Central Giant Cell Granuloma Resistant to Calcitonin Nasal Spray: A Case Report

Lucia Gerzanic1*, Günter Schultes1, Hans Kärcher1 and Doris Zebedin2
1Department of Oral and Maxillofacial Surgery, Medical University of Graz, Auenbruggerplatz, Austria
2Department of Radiology, Medical University of Graz, Auenbruggerplatz, Austria

Abstract

Purpose: We describe successful treatment of a recurrent central giant cell granuloma (CGCG). This is a rare benign intraosseous lesion that occurs before age 30 and can quickly recur as a painless lesion of the mandible. Because of its aggressive growth and tendency to progress as well as its morphological similarity to a giant cell tumour, it justifies radical surgery.

Patients and methods: A female patient aged 18 years presented with a CGCG lesion in the mandible that recurred despite standard treatment with calcitonin nasal spray after enucleation of the initial lesion.

Results: The recurrence in the mandible required radical surgery and reconstruction with a microvascular iliac bone flap; there was no injury to cranial nerves and facial appearance was normal.

Conclusion: Radical surgical treatment of CGCG recurrence is the best option when calcitonin nasal spray fails to prevent recurrence.

Keywords: Central giant cell granulomas; Calcitonin nasal spray; Radical surgical treatment

Introduction

Central giant cell granulomas (CGCGs) of the jaws are rare benign intraosseous lesions that can quickly recur as indolent lesions in mandible, where they are more commonly found than in the maxilla. Conventional treatment is local curettage, which is associated with a high success rate and low recurrence rate [1]. Recurrences have nonetheless been noted and studies suggest recurrence rates up to 20% with local curettage [1]. A more aggressive curettage or enucleation has been recommended, possibly coupled with adjunctive treatment such as liquid nitrogen cryotherapy [2]. To minimize risk of poor esthetic or functional outcome, many clinicians treat aggressive CGCGs with intraosseal triamcinolone, intranasal calcitonin or subcutaneous interferon alpha-2a. Radiation therapy and other chemotherapeutic agents such as methotrexate, doxorubicin, and cyclophosphamide have been employed. Other alternative treatments include intraosseal steroid injections at weekly intervals for six weeks [3-6]. A number of alternative nonsurgical therapies have been advocated for the management of CGCG. Calcitonin antagonizes osteoclastic bone resorption and acts directly on other cell types in this lesion, and calcitonin receptors have been identified on giant cells of the lesion [7,8]. Lim and Gibbins reported that immunohistochemistry suggests that stromal cells or fibroblasts are the etiologic basis of CGCG and that the giant cells themselves may be secondary or reactive [9]. Maerki et al. [10] wrote that it was initially referred to as a "giant cell reparative granuloma", due to the accepted notion of its tendency to repair areas of injury, the term "giant cell granuloma (GCG)" is now more frequently used as this lesion has been found in patients without a history of trauma. In addition, several cases of a destructive rather than reparative nature have been observed. Maerki et al. described a case that supports the theory of trauma and inflammation as risk factors for GCG, so that care must be taken when GCG presents in unusual locations as in a case where it is in the middle cranial fossa in a mixed material arts fighter [10]. Because of its aggressive growth and tendency to progress, the central giant cell granuloma has been described as a benign lesion, although its morphological similarity to a giant cell tumour demands a radical surgical approach. This case report describes successful radical surgery after calcitonin nasal spray failed to prevent recurrence of a CGCG lesion.

