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Mandibulary Eosinophilic Granuloma: Case Series

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Abstract: Eosinophilic granuloma is a proliferation of Langerhans cells in the bones that most commonly involving the skeletal system. The disease generally affects children or young adults with predominance in males and it is characterized by a single or multiple skeletal lesions. This study describes a few cases of mandibular Eosinophilic Granuloma and the effects of surgical curettage of lesions.

Key words: Eosinophilic granuloma, Langerhans cells, granuloma

INTRODUCTION

Eosinophilic granuloma is a proliferation of Langerhans cells in the bones that most commonly involving the skeletal system (Caroli and Ferrante, 2007; Postovsky *et al*., 2001).

It is the localized and benign form of group of Langerhans Cell Histiocytosis (LCH) diseases, which also include Hand-Schuller-Christian syndrome and Letterer-Siwe syndrome (Schroff, 2005; Siessegger *et al*., 2002).

Langerhans cells are dendritic cells deriving from Bone marrow. These cells are not a macrophages or histiocytes, because they express S-100, CD1a and langerin antigens.

However, the most feature of Langerhans cells is the presence of Birbeck granules which are rod-shaped intracellular organelles specific to these cells (Uzan-Gafsou *et al*., 2007; Frater *et al*., 2006; Gunny *et al*., 2004).

The aetiology of the disease remains largely unknown. Eosinophilic granuloma generally affects children or young adults with predominance in males and it is characterized by a single or multiple skeletal lesions (Gunny *et al*., 2004; Ramani *et al*., 2007).

Single lesions are more common than multiple lesions. The most frequent oral location is the posterior part of the mandible (Ramani *et al*., 2002). Patients with mandible lesions are usually asymptomatic or minimally symptomatic.

Clinical oral presentation includes symptoms such as: localized bone pain, adjacent soft tissue swelling, mobile teeth, gingival inflammation, bleeding, hyperplasia, ulceration, toothaches, failure or delayed socket heal following dental extraction (Watzke *et al*., 2000; Unlu *et al*., 1997; Ardekian *et al*., 1999).

A diagnosis of Eosinophilic Granuloma must be confirmed by a biopsy of the tumor, because clinical and radiological features are non-specific (Siessegger *et al*., 2002). Differential diagnosis includes osteolytic lesions such as: Bone cysts, intraosseous hemangioma, osteoblastoma, fibroma, osteomyelitis, ameloblastoma, giant cell granuloma, etc (Gibson and Prayson, 2007).

The management of patients with Eosinophilic Granuloma remains difficult and includes different protocols: surgery, radiation therapy, systemic chemotherapy, systemic and local therapy with corticoids, alone or in combination (Ramani *et al*., 2007; Watzke *et al*., 2000; Ardekian *et al*., 1999).

No studies exist that compare the effectiveness of these treatment modalities, although surgical curettage of lesions alone or in addition with corticosteroids is usually effective in treatment of Eosinophilic Granuloma of bone (Watzke *et al*., 2000; Ardekian *et al*., 1999).

This study describes a case series of mandibular Eosinophilic Granuloma and the effects of surgical curettage of lesions.

CASES SERIES

Case 1: A 43-year-old white man who had a history of pain and swelling in the right posterior parts of the mandible, was referred for assessment by his dentist.

He presented bony osteolytic lesion associated with previous tooth extraction in the right mandibular molar region.

Six months earlier, he had visited his dentist for fever, pain and swelling associated with the teeth 36 (LR6) and 37 (LR6).

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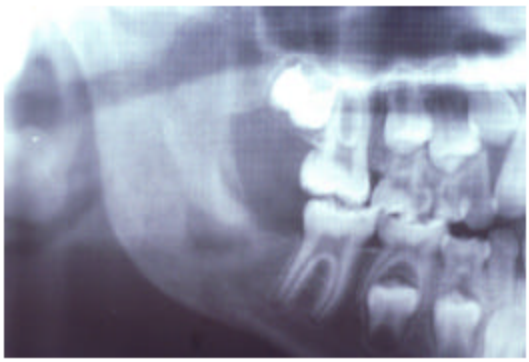

Fig. 1: Mandibular osteolytic lesion

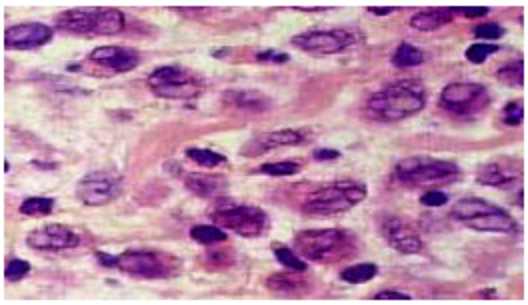

Fig. 2: Cells with pale cytoplasm and eccentric nuclei with nuclear convolutions were found

Those teeth had been extracted but he had noted failure socket heal and increasing of symptomathology. Clinical intraoral examination revealed extensive swelling of the gingiva and alveolar mucosa around the teeth 46 and 47 region.

