A Case of Multiple Eosinophilic Granulomas of Jaws: A Diagnostic Challenge
Sikka Seema, Sikka Pranav, DeviCharan Shetty, Aadithya Urs B

Abstract
Langerhans cell histiocytosis an infrequent disorder complex; includes Letterer-Siwe disease, Hand-Schuller-Christian disease and Eosinophilic granuloma. It has a relative incidence of approximately 2 - 5 cases per million inhabitants per year. Eosinophilic granuloma is the most benign and localized form, may be solitary or multiple, primarily involves the skull and the facial bones. Here, we are presenting a case of patient complaining of just mandibular pain and ulcerations in mouth, the principal differential diagnoses included advanced periodontal disease or a periapical abscess of dental or periodontal origin. But, it was finally diagnosed to be a case of eosinophilic granuloma on histopathology. This implies that a simple case resembling periodontitis can be a serious disease and can lead to grave consequences if not taken seriously.

Key Words: Eosinophilic Granuloma;Bone Diseases;Langerhans-Cells;Histiocytosis;Hematologic Diseases;Leukocyte Disorders;Eosinophilia.


Received on: 12/05/2012 Accepted on: 20/09/2012

Introduction
Langerhans cells histiocytosis (LCH) is an infrequent disease. The relative incidence of LCH is not well known, principally due to the heterogeneous clinical expression. But is estimated that approximately 2-5 cases per million individuals occur per year, being more frequent between the first and third decades of life. Lichtenstein first suggested the term histiocytosis in 1953. The current classification is based only on the number of organs involved and on the number of sites affected in each organ: unifocal eosinophilic granuloma (involving a single organ and a single, generally bony, site), multifocal eosinophilic granuloma (involving multiple sites in a single organ) and acute disseminated histiocytosis (involving multiple organs). Eosinophilic granuloma is considered the most frequent and benign of the clinical forms. It appears as a uni- or multifocal lesion in a single, or occasionally various bones, with or without soft tissue involvement, and without systemic involvement. Eighty percent of cases occur in Caucasians, with predominance in males. It is estimated that it occurs in 75% of the cases in children and young adults under 25 years and prevalent in males. The mandible is a more commonly affected site than the maxilla, especially in patients older than 20 years. In our case the presentation occurred in an Indian female and the synchronous occurrence of the three lesions in both jaws without involvement of other sites; make this case a unique one.

Case Report
A 44 year old female complained of pain in the right back region of lower jaw and right side of upper jaw since two years. Extraoral examination did not reveal any abnormality. Intraoral examination revealed 3 ulcerations present in the mandibular right and left posterior region and right palatal region, measuring 3.5 x 2.5 cm, 3 x 2 cm and 3.5 x 3 cm respectively (Figure 1a, b & c). The ulcerations had an erythematous base and were covered with slough. The shape of the lesions was irregular and borders were not well defined. No purulent discharge could be observed. Regional areas showed severe periodontal loss and teeth mobility. Lymph nodes were tender and palpable bilaterally. Radiographic examination showed extensive alveolar bone loss in the 12 to 17 region, 32 to 38 region and 42 to 48 region (Figure 1d). Bone loss was present till the apical third of the root. It had well demarcated borders. Neurological examination was unremarkable, haematological and biochemical parameters were within the normal limits. At first glance it seemed to be a case of severe periodontal loss of unknown cause. Other disease entities considered were periapical abscess, osteomyelitis, osteolytic metastasis, multiple myeloma, myxoma, ameloblastoma, osteogenetic sarcoma or fibrosarcoma. An
incisional biopsy was performed from the right mandibular vestibular region. Histopathological examination of the representative area revealed an admixture of inflammatory cells including many eosinophils with Langerhans cells. Lymphocytes and mononuclear phagocytes were also found accompanying these cells. Langerhans cells showed somewhat glassy pink cytoplasm, indistinct cell borders and longitudinal coffee-bean grooves in their nuclei with undulating or indented nuclear membranes without presence of any obvious mitotic activity (Figure 1e & f). Based on these findings, a pathologic diagnosis of eosinophilic granuloma was made. The patient was subjected to curettage of the lesions. She revealed an improvement in the symptoms. But the patient was lost to follow up.

Figure 1: The Intraoral examination showed ulceration present in the mandibular right posterior region (a), ulceration present in the left posterior region (b) and in mid right palatal region. The radiographic examination showed extensive alveolar bone loss in the 12 to 17 region, 32 to 38 region and 42 to 48 regions (d). The Photomicrograph showed the presence of granulation tissue containing fibroblasts, mature eosinophils and histiocytic cells (e & f) (H/E x40).

