infiltration of cells, showing ultrastructural and immunohistochemical similarities to Langerhans' cell, in the affected tissues. It exhibits extreme clinical heterogeneity. LCH was historically divided into 3 clinical entities based on extent of tissue involvement and severity of presentation. These 3 entities were eosinophilic granuloma, Hand-Schuler-Christian disease, Letterer-Siwe disease. Owing to similarities of their histologic appearance, they were grouped together under the term histiocytosis X. It was recently changed to LCH, emphasizing the primary cell involved in the disease process. LCH is a rare disease with an incidenceestimated to be 4.0 to 5.4 per million population. Males are affected twice as frequently as females. The disease may occur at any age with peak incidence in children aged 1 to 3 years. We describe an unusual case of a 65-year-old man who presented with painless swelling in anterior region of mandible.
Key words: Langerhan's histiocytosis, Langerhan's giant cells, oral cavity

INTRODUCTION

Langerhans cell histiocytosis (LCH) is a clonal proliferative disease of Langerhans cells (LCs), the primary antigen-presenting cells of the skin.[1] It occurs predominantly, but not exclusively, in children and is quite rare. It represents a spectrum of clinical disorders ranging from a highly aggressive and frequently fatal leukemia-like disease affecting infants to an easily cured solitary lesion of bone. It was originally believed to be a reactive proliferative disorder of histiocytes of unknown cause, hence the name histiocytosis X.[2] It has stimulated considerable debate about its categorization and whether it is a reactive disorder or a truly malignant process.[3,4] Recently it has been classified by the World Health Organization based on the lineage of the specific histiocyte involved: Langerhans cell, undifferentiated cell, dendrocyte or macrophage.[5,6]

CASE REPORT

A 65-year-old man presented after referral by his general dental practitioner with painless swelling in the anterior region of the mandible since 1 year. Swelling was small initially and had increased to the present size.

On further elicitation, the patient gave a history of swelling in the lower anterior region after he had hurt himself with a pin while cleaning his teeth 9 years ago. Patient visited a hospital where incisional biopsy was performed and patient was prescribed medications. Swelling subsided after the biopsy and so patient did not get any treatment done for 3.5 years. Patient reported to our department with a painless swelling in the anterior region of the mandible since 1 year.

Clinical examination [Figure 1a and b] showed a painless swelling measuring 4 cm × 3.5 cm in size in the left anterior mandibular region lateral to the symphysis. Generalized mobility in all the mandibular teeth was noted. Splinting was noted in 31 and 41 teeth [Figure 2]. Extraoral palpation of the mandible showed expansion of the bone with no associated lymphadenopathy.

Erythrocyte sedimentation rate, white cell count and flocculation test were within reference ranges and chest radiograph and gamma globulins were within normal limits, which ruled out systemic involvement.

Radiographs [Figure 3] Orthopantomograph showed extensive bony destruction with radiolucencies involving the anterior part of mandible where the involved teeth had lost their supporting tissue and appeared to be floating in radiolucent

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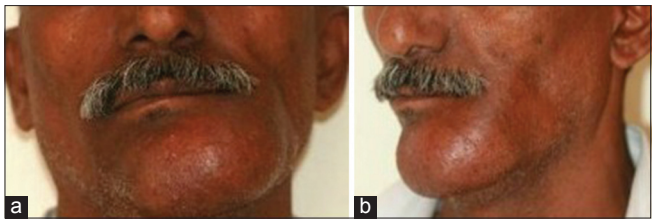

Figure 1: Clinical image of the patient showing the lesion in the left anterior mandibular region. (a) Frontal view and (b) lateral view

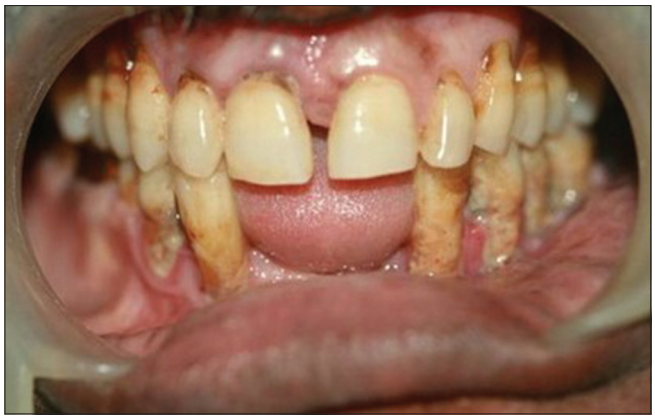

Figure 2: Intraoral examination showed missing lower central and lateral incisor teeth with periodontally compromised teeth

