Case Report

A Case of Central Giant Cell Granuloma Involving the Maxillary Sinus Clinically Masquerading as a Malignant Neoplasm

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Abstract

Central giant cell granuloma is traditionally considered to be a non neoplastic bone lesion. They usually present as a slow growing asymptomatic lesion involving the jaw bones i.e. maxilla and mandible. This paper presents an interesting case of a central giant cell granuloma in a 23 year old female that clinically presented as a swelling in the left side posterior hard palate region and radiographically with complete obliteration of the left maxillary sinus, with extension to infratemporal fossa region mimicking a malignant neoplasm. Controversy surrounding the pathogenesis, histopathological differential diagnosis and evolving differences in potential treatment modalities for this interesting pathology has also been discussed.

Key words: Giant cell granuloma, Jaw bone, Maxillary sinus, Corticosteroids

Introduction

Central giant cell granuloma (CGCG) is a localised benign but sometimes aggressive osteolytic lesion, basically consists of fibro vascular connective tissue with actively proliferating fibroblasts related spindle shaped cells and multinucleated giant cells as its primary cellular components[1]. Most of the CGCGs are asymptomatic slow growing lesion, usually diagnosed during routine radiographic examination or painless expansion of the bone in patients less than 30 years of age. Females are more often affected than males and approximately 70% cases arise in the mandible, followed by the maxilla. Lesion involving the maxillary sinus is extremely a rare occurrence[2]. This article reports an extensive case of CGCG involving the left posterior maxillary alveolus, maxillary sinus and infratemporal fossa region and its management with discussion on the controversies surrounding the pathogenesis, histopathological differential diagnosis or closely related entities and different current potential treatment option available for this entity.

Case description

A 23-years-old female patient reported with a chief complaint of swelling associated with intermittent pain in the left palatal region, approximately for two months. Swelling was initially smaller in for and had progressed to the present size. No history of numbness or abnormal sensation was reported. Clinical examination revealed a facial asymmetry due to a mild, diffuse swelling involving the left malar region. The texture and colour of the overlying skin was normal.

Intraoral examination revealed an obvious swelling involving the left side posterior hard palate region, of size approximately 5X4 cm, extending from second premolar to maxillary tuberosity region and medially upto the mid palatal raphae. The colour of the swelling was normal as that of adjacent mucosa except for the focal redness at the posterior aspect in an otherwise smooth lesion (Fig1). Generally the consistency was soft and boggy with mild tenderness on palpation.

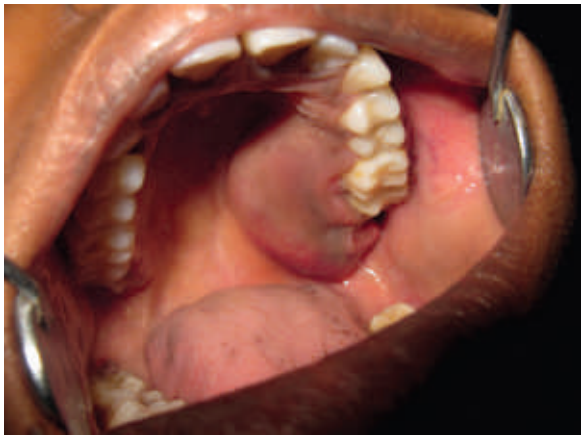

Fig 1 : Well defined smooth surface swelling involving left posterior palate

Thermal vitality test was positive in all maxillary posterior teeth. Panoramic radiograph (OPG) showed a diffuse haziness on the left side posterior maxilla and maxillary sinus region without any teeth displacement and root resorption. (Fig2)

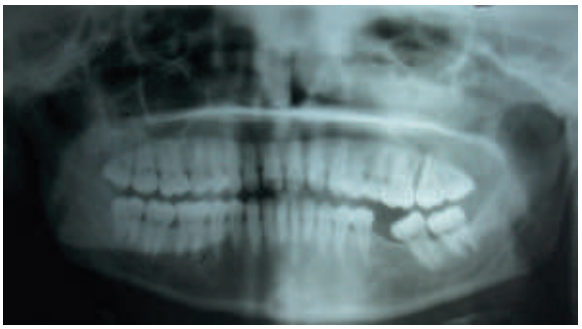

Fig 2 : OPG showing diffuse haziness on the posterior left maxilla and maxillary sinus region (Note – No root resorption or displacement is evident)

CT scan showed an expansile lytic lesion with a thin ossified rim measuring 40×34×38 mm involving the left maxillary antrum and the alveolar process of left maxilla with extra osseous component in the left infratemporal fossa region (Fig3). Deviation of the nasal septum was also noticed towards the right side.

