Article published online: 2022-09-20

CASE REPORT

Clival giant cell tumor - A rare case report and review of literature with respect to current line of management

Mohana Rao Patibandla, Amit Kumar Thotakural, Marabathina Nageswara Rao[1], Gokul Chowdary Addagada[5], Manisha Chowdary Nukavarapu[5], Manas Kumar Panigrahi[2], Shantiveer Uppin[3], Sundaram Challa[3], Srinivas Dandamudi[4]

Departments of Neurosurgery and [3]Pathology, Nizam's Institute of Medical Sciences, Hyderabad, [1]Neurosurgery, NRI Medical College, Mangalagiri, [2]Krishna Institute of Medical Sciences, Secunderabad, Telangana, [4]Radiology, NRI Medical College, Mangalagiri, [5]Guntur Medical College, Guntur, Andhra Pradesh, India

ABSTRACT

Giant-cell tumor (GCT) involving the skull base is rare. Sphenoid bone is the most commonly involved bone followed by petrous temporal bone. Histopathology and radiological features of these lesions are similar to GCT involving bone elsewhere. Unlike other sites, skull base is not an ideal site for the radical surgery. Hence adjuvant treatment has pivotal role. Radiation therapy with intensity-modulated radiation therapy, stereotactic radiosurgery or chemotherapy with adriamycin are promising as described in some case reports. Bisphosphonates showed good control in local recurrence. *In vitro* studies with Zolendronate loaded bone cement and phase 2 trials of Denosumab showed hopeful results, may be useful in future.

Key words: Clivus, giant cell tumor, skull base, sphenoid bone

Introduction

Giant cell tumor (GCT) of bone constitutes 3-7% of all bone tumors and in those head and neck area including skull comprises of 2%.[1] In the head and neck region, GCT occurs principally in the jaw bones and less commonly in the ethmoidal bones, sphenoid bones, zygomatic bones, temporal bones, and frontal bone.[1] Although rare, skull base GCT involves mostly sphenoid bone followed by petrous temporal bone.[2] The common occurrence in the sphenoid bone is due to the enchondral ossification as compared to membranous ossification of other skull bones.[1] GCT arises from the nonosteogenic stromal cells of bone marrow.[1] We present an interesting report of the GCT arising from the clivus in a 20-year-old male with review of literature.

Access this article online	
Quick Response Code:	Website: www.asianjns.org
	DOI: 10.4103/1793-5482.145112

Address for correspondence:
Dr. Amit Kumar Thotakural, Department of Neurosurgery, NRI Medical College, Mangalagiri, Guntur - 522 503, Andhra Pradesh, India. E-mail: doctoramitkumar@gmail.com

Case Report

A 20-year-old male was admitted with a 6 weeks history of left hemicranial headache, associated with vomiting of 10 days duration. There was history of drooping of left eye lid of 1 week duration. On examination, the left eye had partial ptosis and 6th nerve palsy. The remaining ophthalmological and neurological examinations were normal, and the past medical history was not significant. Patient was evaluated with computerized tomogram (CT) and magnetic resonance imaging (MRI) brain. The CT scan showed a homogeneous, expansile mass with lytic bone destruction involving the clivus, sphenoid sinus, sella and nasopharynx with homogeneous well enhancement on contrast administration. There was egg shell calcification noted on the bone window. The MRI brain plain study demonstrated the lesion in the clivus and sphenoid sinus, sella which was isointense on the T1 and

How to cite this article: Patibandla MR, Thotakura AK, Rao MN, Addagada GC, Nukavarapu MC, Panigrahi MK, *et al*. Clival giant cell tumor - A rare case report and review of literature with respect to current line of management. Asian J Neurosurg 2017;12:78-81.