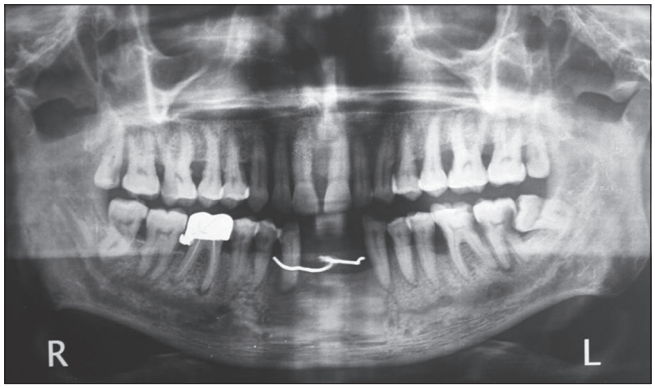

Figure 3: Orthopantomogram showed a radiolucent lesion in the anterior part of the mandible

lesion. The lesion had invaded the cortical rim giving a scooped out appearance, typical of single system LCH.[7] Differential diagnosis of Ewing sarcoma, lymphoma, leukemia, metastatic disease and osteomyelitis were also considered. We decided to further diagnose the condition by taking an incisional biopsy and examining the tissue histologically.

Histopathology

Hematoxylin and eosin stained sections of the lesion revealed marked chronic inflammation with aggregates of histiocytes that showed features of Langerhans cells with their indistinct cell margins and pink cytoplasm. Some of the cells showed cleaved nucleus. Eosinophils were also detected [Figure 4a-c]. Also these cells showed immunoreactivity for S-100 protein [Figure 4d][8,9] and CD 1a [Figure 4e] that suggested that the lesional cells were of Langerhans cells in origin. This indicated a diagnosis of Langerhans cell disease which was compatible with the clinical picture.

Treatment

For the definitive treatment, debulking of the lesion was done under general anesthesia. Local anesthesia was injected at the operative site. Incision extended from mesial surface of canine on right side on alveolar ridge to mesial surface of canine on the left side. Extraction of 33, 34, 35, 36, 37 and 38 was done. Lesion was excised [Figure 5]. Closure was done with 3-0 vicryl. Patient was started on chemotherapy. Follow-up was done at 1 week, 4 weeks, 2 months, 4 months and 6 months intervals and was uneventful [Figures 6 and 7].

DISCUSSION

LCH is a reactive disorder that is characterized by the infiltration and proliferation of dendritic cells, with the appearance of normal Langerhans cells. Despite advances in understanding the clinical picture, disease course and molecular profiling, the etiology and pathogenesis are still poorly understood.[10] A group of disorders of the reticuloendothelial system is termed LCH in accordance with the 1987 proposal of the Writing Group of the Histiocyte Society.[7] These conditions include the so-called Hand–Schuller–Christian disease, eosinophilic granuloma of bone and the Letterer–Siwe disease which were previously known as histiocytosis X. The current nomenclature emphasizes that most of these disorders have the common feature of infiltration of both bone and soft tissues by abnormal collection of Langerhans cells.[11]

LCH is a rare disorder that occurs at all ages, but predominantly affects children and young adults. As adult cases are rare, the clinical features are poorly defined. It can affect almost any bone, but it commonly involves the mandible when the jaw is affected.[12] Mucocutanoeus lesions have been described, usually representing either secondary lesional deposits or extension of the disease process from involved bone to contiguous tissues.[13] Cutaneous lesions have been reported to occur in approximately one-third of cases of LCH, usually coincidental with bone lesions and rarely as the only manifestation of the disease process.[14] Clinically, the skin lesions are described as consisting of either an extensive eruption of crusted papules or of one of several erythematous papules having a tendency towards ulceration.[15] Soft tissue involvement of the oral cavity usually manifests as swelling or ulceration of the gingiva overlying destructive lesions of the jaw bone, usually the mandible, that are clearly evident on radiographic examination.[16,17]

Differential diagnosis for our patient included LCH, Ewing sarcoma, lymphoma, leukemia and osteomyelitis. Our patient had no other systemic involvement as all his laboratory