Patients and Methods

A female patient aged 18 years with a biopsy-proven CGCG was treated with calcitonin nasal spray after enucleation of the mandibular lesion. The indication for additional administration of calcitonin therapy was a clinically and radiographically aggressive variant of CGCG that recurred in the presence of hyperthyroidism. The patient had a biopsy and evaluation for hyperthyroidism (serum phosphate, calcium, parathormone, parathormone related protein) prior to surgical enucleation of the left mandible followed by intranasal salmon calcitonin (100 IU/day) for six months. In spite of the nasal spray, five months after the first operation she developed a recurrent expansive osteolytic process that extended from the first molar to the collum of the left mandible with swelling and pain. The aggressive CGCG lesion grew rapidly and expanded in spite of calcitonin therapy. Calcitonin was stopped and she underwent radical partial resection of the left mandible with a microvascular musculocutaneous iliac bone flap. She was monitored every three months clinically and radiographically; blood samples were taken to assess bone formation and calcium metabolism on the basis of calcium, phosphate, PTH, alkaline phosphatase and osteocalcin. To evaluate bone resorption, 24-h urinary calcium and hydroxyproline were determined every three to six months. She was monitored by PET/CT for regression or recurrence.

*Corresponding author: Lucia Gerzanic, Department of Oral and Maxillofacial Surgery, Medical University of Graz, Auenbruggerplatz 12, A-8036 Graz, Austria, Tel: 00436641124229; Fax: 0043/316/385/351; E-mail: lucia.gerzanic@medunigraz.at

Received July 19, 2013; Accepted September 14, 2013; Published September 18, 2013

Citation: Gerzanic L, Schultes G, Kärcher H, Zebedin D (2013) Central Giant Cell Granuloma Resistant to Calcitonin Nasal Spray: A Case Report. Anaplastology 2: 119. doi: 10.4172/2161-1173.1000119

Copyright: © 2013 Al-Sukhun J, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.
Results

This 18-year-old woman has been followed for three years after first presenting with an aggressive lesion that was enucleated surgically and proved upon biopsy to be a central giant cell granuloma. The criteria for choosing the patient for additional administration of calcitonin were a clinically and radiographically aggressive variant of CGCG and a recurrent CGCG along with a suspicion of hyperparathyroidism. A work-up at our hospital’s Division of Endocrinology and Nuclear Medicine failed to confirm this. Our patient was evaluated radiologically and clinically every three months. Orthopantomography after 5 months showed a recurrent lesion more than 4 cm in length and 2 cm in height that was growing rapidly and aggressively in the left mandible (Figure 1), although calcitonin nasal spray had been initiated immediately after the enucleation. Absorption of the nasal spray is known to be erratic and varies between 20% and 100%. The calcitonin spray was discontinued and the patient underwent radical surgery (Figure 2) with a microvascular iliac bone flap (Figure 3). Healing after the second intervention was uneventful and she regained normal facial appearance after resolution of the postoperative edema (Figure 4). The function of the cranial nerves was preserved.

Discussion

Central giant cell granulomas (CGCG) of the jaws are histologically benign lesions characterized by the presence of giant cells in the richly vascularized stroma of the spindle cells. They are morphologically similar to giant cell tumours of the long bones. The giant cell reparative granuloma [11] as it was originally called is not a granuloma in the histologic sense. It is not reparative clinically, apparently demonstrating neoplastic tendencies [12]. Some studies consider giant cell tumors to be a manifestation of the central giant cell granuloma because of the histopathology, whereby age and local factors are responsible for varying clinical characteristics [1,13,14]. The differential diagnosis of CGCL includes the so-called “brown tumor of hyperparathyroidism” (BTOH), peripheral giant cell granuloma, and giant cell tumor of bone. The end result of PTH secretion is osteoclast proliferation, bone resorption, and calcium liberation. Pathologically sustained PTH elevation causes BTOH, which consists of mononuclear osteoclast precursors and multinucleated differentiated osteoclasts. None of these differential diagnoses was confirmed. Intranasal calcitonin spray is the usual postoperative treatment; it can be self-administered and has minimal side effects [15-17]. At present, the nature of the CGCG is unknown, and it is still not known whether the central giant cell granuloma represents an inflammatory, reactive, infective, or neoplastic process. Some authors describe the CGCG as a progressive lesion with potential for aggression. In our case, radical surgery for CGCG with preservation of function and normal facial appearance was effective. In view of the recurrence after the initial enucleation, there was no reason to continue the calcitonin after radical surgery, as it had not prevented recurrence after the first surgery and resistance to the spray had apparently developed.