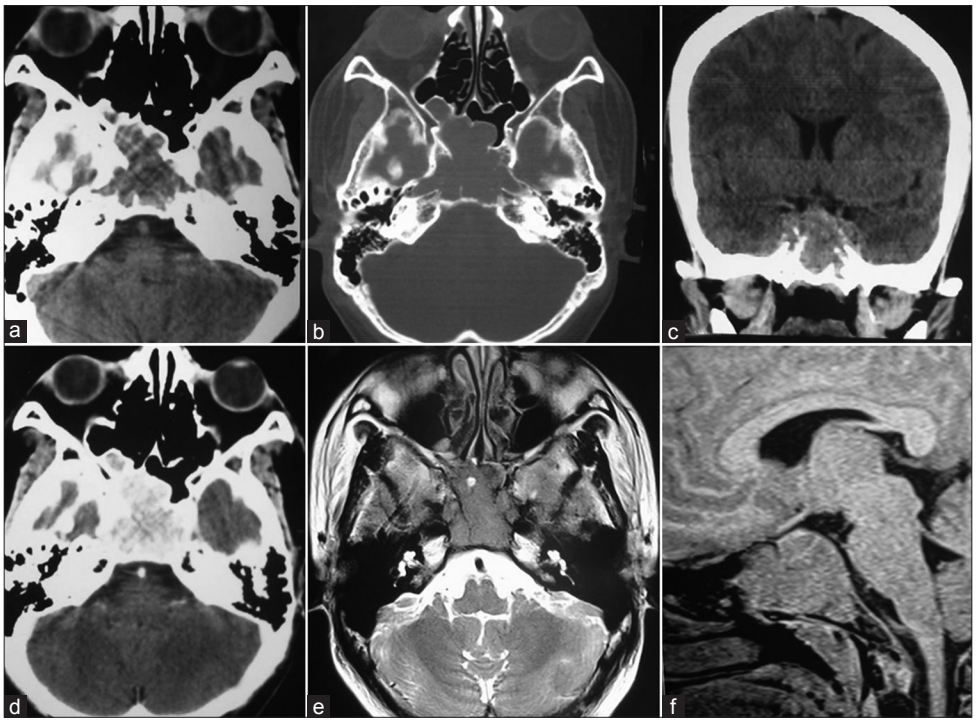

Figure 1: CT scan Brain plain study axial section normal window (a) and bone window (b) showing isodense lesion in clivus with expansion of bone and peripheral egg shell calcification and extension to sphenoid and nasopharynx, coronal section (c) showing extension of lesion to bilateral cavernous sinuses, axial section contrast study (d) showing uniform well enhancement of lesion. MRI Brain plain T2WI axial section (e) and T1 WI sagittal section (f) showing well defined isointense clival lesion on T1 and T2 WI

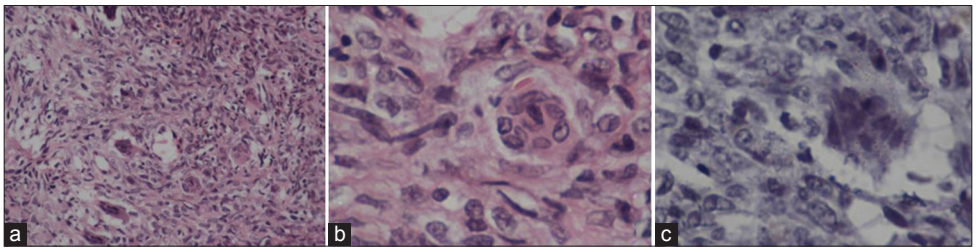

Figure 2: Histopathological examination with different magnification x100 and x400 showing mononuclear cells and osteoclast like giant cells with similar nucleoli. EMA stain was negative

T2 weighted images [Figure 1]. Patient underwent a bilateral transnasal transsphenoidal subtotal resection of the tumor. Grossly, the tumor tissue was firm, reddish brown, friable, and moderately vascular. The histopathological examination showed osteoclastic giant cells, fibroblastic spindle and round cells without atypia and mitoses. Osteoclastic giant cells contains nearly 30 to 40 nuclei with scanty cytoplasm, spindle cells contain abundant cytoplasm with collagen. These histopathological features are consistent with a benign GCT [Figure 2]. At the time of discharge, patient had recovery of VI nerve palsy with persistent left upper eyelid drooping. Post-operatively, patient was treated with intensity-modulated radiation therapy (IMRT) for the residual lesion. A 3-month follow-up examination revealed that the patient is free from symptoms.