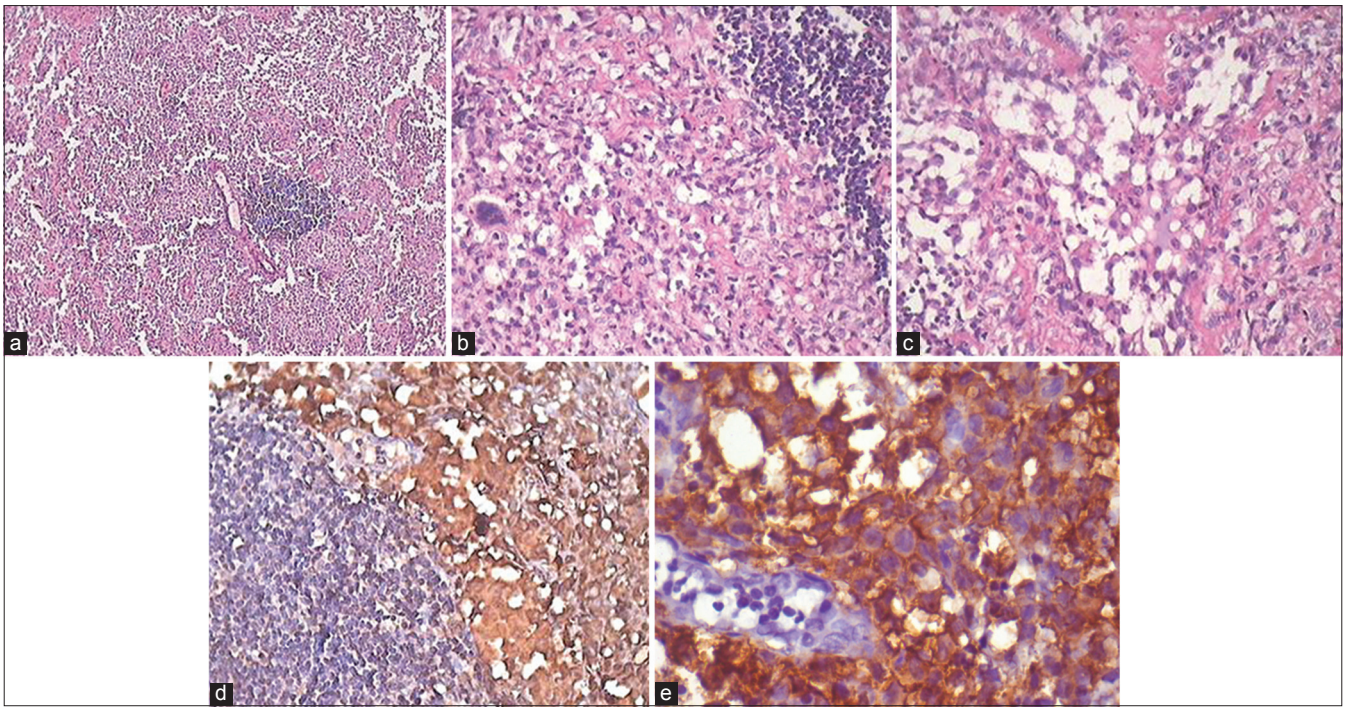

Figure 4: Intraoperative view: Incisional biopsy taken at the site of the lesion.(a) Low power view of the histological section showed marked cellular infiltrate in the connective tissue (H&E stain, x40)(b) Photomicrograph shows aggregates of histiocytes along with lymphocytes (H&E stain, x100). (c) High power view shows aggregates of histiocytes with indistinct cell borders and pale eosinophilic cytoplasm (H&E stain, ×400). (d) The histiocytic cells showing positivity for S-100 protein (IHC stain, ×100). (e) The aggregates of histiocytes were positive for CD 1a protein (IHC stain, ×400)

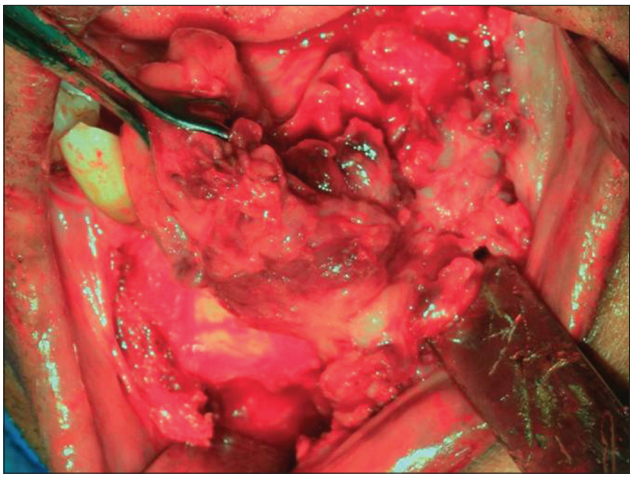

Figure 5: Intraoperative view showing debulking of the lesion

findings were within normal ranges and his chest radiograph and gamma globulins were within normal limits. So leukemia was ruled out. Burkitt's lymphoma was also considered, but it usually attacks the maxilla instead of the mandible. 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 the mandible. So it was rather a far possibility. The other differential diagnosis was of osteomyelitis. But his condition was not associated with any tooth infection. An incisional biopsy was thus taken to confirm the diagnosis.

