Eosinophilic Granuloma of Mandible: A Diagnostic Challenge

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Citation

Bajracharya B, Poudel P, Bajracharya D, Bhattacharyya S, Shakya P. Eosinophilic Granuloma of Mandible: A Diagnostic Challenge. *Kathmandu Univ Med J.* 2018;62(2):201-3.

ABSTRACT

Eosinophilic Granuloma is the mildest and localized form of Langerhans Cell Histiocytosis and is characterized by clonal proliferation of Langerhans cells. It is a rare disease, accounting for less than 1% of all the osseous neoplasms. It has predilection for the axial skeleton and incidence in jaws is just 7.9%. It lacks pathognomonic clinical and radiographic trait and hence is difficult to make a correct diagnosis without histopathological and immunohistochemical examination. This report describes a case of Eosinophilic Granuloma of mandible in 30 years old male who presented with complain of unhealed extraction wound and was clinically diagnosed as chronic suppurative osteomyelitis. The final diagnosis of Eosinophilic Granuloma was made only after histopathological and immunohistochemical evaluations.

KEY WORDS

Eosinophilic granuloma, Immunohistochemistry, Langerhans cell histiocytosis

INTRODUCTION

Langerhans cell histiocytosis (LCH) is a rare disease of reticuloendothelial system resulting from clonal proliferation of Langerhans cells. This disease of unknown etiology has diverse manifestations.[1] Eosinophilic Granuloma (EG) is localized and mildest form of LCH, accounting for less than 1% of all osseous neoplasms.[2] It has predilection for the axial skeleton, and has higher incidence among young children. 7.9% of all the cases of osseous EG involves the jaws, most commonly in the body and the angle of the mandible.[3] It may present clinically with wide variety of non-specific signs and symptoms such as pain, loose tooth, edema, gingival bleeding and ulcers. Radiographic appearance of EG is quite variable and can be mistaken for osteomyelitis, radicular cyst and malignancies.[4] In our report, we present an unusual case of EG of the mandible and discuss the importance of histopathological and immunohistochemical examination in its diagnosis.

CASE REPORT

A 30 year old male presented to the department of Oral Medicine, People's Dental College, on 26/11/2014, with complain of unhealed extraction wound in the right side of lower jaw since four months. His medical history was not significant. Clinical examination revealed missing 47, 48 and unhealed extraction wound in the same area. 45 and 46 were mobile and tender. There was tender gingival swelling w.r.t 45, 46, 47 and 48. There was no regional lymphadenopathy. The patient was given several trials of antibiotics but there was no improvement. He then underwent extraction of 45 and 46. Based on the clinical findings, diagnosis of Chronic Suppurative Osteomyelitis was given and Intra Osseous Squamous Cell Carcinoma and central Giant cell granuloma were kept as differentials. As there was no improvement even after one week of extraction, complete blood count, CBCT and biopsy were advised.

Blood biochemistry was within normal limits. CBCT revealed lytic areas with ill-defined ragged border and irregular margin. The lesion extended from distal aspect of 44 to the right ramus and inferior aspect of coronoid process of mandible. It was 59.20 mm antero-posteriorly, 32.80 mm superio-inferiorly and 13.20 mm bucco-lingually. Buccal and lingual cortical plates showed thinning and perforation but without significant expansion (fig: 1). The internal structure of the lesion was homogeneous with no evidence of calcification. CBCT gave the impression of intraosseous carcinoma and chronic suppurative osteomyelitis.

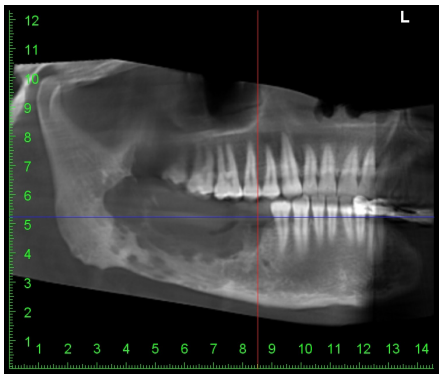

Figure 1. Showing lytic area with ill-defined border

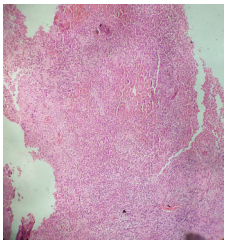

Figure 2. Loose connective tissue stroma showing sheets of histiocytes (hematoxylin-eosin, original magnification x100)

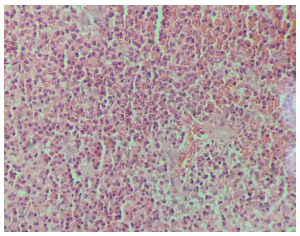

Figure 3. Figure 3. Sheets of histiocytes showing vesiculated nucleoli (hematoxylin-eosin, original magnification x100)

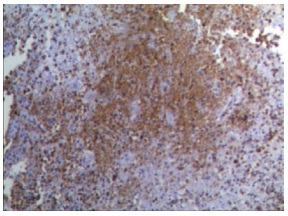

Figure 4. CD1a expression by Langerhans cells (IHC, original magnification x100)

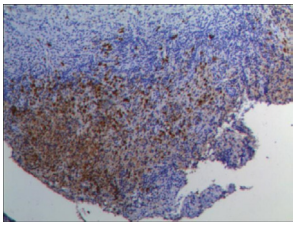

Figure 5. S100P expression by Langerhans cells (IHC, original magnification x100)