Discussion

This tumor is also known as GCT of epiphysis, localized osteitis fibrosa cystica or osteoclastoma. GCT is a solitary lucent lesion with osteoclast-like giant cells and stromal cells. The exact etiology of the GCT is not known but presumed to be due to parathyroid hormone related protein, increased receptor activator of nuclear factor-κB ligand (RANKL) expression by stromal cells of GCT of bone, which in turn causes the resorption of bone.[3]

GCT of the clival and sphenoid bone are generally present with the headache, III, IV, VI cranial nerves, visual loss, and proptosis due to involvement of sphenoid bone, sphenoclival junction, and middle cranial fossa.[1,2] According to Canpanascci *et al*., GCT is radiologically graded into three grades. Grade 1 - tumor

Table 1: Previously reported cases of skullbase

Year	Patient details	Location	Surgery	RT	CT	Recurence	Outcome/total survival
Zorlu *et al*.[2]	14/F	Sphenoid and clivus	STR	RT on recurrence	-	Recurrent after surgery and RT	Alive WD/2 years
Gupta *et al*.[17]	17/F	Clivus	STR	3D-CRT	-	-	Alive/2 yrs
Present case	20/M	Clivus	STR	57 Gy	-	-	Alive WD/6 months

CT – Chemotherapy; f – Female; GTR – Gross total resection; Gy – Grey; M – Male; NED – No evidence of disease; RT – Radiotherapy; STR – Subtotal resection; WD – With disease; Yrs – Years

associated with a well defined margin and thin rim of mature bone; Grade 2 - tumor is well defined but has no radiopaque rim; Grade 3 - tumor with fuzzy borders. Our case corresponds to grade 2, which has moderate prognosis according to Canpanascci.[4]

Histopathologically tumor shows osteoclastic giant cells that contain more than 15 round to oval shaped nuclei per cell, never show mitotic activity and probably formed from fusion of stromal cells. GCT also characteristically contains stromal cells, which have single nucleus, arranged in storiform pattern with 5 to 10 mitoses per high power field, express intracellular adhesion molecule-1. Hemorrhage, hemosiderin and even necrosis may be seen. Upto 50% may have reactive osteoid laid down in trabecular pattern. Immunohistochemistry, though not essential to diagnose, may show positive stain for betacatenin, cyclin D1, MMP – 1, MMP – 13, CD 34, P53, PDGFA, and C-kit. Recent study has shown that CCAAT/enhancer binding protein beta (C/EBPbeta) is a RANKL promoter activator in stromal cells of GCT of bone and which plays an important role in the osteolytic characteristics and pathological causes of GCT of bone.[5] MMP – 13 is a principal proteinase present in GCT and Runx2 may play a crucial role in cytokine-mediated MMP-13 expression in GCT stromal cells.[6] Presence of P53 indicates high risk of local recurrence and metastasis in GCT.[7] Approximately, 84% of GCT show telomeric fusion in various chromosomes like 11p, 13p, 15p, 18p, 19p, and 21p, with telomere length reduction[8] (more in grade 3 than grade 1 and 2), and centromere amplification[9] (higher in recurrent and malignant GCT). Differential diagnoses for GCT are Brown tumor, Osteoblastoma, Aneurysmal bone cyst, Giant cell rich fibrosarcoma and Dedifferentiated chondrosarcoma.

GCT work up should include detailed history, physical examination, serum calcium and phosphate levels, serum parathyroid hormone level, bone scan, chest X-ray, CT, and MRI. Treatment modalities include enbloc resection, curettage, curettage and adjuvant chemotherapy (doxorubicin, cisplatin, methotrexate, zolendronate, and raloxefine) or radiotherapy.[10] Recurrence in long bone GCT is increased in the ascending order with enbloc resection, subtotal resection with adjuvant treatment (chemotherapy or radiotherapy), curettage with PMMA cement and only curettage.[2,10] Giant cell tumor is associated with soft tissue recurrence and lung metastasis.[11] Due to inadequate availability of literature the definitive treatment for skull base GCT is uncertain.[2] Radiotherapy has vital role as showed in previous case reports of skull base GCT.[2] In one study, unresenctable lesions treated with 57.6 Gy mean dose IMRT for sphenoid lesion and followed for 60 months showed good tumor control and no side effects.[12] There were case reports showing usage of gamma knife radiosurgery for petrous bone GCT.[13] Chemotherapy with adriamycin in previous skull base GCT showed good control in one study.[2] Bisphosphonates may be useful in decreasing local recurrence when compared with placebo (4.2% vs 30%), mechanism appears to be apoptosis of spindle cells in GCT.[14] *In vitro* studies with zolendronate loaded bone cement[15] and phase 2 trial of Denosumab[16] showed promising results in the control of the GCT, may be useful in future for unresectable tumors. In long bone tumors GCT metastasize to lungs in 1-9%. Malignant transformation of GCT has been reported, mostly due to adjuvant radiotherapy. As radical surgery is difficult unlike other sites, adjuvant treatment has pivotal role.[18]