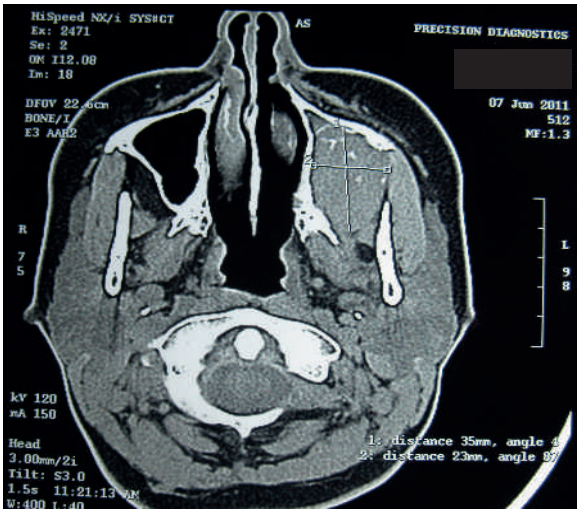

Fig 3 : CT scan showing obliteration of left maxillary sinus with destruction of posterior wall of the sinus (Before steroid injection)

Based on the clinical and radiographic presentation, a provisional diagnosis of primary malignancy of left maxillary sinus region or a salivary gland malignancy extending to involve the maxillary sinus and infratemporal fossa region was made. The differential diagnosis includes ameloblastoma, odontogenic myxoma, odontogenic keratocyst, ossifying fibroma and hemangioma.

An incisional biopsy under local anaesthesia was taken from the left maxillary sinus by creating a small window through the anterior wall. Profuse bleeding was encountered during biopsy and the hemostasis was achieved with the surgipack. Histopathological examination showed proliferating plump spindle cells and unequally distributed multinucleated giant cells in the fibrous stroma (Fig4). The giant cells were varying in shape, size, and consists of varying no of nuclei usually ranging from 10-15. Focal hemorrhagic areas and peripheral reactive bone were present. No evidence of pleomorphism, abnormal nuclear cytoplasmic ratio, and atypical mitotic figures were noticed.

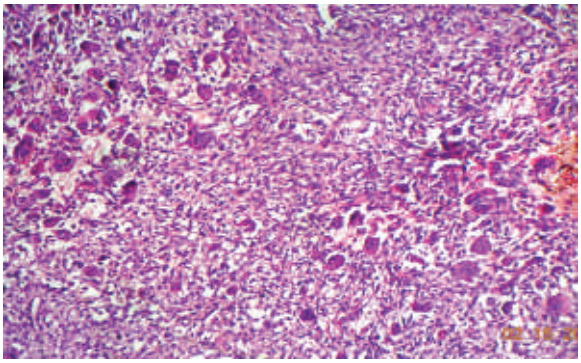

Fig 4 : Numerous unevenly distributed multinucleated giant cells within a background of plump proliferating spindle cells (H&E × 20)

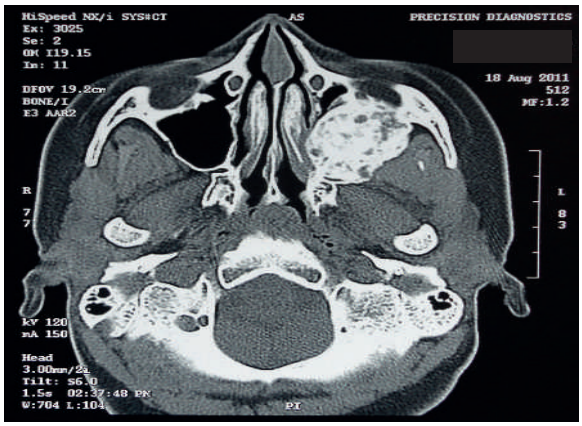

Fig 5 : CT scan showing diffuse radio opaque areas within the lesion after intralesional corticosteroid injection

Patient was referred for serum calcium and parathormone level to rule out hyperparathyroidism and the report was found to be within the normal range.
Based on the histopathology and serum biochemical investigation, a diagnosis of central giant cell granuloma was given.