Subsequently a panoramic radiograph confirmed the presence of osteolytic lesion which suggested a tumor (Fig. 1).

Computed tomography and scintigraphy showed no other lesion. Patient was treated by surgical curettage.

The lesion appeared as a single regular nodule in the right mandibular jaw.

A representative biopsy specimen was taken from the osteolytic process and it was referred for histologic examination.

Histiologically cells with pale cytoplasm and eccentric nuclei with nuclear convolutions were found (Fig. 2).

Ultrastructural studies demonstrate Birbeck granules and immunohistologically these cells stained for S100, langerin and CD1a (Fig. 3).

The diagnosis of Eosinophilic Granuloma was carried out, relying on histopathological and immunohistochemical evaluations.

Clinical and radiographic follow-up were done in the first 6 months, 1 year, 2 years and 5 years postoperative with excellent prognosis.

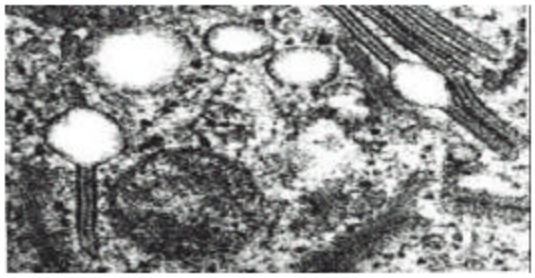

Fig. 3: Birbeck granules

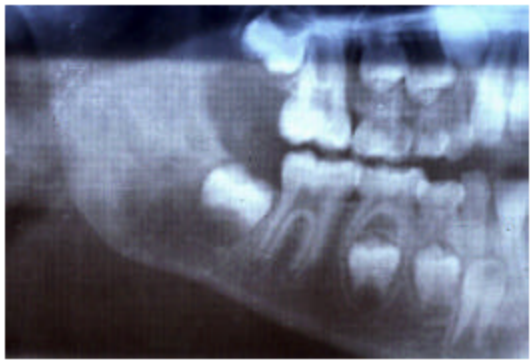

Fig. 4: A radiolucency in the mandible angle region

Case 2: A 8-year-old white man who had an asymptomatic osteolytic lesion localized in the right mandibular molar region, was referred for assessment by his local dental practitioner. Osteolytic lesion was revealed incidentally during the orthopantomography carried out for orthodontic examination.

Intraoral examination shows no clinical signs of lesions. A radiolucency in the mandible angle region was observed in the panoramic radiograph apparently causing no displacement of the second Lower Right Molar (LR7) germ (Fig. 4).

Computed tomography and scintigraphy confirmed that lesion was single. The treatment was by curettage and extraction of the germs of the 47, as the bony support of the tooth was lost (Fig. 5). Specimens taken for examination showed dendritic cells with eosinophilic cytoplasm. Immunohistochemically these cells are stained with langerin, S-100 protein and CD1a.

The identification of Birbeck granules on electron microscopic study demonstrated that these cells were Langerhans cells.

Clinical, radiographic and pathological features demonstrate diagnosis of Eosinophilic Granuloma. Clinical and radiographic follow-up were done in the first 6 months; 1 year; 2 years; and 3 years postoperative with excellent prognosis.

