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內文:

Abstract

✧ Initially, the lesions presented concurrently in the maxilla and mandible with subsequent recurrence in the mandible. Now, two recurrences are seen in the maxillary sinus and ethmoid region.

Introduction

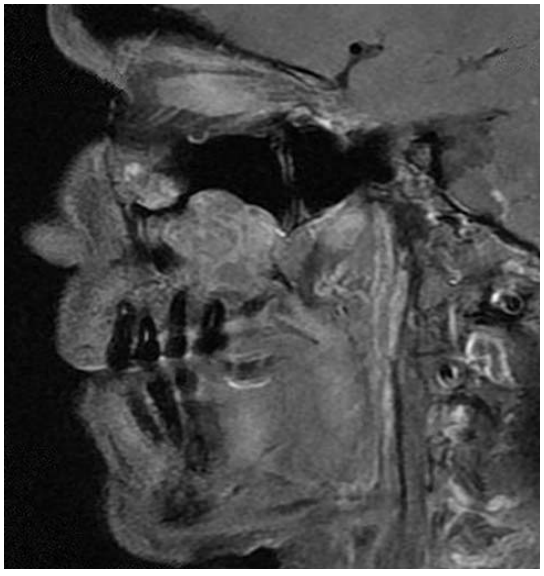
✧ **Central giant cell granuloma (CGCG)**

- Female : male = 2:1
- Most frequently under the age of 30 years. (One study of 38 patients shows 74% to be less than 30 years of age and 61% to be less than 20 years of age.)
- Lesion: solitary radiolucency with a multilocular appearance or less commonly, a unilocular appearance
- Site: more prevalent in the anterior than the posterior jaws, often crossing the midline, and the mandible is more commonly affected than the maxilla. This lesion has also been reported in the small bones of the hands and feet.
- The behavior of CGCG is variable, most commonly producing asymptomatic expansion of the jaws. However, it can be clinically aggressive, associated with pain, osseous destruction, cortical perforation, root resorption, and recurrence.
- Cases of CGCG occurring with neurofibromatosis (type 1), Noonan-like syndrome, or both have been reported.
- Treatment:
  1. simple curettage or curettage with peripheral ostectomy;
  2. Resection for lesions of the maxilla or paranasal sinuses has been advocated as the thin bony cortices and sinuses do not provide a good anatomic barrier
  3. Corticosteroids and calcitonin are used for non-surgical management

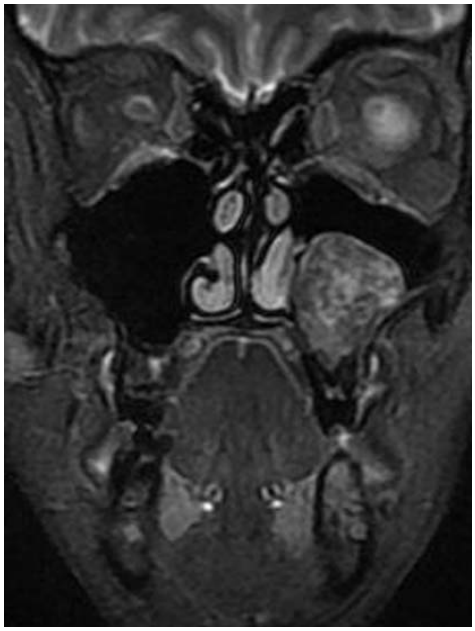
4. Interferon alpha therapy has also been used as a postoperative adjuvant and to prevent tumor progression

Report of a Case

- ✧ A 42-year-old female with a history of multifocal giant cell lesions in the left mandible and left maxilla.
- ✧ A year after her initial diagnosis and treatment, a recurrent lesion was noted in the left mandible and subsequently curetted.
- ✧ Two and a half years after the initial lesions, this was the second recurrent episode. the patient presented with two distinct lesions the larger, inferior lesion filling much of the maxillary sinus and the smaller, superior lesion adjacent to the ethmoid region.
- ✧ A comprehensive laboratory assessment:
  - ■ calcium (serum) 9.8 (normal 8.5–10.4 mg/dl),
  - ■ PTH (intact) 58 pg/ml (normal 12–65 pg/ml),
  - ■ phosphorus(serum) 2.9 mg/dl (normal 2.5–4.5 mg/dl),
  - ■ albumin 5.1 (normal 3.7–5.1 g/dl),
  - ■ urine calcium level of 6.4 mg/dl (normal, not established),
  - ■ urine 24 h calcium 185.4 mg/24 h (normal 100.0–300.00 mg/24 h).
  - ■ bilirubin of 1.8 mg/dl (normal 0.1–1.2 mg/dl)
- ✧ The patient had known Gilbert's syndrome.
- ✧ MRI