Considering the posterior extension of the lesion till the infratemporal fossa region and the macroscopic nature of CGCG i.e. it does not grow as a uniform solid mass, with the stroma composed of loose fibrous tissue intermixed with abundant hemorrhagic areas, the initial treatment plan was to consolidate the lesion and possibly decrease lesion size using intralesional corticosteroids followed by the surgical removal of the lesion.

Hence the patient was started on with the initial treatment of intralesional corticosteroids as recommended by Terry and Jacoway[3] i.e. equal parts of Triamcinolone acetonide (10mg/1ml) and local anaesthetic (2% lignocaine with 1 in 200,000 adrenaline) 2ml per 2cm of the lesion was given as weekly regimen for 6 weeks.

Patient was carefully monitored for steroid induced side effects and the course was fairly uneventful. CT scan was taken one week after the last injection (7th week from starting) and on interpretation revealed diffuse radio opaque areas within the lesion which indicate consolidation of the lesion compared to the initial presentation (Fig5). Patient was informed about

the improvement, surgical removal of the lesion was planned and through an intraoral approach the lesion was removed thorough surgical curettage (Fig 6&7) Patient is under regular follow up and till to date there is no recurrence.

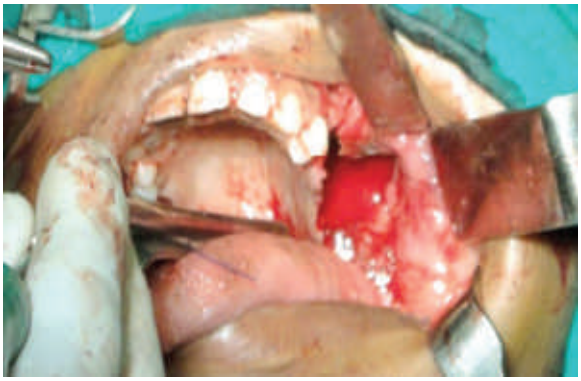

Fig 6: Intraoral surgical curettage of the lesion

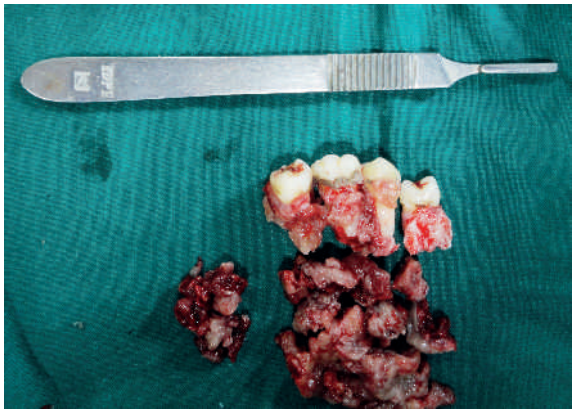

Fig 7 : Gross specimen after surgical removal of the lesion

Discussion

The term central giant cell reparative granuloma was initially coined by Jaffe in 1953 to describe a tumor of the jaw bones that had previously been diagnosed as giant cell tumor of bone. In 1962, Ackerman and Spjut described the first two cases involving the small tubular bones of hand, for which they coined the term "giant cell reaction"[4]

The most interesting aspect of this pathology is that its etiopathogeneis which still remains elusive. Earliest theories has suggested that the lesion may be derived from the odontoclasts that were responsible for the resorption of the deciduous teeth based on the facts that they occur more commonly in the deciduous teeth bearing regions of the jaws and in most cases the period of onset was found to be either during the time of exfoliation or few years after the exfoliation of deciduous teeth.

Traditionally it has been hypothesized that the giant-cell-rich areas represent a reaction to recent haemorrhage due to trauma and the fibroblastic component represents the older or the healing part of the lesion which lead to its description by the term called "Central giant cell reparative granuloma". But the fact that almost every lesion does not regresse without an intervention, lead to the removal of the term "reparative" from its original description [5]

J.A Regezi et al has speculated that there could be separately a reactive and neoplastic form or a subset of tumours that behave as a neoplasm developing from a reactive lesion through an epigenetic event in spindle mesenchymal cells[6]. Recently, cytogenetic abnormalities have been identified in a giant cell granuloma, raising the possibility that this tumor may indeed be neoplastic[7].