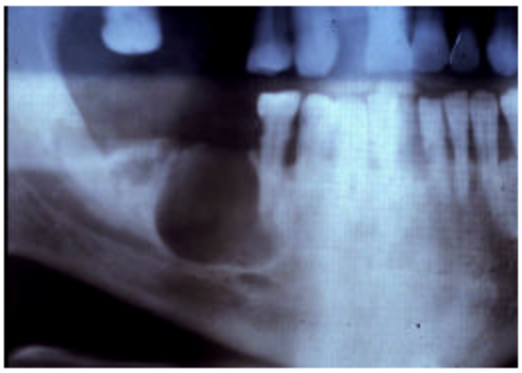

Fig. 5: Curettage and extraction of the germs of the 47

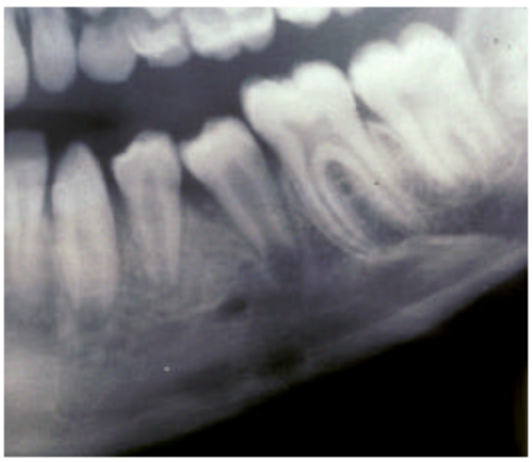

Fig. 6: Panoramic radiograph showed multiple lytic lesions in the left posterior parts of the mandible

Case 3: A 12-year-old female was referred to our Department for multiple asymptomatic osteolytic lesions associated with the right posterior parts of the mandible. Osteolytic lesion was revealed incidentally by her paediatric dentist during the examination of a orthopantomography. Intraoral examination shows no clinical signs of lesions.

Panoramic radiograph showed multiple lytic lesions in the left posterior parts of the mandible (Fig. 6). Computed tomography and scintigraphy revealed no other lesion. The lesions were treated by surgical curettage. Specimens taken for examination showed the presence of Langerhans cells. The diagnosis of Eosinophilic Granuloma was carried out on the basis of clinical, radiographic and pathological features. Clinical and radiographic follow-up were done in the first 6 months 1 year 2 years and 5 years postoperative with excellent prognosis.

Comment: Dendritic cell neoplasms are rare tumours that World Health Organization (WHO) classifies into five groups: Langerhans' cell histiocytosis, Langerhans' cell sarcoma, Interdigitating dendritic cell sarcoma/tumour, Follicular dendritic cell sarcoma/tumour and Dendritic cell sarcoma (Kairouz *et al*., 2007).

Among these diseases, Langerhans' cell histiocytosis plays a important role. Langerhans Cell Histiocytosis (LCH) is a rare disorder characterized by an uncontrolled clonal proliferation of Langerhans cells, that occurs in several organ systems including the lung, bone, liver, lymph nodes and brain (Gunny *et al*., 2004; Da Costa *et al*., 2007; Kim *et al*., 2006).

Today aetiology and pathogenesis is still unclear. In Da Costa *et al*. (2007) observed that " the clonal nature of LCH could support the hypothesis that it is a neoplastic disease with unlimited growth potential (Da Costa *et al*., 2007). According to this Neoplastic hypothesis are the results of a study of Amir *et al*. (2007).

In 2007 these authors examined expression of various gene products that play a role in cell cycle and cell death and their association with any bone diseases.

In this study, Amir and Weintraub (2007) suggested that cell proliferation and suppression of apoptosis may be mechanisms of cell survival in the more aggressive forms of LCH.

Some authors reported cases of patients with multisystem LCH with spontaneous resolution of lesions (Gunny *et al*., 2004; Yamaguchi *et al*., 2004).

Spontaneous resolution is only apparently in contrast with neoplastic hypothesis, as spontaneous regression of neoplastic lesions is sometimes described in literature.

Cao *et al*. (2005) studies the potential etiological factors and clinical features of gastric eosinophilic granuloma. These authors suggest that *H. pylori* infection, estrogen status and local allergic reactions may be associated with the development of gastric eosinophilic granuloma (Cao *et al*., 2005).

Other aetiological hypothesis sustains the role of virus such as HHV-6, HHV-8 and EBV (Csire *et al*., 2007; Sakata *et al*., 2007). Eosinophilic granuloma represents a localised form of Langerhans Cell Histiocytoses (LCH) that most commonly involving the skeletal system in childhood.

Primary skull lesions are rare in the pediatric population. The diagnosis eosiniphilic granuloma is very difficult and might be made only by bone biopsy. In fact clinical and imaging studies do not reveal abnormalities in other organs. The differential diagnosis of these lesions includes both congenital and acquired osteolytic lesions.

Multifocal cases of Eosinophilic granuloma stresses the importance of scintigraphy and CT as complementary methods that enable one to make an assessment of the extent of the disease and thereby for biopsy planning, diagnosis and therapy.

The excellent prognosis does not dispense on regularly follow up. Further clinical study is required to establish the aetiology and pathogenesis of this rare disorder. These studies will have to establish if Langerhans cell histiocytosis is a neoplastic, an immune or an infective disease. This is very important for the prophylactic and therapeutic strategies.

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