←Fig. 1 T1 weighted MRI of the tumors on sagittal section demonstrating proximity to the dentition and the ethmoid region



→Fig. 2 T2 weighted MRI of the larger inferior lesion on coronal section demonstrating deviation of inferior turbinate

- ✧ The larger of the two recurrent lesions

was 3.1 x 2.9 x 2.6 cm encompassing the roots of the maxillary posterior teeth and deviating the inferior turbinate.

- ✧ The second lesion was 2.4 x 2.3 x 2.1 cm and was located inferior to the medial floor of the left orbit.
- ✧ Treatment:
  - ■ Using an image guidance mask
  - ■ left endoscopic ethmoidectomy
  - ■ via intraoral approach
  - ■ after remove, stripping of the maxillary sinus mucosa to bone
  - ■ The maxillary sinus was reconstructed with demineralized bone matrix and autogenous platelet rich plasma.
- ✧ Histologically similar
- ✧ The hypercellular fibrous stroma was composed of mononuclear spindle shaped cells and scattered ovoid cells.

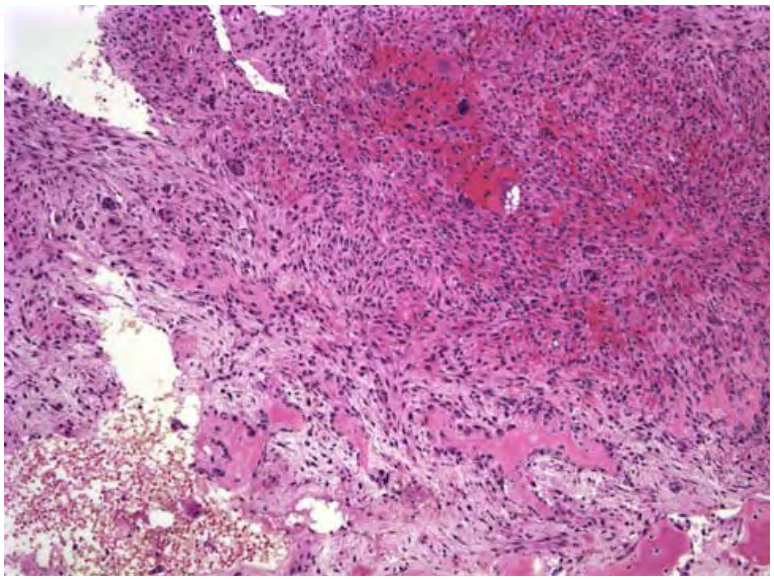


Fig. 3 Photomicrograph from first recurrence of the left maxillary CGCG showing multinucleated giant cells in a spindle or ovoid shaped fibrovascular connective tissue stroma (H&E, x10)

- ✧ Cystic areas of extravasated nonendothelialized hemorrhage, resembling an aneurismal bone cyst, and minimal mitotic activity were observed but no cellular atypia was observed.

Discussion

- ✧ Initially, CGCG was not distinguished from the giant cell tumor of the extragnathic skeleton
- ✧ Jaffe: giant cell reparative granuloma
- ✧ the more neutral term ‘‘central giant cell lesion’’ to describe this process, but most accept CGCG.

- ✧ CGCG has been proposed to be both a reactive response, to hemorrhage or trauma, and a neoplasm
- ✧ Some have proposed that giant cell granuloma of the jaws and giant cell tumors (GCT) of the extragnathic skeleton are part of a spectrum of a single lesion, modified by anatomic site
- ✧ others have viewed CGCGs and GCTs of the extragnathic skeleton as distinct lesions
- ✧ Table 1 Comparison of giant cell tumor and central giant cell granuloma

	Giant cell tumor	Central giant cell granuloma
Location	Sphenoid, temporal, ethmoid bones (endochondral ossification, not membranous in origin) Jaws in Paget disease	Jaws, anterior mandible
Giant cells	Evenly distributed	Fewer, smaller giant cells, unevenly distributed
Stromal cells	Monocytes, osteoclasts No intercellular collagen	Fibroblasts producing collagen; Numerous capillaries
Osteoid	No	Yes