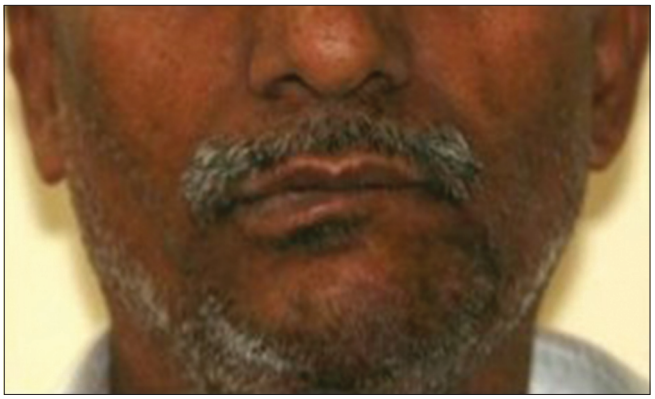

Figure 6: Postoperative extraoral view: No recurrence of the lesion was noted during the follow-up

The diagnosis of LCH was confirmed histologically by tissue biopsy. Hematoxylin and eosin stained sections showed features of Langerhans cells which include cells with pale eosinophilic cytoplasm with indistinct cell borders and rounded or indented nuclei. Varying number of eosinophils and other inflammatory cells like plasma cells, lymphocytes and multinucleated giant cells can also be seen. Unique features of these cells include cytoplasmic immunostaining with S-100 antigen that distinguishes them from other histiocytes. The presence of HX bodies or Birbeck's granules (rod-shaped with characteristic periodicity and sometimes with a dilated terminal end called tennis racket appearance, intracellular in location and identified by electron

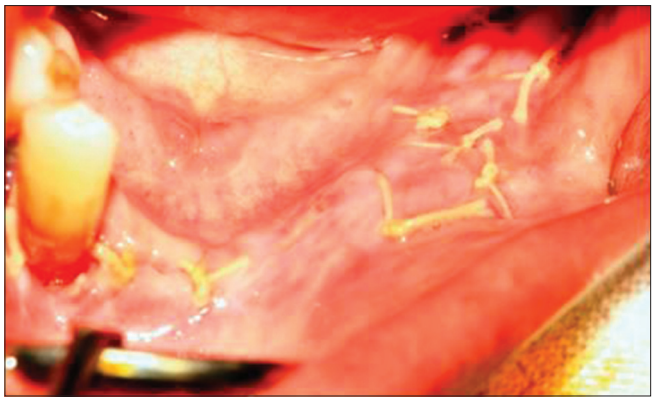

Figure 7: Postoperative intraoral view: No recurrence of the lesion was noted during the follow-up

microscopy) and the presence of CD1a antigen on the cell surface and HLA-DR positivity confirms the Langerhans cell origin of the disease.[8]

LCH affects only 1–2/millions of population. Thirty percent of cases present with lesions that affect the jaws and the diagnosis must be confirmed by biopsy.[3] The condition maybe a single system disease that affects bone, with or without involvement of lymph nodes, or multisystem disease that is disseminated throughout the body.[3-5] In a recent report from the Registry of the Histiocyte Society for adults, the 5-year survival rate for patients without pulmonary involvement was 100%.[18] Since the disease is much more common in children, most studies of treatment relate to data collected from juvenile cases and a definitive treatment regimen is yet to be established. Currently single lesions are managed with simple biopsy, excision or curettage; but chemotherapy is the preferred option for multiple lesions.[19] However, while children respond well to chemotherapy, the disease in adults tends to follow a more chronic pattern with periods of relapse and remission. The use of radiotherapy is reserved for nonresponsive lesions or single lesions that are inaccessible for surgical curettage. Owing to its rarity and varied presentation, management of histiocytosis is multidisciplinary. It is only through the collation of international data and good cross specialty communication that a definitive and appropriate adult treatment regimen will be established for this unusual disease in adults.[3,19]

CONCLUSION

LCH occurs in bone, lung, skin, lymph nodes and the liver. Involvement of the thyroid, thymus and other sites is also possible but is rare. The standard treatment differs with the type of disease. It is generally believed that patients with isolated LCH of the bone require minimal treatment, which usually includes biopsy followed by curettage. However, the disease may recur at the same site or new lesions may appear elsewhere. Even, after certain circumstances, surgery is rarely required and there are several alternative therapies. Many approaches such as low-dose radiation therapy (between 400 and 800cGy), nonsteroidal anti-inflammatory drugs, intralesional injection of a steroid or systemic cytotoxic agents can be tried. Excellent results can be obtained with radiation therapy in the management of localized histiocytosis, which is usually found in bone. When the disease is more widespread, radiation therapy is an effective adjunct to systemic chemotherapy, particularly for the control of local symptoms. Doses in the range of 600–1,000 rads are effective for achieving local control in most instances. After we confirmed that there are no lesions in other organs, we made a decision that excision of the lesion plus chemotherapy was appropriate, because the disease was localized to the oral cavity. After this treatment, the patient's symptoms were controlled. No recurrence at the site was seen. Therefore, we conclude by saying that surgical treatment may be best for this type of LCH based on the results in the present case. Long-term follow-up of these type of patients is required.

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