Conclusions

We can offer no explanation as to why the patient had no recurrence after radical surgery but suggest that this is the best treatment option when enucleation of a CGCG and calcitonin spray are ineffective.
References

1. Whitaker SB, Waldron CA (1993) Central giant cell lesions of the jaws. A clinical, radiologic, and histopathologic study. Oral Surg Oral Med Oral Pathol 75: 199-208.
2. Schmidt BL, Pogrel MA (2001) The use of enucleation and liquid nitrogen cryotherapy in the management of odontogenic keratocysts. J Oral Maxillofac Surg 59: 720-725.
3. Jakoway JR, Howell FV, Terry BC (1988); Central giant cell granuloma: An alternative to surgical therapy. Oral Surg Oral Med Oral Pathol 66: 572.
4. Terry BC, Jacoway JR (1994) Management of central giant cell lesions: An alternative to surgical therapy. Oral Maxillofac Surg Clin North Am 6: 579.
5. Kermer C, Millesi W, Watzke IM (1994) Local injection of corticosteroids for central giant cell granuloma. A case report. Int J Oral Maxillofac Surg 23: 366-368.
6. Carlos R, Sedano HO (2002) Intralesional corticosteroids as an alternative treatment for central giant cell granuloma. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 93: 161-166.
7. Pogrel MA, Reggezi JA, Harris ST, Goldring SR (1999) Calcitonin treatment for central giant cell granulomas of the mandible: report of two cases. J Oral Maxillofac Surg 57: 848-853.
8. Flanagan AM, Nui B, Tinkler SM, Horton MA, Williams DM, et al. (1988) The multinucleate cells in giant cell granulomas of the jaw are osteoclasts. Cancer 62: 1139-1145.
9. Lim L, Gibbins JR (1995) Immunohistochemical and ultrastructural evidence of a modified microvasculature in the giant cell granuloma of the jaws. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 79: 190-198.
10. Maerki J, Riddle ND, Newman J, Husson MA, Lee JY (2012) Giant cell granuloma of the temporal bone in a mixed martial arts fighter. J Neurol Surg Rep 73: 60-63.
11. Jaffe HL (1953) Giant-cell reparative granuloma, traumatic bone cyst, and fibrous (fibro-oseous) dysplasia of the jawbones. Oral Surg Oral Med Oral Pathol 6: 159-175.
12. Thawley SE, Panje WR, Batsakis JG (1999) Comprehensive management of head and neck tumors. Philadelphia, PA WB Saunders, USA.
13. Auclair PL, Cuenin P, Kratochvil FJ, Stater LJ, Ellis GL (1988) A clinical and histomorphologic comparison of the central giant cell granuloma and the giant cell tumor. Oral Surg Oral Med Oral Pathol 66: 197-208.
14. Al Sheddi M, Mosadomi H, Al Dayel F (2004) Central giant cell granuloma of the jaws and giant cell tumor of long bones. A clinicopathologic, cytometric and immunohistochemical comparative study. Oral Surg Oral Surg Med Oral Pathol Oral Radiol Endod 98: 195-196.
15. De Lange J, Rosenberg AJ, van den Akker HP, Koole R, Wirds JJ, et al. (1999) Treatment of central giant cell granuloma of the jaw with calcitonin. Int J Oral Maxillofac Surg 28: 372-376.
16. Allon DM, Anavi Y, Calderon S (2009) Central giant cell lesion of the jaw: nonsurgical treatment with calcitonin nasal spray. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 107: 811-818.
17. de Lange J, van den Akker HP, Veldhuijzen van Zanten GO, Engelshove HA, van den Berg H, et al. (2006) Calcitonin therapy in central giant cell granuloma of the jaw: a randomized double-blind placebo-controlled study. Int J Oral Maxillofac Surg 35: 791-795.