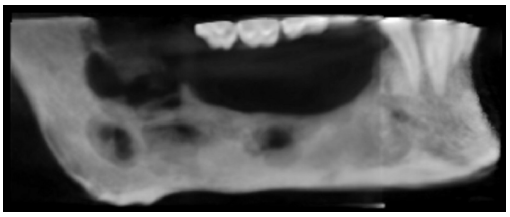

Figure 6. Postoperative CBCT after five months showing bone formation in previous lytic area

Histopathological examination revealed sheets of histiocytes having vesiculated nucleoli. The supporting stroma was loose with abundant eosinophilic infiltration (fig: 2, 3). Areas of hemorrhage were noted. Based on these findings histopathological diagnosis of Eosinophilic granuloma was given. But as EG is rare in jaws, to confirm the diagnosis, immunohistochemistry was done using horse radish peroxidase polymer. It showed positivity for CD 1A and S-100 whereas CD45 was negative (fig: 4, 5). These findings were consistent with Eosinophilic Granuloma. Hence diagnosis of Eosinophilic granuloma of mandible was confirmed.

The lesion was managed by surgical curettage. The post treatment period remained uneventful and patient was kept under regular follow up. Five months after the treatment, clinical examinations disclosed completely healed oral lesions and CBCT showed bone formation in previous lytic areas (fig: 6). Hence, patient responded favourably to therapy and showed no signs of recurrence.

DISCUSSION

The Writing Group of the Histiocyte Society introduced the term "Langerhans cell histiocytosis", replacing the term "histiocytosis X". LCH encompasses three disorders: Eosinophilic granuloma, Hand-Schüller-Christian disease and Letterer-Siwe disease.[5] The term 'Eosinophilic Granuloma of bone' was first introduced by Lichtenstein and Jeffe in 1940.[6] Accounting for 60% to 70% of all LCH cases, EG can present as either solitary (50% to 75%) or multifocal bone lesion.[7] They arise from clonal proliferation of Langerhans cells. These cells can be identified under the electron microscope by the presence of Birbeck granules, which are racket-shaped cytoplasmic inclusions. The reason for proliferation of these cells in LCH is still unknown. However, various etiological factors have been suggested, including immunological reactions, bacteria, viruses and genetic factors.[8]

EG of bone is a rare disease with incidence rate of one to two per million population per year.[8] It occurs predominantly in children. 60% of EG patients having solitary lesions are less than 10 years in age. In our cases, the patient was 30 years old, which is an unusual age for EG. It has predilection for males (male:female = 2:1).[9] EG can occur as unifocal or multifocal lesion, the former being more common. Bones of the axial skeleton are usually affected.[3]

In the maxillofacial region, EG is mostly asymptomatic and is usually discovered incidentally while performing radiographic examination for other indications. When symptomatic, it may present in a various ways including pain, swelling, gingival inflammation, ulceration, and even pathological fracture. It can also present as periodontal destruction with recession of gingival and loss of alveolar bone.[7] Common dental symptoms are mobile teeth, premature exfoliation and delayed healing after tooth

extraction, which is similar to our case. Laboratory analyses are usually noncontributory. Elevated ESR and leukocytosis are common findings that can lead to the false impression of focal infective lesions. It should be noted that eosinophilia in the peripheral blood analysis is not a consistent finding in EG.[10]

The radiographic feature of EG is variable, depending on the stage of the disease. Initially it presents as a centrally located small lytic process, with poorly delineated rough borders. In the midphase, borders become more sharply delineated. As it progresses to late phase, resolution of periosteal lamellations takes place resulting in sharper delineation of border. Thick crust of sclerotic tissue can be seen occasionally.[11] When the lesion involves the alveolar crest, it shows characteristic "scooped out" appearance. Extensive alveolar involvement can result in floating in air appearance of teeth.[6] Rarely pathological fracture is also seen. Since the radiologic features of EG is not specific, diagnosis on the basis of radiologic finding is only speculative.[12]

In EG of jaws, clinical and radiographic features are not specific, as they mimic various diseases including osteomyelitis, odontogenic cysts, bone cysts, primary bone tumors and lymphomas, which was similar to our case, where, based on clinical and radiographic findings, diagnosis of chronic suppurative osteomyelitis was made. In such situations, histopathological examination of the lesion is crucial.[13] The classic histopathologic feature of EG is the presence of histiocytes, which grow in sheets and sheet-like collection. These large mononuclear histiocytes are round or oval in shape with elongated nucleus and longitudinal grooves and folds (Langerhans cells). Numerous eosinophils along with other inflammatory cell population of plasma cells and lymphocytes may be present.[14] As the lesion matures, fibrosis occurs and eosinophils become less numerous.[7] On immunohistochemical analysis, the Langerhans cells are positive for S-100, CD207 and CD1a. Negativity for CD45 is the finding that specifies the diagnosis.[15] In our case, the association of S-100 and CD1a and absence of CD45, confirmed the histopathologic diagnosis.

The management of EG is equally disputable, as different studies have shown different therapeutic approaches claiming effectiveness. Mode of treatment depends on the presentation of the disease. When untreated, it can resolve spontaneously or disseminate with severe or even fatal consequences. The preferred method of treatment for focal lesion is curettage or resection of affected bone. In cases of symptomatic lesions associated with risk of functional abnormality, fracture or cosmetic disfigurement, radiotherapy at relatively low dose is indicated. When there is local recurrence or when surgical treatment is not possible, radiotherapy is advised.[16] Another modality of managing local recurrent EG is intralesional injection of steroids.[2]

Prognosis for localized disease is good. However, there have been reports of late reactivation in patients considered to be cured of EG. Hence, long-term follow-up should be advised. Studies have proposed monoclonal antibodies directed against CD1a or CD207 as a potential treatment modality for EG. However, further research is needed to prove its effectiveness in the treatment of EG.[17]

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