

Case Report

Calcitonin as an Adjuvant Therapy after Surgical Excision of Central Giant Cell Granuloma of Mandible: A Clinical Case Report

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Abstract

As defined by World Health Organization, Central Giant Cell Granuloma (CGCG) is an intraosseous lesion consisting of cellular fibrous tissue that contains multiple foci of hemorrhage, aggregations of multinucleated giant cells, and occasionally trabeculae of woven bone. Management of CGCG varies from a simple curettage in nonaggressive cases to complex surgical options in more aggressive forms. Several non-surgical treatment protocols have been suggested based on various biologic behavior of giant cell granuloma including Interferon therapy, administration of calcitonin or steroids. In this case a conservative treatment consisting of curettage and calcitonin therapy was administered in the treatment of a large CGCG lesion to prevent consequences of radical resection.

INTRODUCTION

In 1953 Jaffe firstly described Giant cell granuloma as central giant cell reparative granuloma (CGCG) [1], and World Health Organization defines it as an intraosseous lesion consisting of cellular fibrous tissue that contains multiple foci of hemorrhage, aggregations of multinucleated giant cells, and occasionally trabeculae of woven bone [2]. This benign osteolytic lesion includes less than 7% of jaw lesions [3]. CGCG is more likely to develop in women; it is also more common in the mandible, from anterior site of first molar which often crosses the midline [4]. It is most common in adolescents especially women under thirteens [3,5,6]. Its radiographic features include a unilocular or multilocular radiolucency with well-defined borders [8]. Histologically, CGCG has fibroblastic, osteoblastic and osteoclast potentials predominant, high vascular elements and hemorrhage. It has a spindle shaped cellular stroma containing osteoclast-like multinucleated giant cells with obvious inflammatory cells infiltration [2,4].

Cherubism, Brown tumor of hyperparathyroidism, fibrous dysplasia and aneurismal bone cyst also share some similar histologic features [4,9]. These lesions differ in other clinical aspects; as Cherubism is a bilateral painless mandibular or maxillary swelling which causes intraoral alveolar masses and is more common in childhood [3,4]. Normal levels of calcium,

phosphate and alkaline phosphatase rule out the Brown tumor of hyperparathyroidism [4]. Choung et al., divided central giant cell lesions into two groups of aggressive and non-aggressive types based on the biologic behaviors, growth and recurrence rates [7]. Aggressive lesions are associated with pain, tooth mobility, rapid growth rate, root resorption, cortical perforation and 13-49% risk of recurrence [3,7]. Several treatment methods have been suggested for treatment of CGCG during the recent decades. Management of CGCG varies from a simple curettage in non-aggressive cases to complex surgical enucleation in more aggressive forms. Surgical procedures include: excision, curettage and peripheral osteotomy. Simple curettage or radiation therapy can be applied in treatment of inaccessible or non-resectable maxillary lesions [9]. Becelli et al., used autologous iliac crest bone graft to reconstruct the mandible after the excision of a CGCG. It has also been suggested in the literature that the use of curettage along with cryosurgery can be applied to treat aggressive lesions [5]. The Recurrence rate of CGCG following initial conservative surgery is 12-37 % [4]. According to various theories about biologic behavior and possible nature of CGCG a number of non-surgical treatment protocols have been suggested. Harris was the first who applied calcitonin for treatment of CGCG [10]. Antiangiogenic properties of Interferon $\alpha 2$ was the cause of INF therapy protocols for CGCG treatment [11]. Steroids are also used

in the treatment of CGCG due to their anti-inflammatory and anti-angiogenic properties [12,13].

CASE PRESENTATION

A 33-year-old woman was referred to Alzahra hospital, Isfahan, Iran with the chief complaint of localized intraoral increasing swelling accompanied by paresthesia in the left side parasymphysis of the mandible and aching sensation in lower incisors during the 3 months prior to admission. The patient had no relevant medical history and was not using any medications. Also, no history of traumatic injury or hemorrhage was reported. Extra oral examinations revealed mild facial asymmetry and no lymphadenopathy were noted. Mandibular left 3rd molar had been extracted 3 months before the problem started. Intraoral examinations revealed a bony-hard, reddish, non-tender mass with no tooth displacement or mobility within the adjacent dentition (Figure 1). The result of the vitality test was normal and similar to the opposite quadrant teeth.