Discussion
The term Langerhans cell histiocytosis encompasses eosinophilic granuloma and two clinical syndromes: Hand-Schüller-Christian and Letterer-Siwe disease. All these diseases seem to represent similar processes in which the proliferating cells have the structural and functional features of Langerhans cells. They differ in their proliferating properties, ranging from a solitary focus (eosinophilic granuloma) to disseminated multifocal skeletal (Hand-Schüller-Christian) and disseminated multifocal skeletal and extra skeletal disease (Letterer-Siwe disease). These three basic conditions in fact represent clinical stages of the same process. This disease primarily affects young individuals during the first
three decades of life out of which fifty per cent are in first decade. The craniofacial bones are most frequently affected and other common sites include the mandible, vertebral bodies, ribs, pelvis and femur. The lesions are lytic and have sharply demarcated punched out intramedullary defects. They are rarely intracortical and sometimes a thin sclerotic rim can be seen. Larger lesions can erode or even completely disrupt the cortex and expand into the adjacent soft tissue. In rare instances lesions have a moth-eaten appearance.\textsuperscript{11}

Alveolar bone lesions form the basis for all the associated periodontal involvement in these patients. As new osteolytic areas develop, accompanying gingival ulceration and inflammation are observed, such that all the quadrants of the oral cavity are affected to a greater or lesser degree, even though the process began initially in only one quadrant.\textsuperscript{1} Dagenais et al. observed slight radicular resorption associated with these lesions in 53\% of cases studied, seen in the retro alveolar radiographs as images typical of a periodontal lesion.\textsuperscript{3} As a consequence of the alveolar bone loss, these patients manifest gingival inflammation, ulceration, destruction of the keratinized gingiva, gingival recession with periodontal pockets and bleeding of the oral soft tissues, associated with pain and even swelling. As a result of this loss of bone support, the teeth begin to progressively move giving rise to the characteristic ‘floating teeth’, completely surrounded by a radiolucent defect accompanied by dental displacement, odontalgia and on occasions cervical adenopathies. This excessive mobility gives rise to the inevitable premature loss of these teeth.\textsuperscript{1}

The pathogenesis of LCH is unknown, and various hypotheses have been proposed about its possible etiology. It may be caused by a dysfunction of the immune system, representing a hypersensitive reaction to an unknown antigen, with stimulation of the histiocytes – macrophage system.\textsuperscript{12,13} Deficiency of suppressor lymphocytes (T8), altered immunoglobins, autoantibodies, anomalous lymphocytic response to various mitogens and structural changes in the thymus in all the advanced forms have been found in LCH patients.\textsuperscript{3} An inflammatory origin is also suspected due to the microscopic characteristics and clinical evolution; or a bacteriological origin, although no specific causal microorganisms have been identified.\textsuperscript{12,13}

The differential diagnosis of oral unifocal lesions of LCH involving bone in adults can include pathologies like advanced periodontal disease. Periapical abscess, osteolytic metastasis, multiple myeloma, myxoma, ameloblastoma, osteogenic sarcoma and fibrosarcoma.\textsuperscript{1} The diagnosis is confirmed by histological study supported by clinical and radiographic examination. Biopsy by conventional microscopy shows areas of fibrous tissue related with a mixed inflammatory infiltrate. Non-malignant histiocytic proliferation is seen together with the Langerhans cells (with Birbeck granules). These large mononuclear histiocytic cells are round or oval in shape, with a vesicular nucleus, a moderate quantity of eosinophilic cytoplasm, and laminated or dispersed distribution. Abundant eosinophils and other inflammatory cells such as lymphocytes and mononuclear phagocytes may be found accompanying these cells. Electron microscopy reveals Birbeck granules in the lesional cells, described as organelles with rod-shaped or tennis-racket morphology that could represent structural changes of the membrane following contact with an antigen. The percentage of histiocytes with Birbeck granules is not related with prognosis. Using immunohistochemical techniques, the mononuclear histiocytic cells show positivity to markers S-100 and/or CD1a, and demonstrate ATPase activity of the cellular membrane.\textsuperscript{1}

The treatment modalities have varied from non surgical treatment like corticosteroids, antibiotics to surgical curettage, chemotherapy and radiation therapy.\textsuperscript{14-17} The prognosis of LCH is difficult to assess since this is a rare disease with high clinical variability. In the majority of patients LCH is a self-limiting process, although often with alternating phases of relapse and remission. The course of the disease is unpredictable and can evolve with multiple reactivations.\textsuperscript{11}

**Conclusion**

Thus the diagnosis of eosinophilic granuloma in a lesion simulating periodontal disease is a must to prevent unnecessary delay in the diagnosis and management of such lesions. This lesion should be differentiated from other diseases and tumors which can cause similar alveolar bone loss, keeping in mind the different
treatment strategies to be applied in such diseases. Also, the dentist should apply a multidisciplinary approach in such lesions as these may present only an early sign of widespread case of Langerhans cell histiocytosis.

Author Affiliations
1. Dr. Sikka Seema, Senior Lecturer, Department of Oral & Maxillofacial Pathology, I.T.S. College of Dental Science and Research, Muradnagar, Ghaziabad. 2. Dr. Sikka Pranav, Assistant Professor, Department of Pharmacology, LLRM Medical College, Meerut. 3. Dr. Devicharan Shetty, Professor & Head, Department of Oral & Maxillofacial Pathology, I.T.S. College of Dental Science and Research, Muradnagar, Ghaziabad, Uttar Pradesh. 4. Dr. Aadithya Urs B, Professor, Department of Oral & Maxillofacial Pathology, Maulana Azad Dental College and Hospital, New Delhi, India.

Acknowledgement
We would like to thank all the staff members from Department of Oral Pathology for their support & cooperation.

References

Corresponding Author
Dr. Seema Sikka, Senior lecturer, Department of Oral & Maxillofacial Pathology, I.T.S. - C.D.S.R., Muradnagar, Ghaziabad, UP, India.
E mail: simu50@yahoo.com

Source of Support: Nil, Conflict of Interest: None Declared.