Though little is known about the exact etiology and the nature of CGCG, recent molecular studies have shown that the active proliferating component in the CGCG is the fibroblast related spindle cells which secrete cytokine such as monocyte chemoattractant protein (MCP) that recruits monocytes from the blood vessels which fuses to form the multinucleated giant cells i.e osteoclasts[6].

And also it has been shown that osteoclastogenesis is under the influence of osteoprotegerin and its antagonist receptor activator of nuclear factor of kappa B (RANK) ligand via an osteoclast receptor known as RANK[6].

From a differential diagnosis standpoint, severel lesions have to be considered when entertaining a diagnosis of CGCG.

Aneurysmal bone cyst (ABC) tends to occur in the same age group and also has slight female predilection but the most striking feature in the ABC is the presence of large blood filled spaces and thrombosis. These blood filled spaces are typically bordered by fibrous septa of cellular tissue that may consist of osteiod or woven bone which are oriented along its long axis.

The microscopic and radiographic feature of brown tumor of hyperparathyroidism is nearly identical and is therefore necessary always to rule out primary and secondary hyperparathyroidism viz due to parathyroid disease and chronic renal failure by determining the serum calcium, phosphorus and parathormone level.

A diagnosis of cherubism should be entertained whenever evaluating central giant lesion of the jaw but the classical multifocal involvement and the age of occurrence in a childhood usually between 2-7 years old, allows easy distinction of this entity from CGCG.

Though surgical curettage, excision or resection were considered as the conventional treatment modalities for CGCG, several medical treatment options are now available, mainly due to the current understanding about the molecular biology of the cellular components of the lesions.

One of the potential medical treatment options that have been tried in CGCG either alone or in combination with surgery and reported with a reasonably good success rate is intralesional corticosteroids. The rationale of using steroid in the CGCG is based on the fact that the giant cells express glucocorticoid receptors and it has been hypothesized that steroid inhibits the production of extracellular bone resorption mediating

lysosomal proteases by giant cells and also induce apoptosis of osteoclast (giant) like cells[8].

Though few authors[9] have reported, complete regression of the CGCG with intralesional steroid alone, in the present case the steroid was given mainly to consolidate and decrease the lesion size to facilitate its complete surgical removal.

The option between steroid alone or combined surgical and steroid treatment for CGCG entirely depends on the individual case, and how well the patient responds to the initial course of steroid injection.

Adolescent patient, moderately sized lesion in the site that can be evaluated with the simple radiograph (less exposure & cost effective), good patient compliance, with good treatment response, intralesional corticosteroid alone may be a potential option and can be given till the complete regression of the lesion. Practically the most important problem with this steroid alone option is the constant follow up that may extend for 3-6 years with the associated chance for lack of patient compliance.

The fact that the multinucleated giant cells in CGCG are basically osteoclasts and expresses calcitonin receptors forms the basis for the use of calcitonin in CGCG to inhibits the giant cell function. Harris M[10] reported four cases of CGCG treated by calcitonin where a complete remission was achieved. However the literature evidence shows that therapeutic response to calcitonin is variable and is influenced by mode of administration i.e. intravenous, subcutaneous or as nasal spray.

Presuming CGCG as a vascular lesion Interferon α also has been used in the treatment of CGCG[1]. Another promising treatment modality for CGCG in future may be administration of osteoprotegerin which is an antagonist for RANK ligand and by binding to RANK receptor on osteoclasts (giant cell) potentially inhibits its function. i.e. bone resorption[11]. In future further research should focus on gene and protein expression in CGCG to develop new medical therapeutic agents with predictable results.

Conclusion

It is essential to be aware of the fact that CGCG rarely can present as an extensive lesion involving maxillary sinus, infratemporal fossa region mimicking malignant neoplasm, this possibility should also be considered in the differential diagnosis for similar clinical presentation.We also favour the use of intralesional corticosteroids as an initial treatment option for CGCG especially for an extensive lesion to consolidate and decrease the size of the lesion to facilitate the surgical removal and to reduce the post surgical morbidity.

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