Radiographic investigations with panoramic radiograph showed a well-defined intraosseous radiolucent mass with radio opaque borders extending from the mesial root surface of the 2nd mandibular right premolar to the mesial root surface of the left lower canine leading to root resorption (Figure 2). Laboratory test levels of calcium and phosphorus were within the normal range which ruled out a brown tumor of primary hyperparathyroidism, however 25-hydroxy vitamin D level was insufficient. Therefore, Vitamin D (AsalDaroo Kish, Tehran, Iran) was prescribed for 6-8 weeks.

Incisional biopsy was performed under local anesthesia (lidocaine 2% with 1/80000 epinephrine, Daroopaksh, Tehran, Iran). Histopathological exams revealed a fibrotic stroma with the presence of bony spicules and multi-nucleated giant cells. Clinical, radiographic and microscopic results confirmed the diagnosis of a CGCG. Presence of highly cellular connective tissue with high osteoblastic activity in specimens increased the risk of relapsing so regular follow up with radiographic examination was suggested.

Treatment was started with excisional biopsy under general anaesthesia. After complete excision of the lesion, 1 ml calcitonin (Salmon) was injected in the site (Figure 3). All the teeth involved



Figure 1 Photograph of the patient.



Figure 2 Panoramic radiograph of the patient depicting the tumor extending from the mesial root surface of the 2nd mandibular right premolar to the mesial root surface of the left lower canine.



Figure 3 Clinical image demonstrating injection of calcitonin to the lesion.

in the lesion remained intact during the surgery. The patient received calcitonin subcutaneously for one month after the surgery.

After 3 months follow up, the lesion was completely regressed, clinical examination was normal and radiographic investigation revealed complete healing of the surgical defect with no signs of recurrence. 6-month follow up reports revealed continuous bone healing and no evidence of recurrence was observed.

DISCUSSION

CGCG is a benign lesion of the jaw with fibroblastic, osteoblastic and osteoclastic activities, most occurring in the anterior mandible in women younger than thirty [3,4].

One of the major complications of CGCG is its recurrence after treatments [14]. According to various theories about biologic behavior of CGCG, a number of non-surgical treatment procedures have been suggested including:

(A) radiation therapy which was firstly suggested by Herendeen however due to an increased risk of malignancy it is not recommended for treatment of CGCG unless for inaccessible or non resectable lesions [9].

(B) Antiangiogenic properties of interferon $\alpha 2$ can be effective

in the treatment of this proliferative vascular lesion [15]; Kaban et al., applied interferon $\alpha 2$ in 8 patients with CGCG of mandible. They enucleated lesions and administered interferon $\alpha 2$ daily subcutaneously for 6-8 months. In 7 patients who completed the treatment course, follow up results revealed successful curing [11].

(C) Jacoway described the use of corticosteroids in the treatment of CGCG. This treatment protocol included 6 intra-lesion injections of equal parts of triamcinolone acetonide accompanied by local anesthetic over a period of 6 weeks [13,16].

(D) Calcitonin therapy for CGCG was firstly described by Harris [10]. The use of calcitonin is justified by the presence of giant cells receptors for calcitonin and also its anti-osteoclastic properties [12,13]. The first generation of calcitonin was synthetic human type which is no longer on the market. The salmon calcitonin is much more effective than the human synthetic calcitonin. Due to published studies, 50 IU of salmon calcitonin seems to be equivalent to 75-90 IU of human calcitonin. However, the benefit of human calcitonin is its less immunogenic reactivity [1]. It has been stated that salmon calcitonin represents similar effects on the inhibition of osteoclastic bone resorption in comparison to human calcitonin [17].

It has been stated that the route of calcitonin administration (subcutaneous injections or nasal spray) might influence the therapeutic outcomes. The subcutaneous injection causes 70% bioavailability is compared to 3% to 25% in a nasal spray. Therefore, the subcutaneous injection was ordered in the treatment protocol [1].

Porgel et al., used a successful calcitonin therapy protocol for 10 patients: 9 receiving daily subcutaneous, and 1 using nasal spray. Results revealed a positive effect on resolution of the lesion, although long term assessment is needed [12]. In another clinical trial study by Tabrizi et al., 12 patients underwent curettage and intra nasal calcitonin therapy (200IU/day once a day) for 3 months after surgery. After 5 years follow up, recurrence was observed only in one of the patients out of 12 [14]. In presented case, a conservative treatment combining excision and calcitonin therapy was preferred to prevent following consequences of resection and aggressive surgical procedures. The results and follow up data revealed no signs of recurrence along-side complete healing of the lesion after 6 months follow up. This method could be effective substitute for the resection in aggressive CGCG cases and prevents morbidity, loss of function and psychological side effects of aggressive surgical procedures.

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