- ✧ Histologically, CGCG resembles the giant cell lesion of hyperparathyroidism, cherubism, and aneurysmal bone cyst, which must be excluded.
- ✧ Multiple central giant cell lesions have been reported in association with Noonan-like/multiple giant cell lesion syndrome, and other features of the disease include a short stature, webbed neck, cubitus valgus, pulmonic stenosis, and multiple lentigenes
- ✧ Supporting the theory that the multinucleated giant cells are derived from macrophages is the immunoreactive response to muramidase, a-1 antichymotrypsin, and a-1 antitrypsin
- ✧ Aggressive and nonaggressive CGCGs stained for antibodies to CD34, CD68, factor Xllla, and smooth muscle actin, prolyl 4-hydroxylase, Ki-67, p53 protein, RANK, and glucocorticoid receptor alpha have revealed no phenotypic differences between the types
- ✧ Immunohistochemical staining for c-Src, a protein thought to be required for osteoclast activation, has yielded no quantitative difference between CGCG,

GCT, or cherubism

- ✧ SH3BP2 gene is commonly found to be mutated in cherubism, and its transcripts and proteins have been found to be expressed in GCT and CGCG.
- ✧ The mononuclear stromal cells display strong p63 immunostaining in GCTs, but this has not been detected in CGCGs
- ✧ P63 is one immunohistochemical stain that may help distinguish GCT from CGCG, while also suggesting a differing pathogenesis.
- ✧ Previous cases of multiple giant cell lesions may represent:
  1. Unusual reports of cherubism
  2. Association with a syndrome or genetic condition
  3. A single lesion of a jaw separated by normal bone
  4. Association with elevated PTHrP
  5. True giant cell tumors originating in the maxillofacial region,
  6. Multifocality resulting from hematogenous spread due to inadequate treatment
- ✧ Smith et al. have proposed a new term, ‘‘craniofacial giant cell dysplasia,’’ to describe the multifocal central giant cell of the jaws.
- ✧ Miloro and Quinn advocate dividing multifocal central giant cell lesions into synchronous or metachronous lesions: metachronous lesions are more likely to represent a recurrence due to inadequate initial treatment or tumor seeding, whereas synchronous lesions are more likely to represent true multifocality.
- ✧ Table 2 Characteristics of multifocal central giant cell granulomas

Reference	Age/Sex	Location at initial presentation	Recurrence
Davis and Tideman [43]	31/F	R mandibular body	4 months L maxilla 1 year L maxilla 2 years R mandible
Smith et al. [40]	41/F	R mandibular angle	9 years L maxillary sinus, nasal bone, orbital floor and R maxillary sinus
Martins et al. [35]	35/F	L maxilla R mandible	5 years follow-up no recurrence
Loukota [44]	25/F	R mandible	10 months L maxilla No additional recurrence at 2 years
Wise and Bridebord [45]	23/M	L mandibular body L and R nasomaxillary area	4 years follow-up no recurrence
Miloro and Quinn [34]	37/F	L maxilla Ant. mandible	1 year L maxilla and ant mandible
Bilodeau, Chowdhury, and Collins	42/F	L mandible L maxilla	1 year L mandible 2 years L maxillary sinus/ethmoid region

- ✧ female predominance, representing six of the seven patients.
- ✧ The mean age in our review of published multifocal cases was 33 years, with only two of the seven patients younger than 30 years of age
- ✧ Multifocal CGCGs are more aggressive than solitary CGCGs as exhibited by increased recurrence and osseous destruction → should be treated with more

aggressive surgical therapy as in five of seven cases the patients had a recurrence.

✧ Central giant cell granuloma remains a challenge for pathologists.

✧ multiple conditions that must be ruled out clinically

題號	題目
1	關於 central giant cell granuloma(CGCG), 下列何者為非? (A) Ranging from 2 to 80 years of age (B) Majority in females (C) Mostly arise in the mandible (D) Most giant cell granulomas of the jaws are symptomatic.
答案(D)	出處：Oral & Maxillofacial Pathology, 2nd edition ,p545
題號	題目
2	關於 central giant cell granuloma 與 giant cell tumor 的比較, 下列何者為非?
	(A) central giant cell granuloma 的好發部位是 jaws, anterior mandible (B) central giant cell granuloma 含有 osteoid,而 giant cell tumor 沒有 (C) central giant cell granuloma 的 giant cells 分布均勻 (D) central giant cell granuloma 的 stromal cells 中,fibroblasts producing collagen, 且含有 numerous capillaries
答案(C)	出處：From this journal Ans: the giant cells are more evenly distributed in the GCT