Previously reported cases were tabulated in Table 1.

Conclusions

GCT involving the skull base is rare. Sphenoid bone is the most common bone involved followed by petrous temporal bone. As radical surgery is difficult unlike other sites, adjuvant treatment has pivotal role. Radiation therapy with IMRT, stereotactic radiosurgery, and chemotherapy with adriamycin is useful. Bisphosphonates may have a role in the control of local recurrence.

Contribution statement

All authors contribute in either of 1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content; and 3) final approval of the version to be published.

FUNDING STATEMENT: This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Weber AL, Hug EB, Muenter MW, Curtin HD. Giant-cell tumors of the sphenoid bone in four children: Radiological, clinical, and pathological findings. Skull Base surg 1997;7:163-73.
2. Zorlu F, Selek U, Soylemezoglu F, Oge K. Malignant giant cell tumor of the skull base originating from clivus and sphenoid bone. J Neurooncol 2006;76:149-52.
3. Cowan RW, Singh G, Ghert M. PTHrP increases RANKL expression by stromal cells from giant cell tumor of bone. J Orthop Res 2012;30:877-84.
4. Campanacci M, Baldini N, Boriani S, Sudanese A. Giant cell tumor of bone. J Bone Joint Surg Am 1987;69:106-14.
5. Ng PK, Tsui SK, Lau CP, Wong CH, Wong WH, Huang L, *et al*. CCAAT/enhancer binding protein beta is up-regulated in giant cell tumor of bone and regulates RANKL expression. J Cell Biochem 2010;110:438-46.
6. Mak IW, Cowan RW, Popovic S, Colterjohn N, Singh G, Ghert M. Upregulation of MMP-13 via Runx2 in the stromal cell of Giant Cell Tumor of bone. Bone 2009;45:377-86.
7. Papanastassiou I, Ioannou M, Papagelopoulos PJ, Arealis G, Mihas C, Iakovidou I, *et al*. P53 expression as a prognostic marker in giant cell tumor of bone: A pilot study. Orthopedics 2010;33:doi: 10.3928/01477447-20100329-15.
8. Matsuo T, Hiyama E, Sugita T, Shimose S, Kubo T, Mochizuki Y, *et al*. Telomeric activity in giant cell tumors of bone. Ann Surg Oncol 2007;14:2896-902.
9. Moskovszky L, Dezsö K, Athanasou N, Szendröi M, Kopper L, Kliskey K, *et al*. Centrosome abnormalities in giant cell tumour of bone: Possible association with chromosomal instability. Mod Pathol 2010;23:359-66.
10. Suehara Y, Nozawa M, Kim SG, Nagayama M, Kojima T, Torigoe T, *et al*. Late recurrence of giant cell tumor of bone after curettage and adjuvant treatment: A case report. J Orthop Surg 2010;18:122-5.
11. Abdel-Motaal MM, Othman AS, Katchy MK, Jassar AK. Soft-tissue recurrence of giant cell tumor of bone associated with pulmonary metastases. Gulf J Oncolog 2009;5:49-53.
12. Roeder F, Timke C, Zwicker F, Thieke C, Bischof M, Debus J, *et al*. Intensity modulated radiotherapy (IMRT) in benign giant cell tumors: A single institution case series and a short review of the literature. Radiat Oncol 2010;5:18.
13. Kim IY, Jung S, Jung TY, Moon KS, Jang WY, Park SJ, *et al*. Gamma knife radiosurgery for giant cell tumor of the petrous bone. Clin Neurol Neurosurg 2012;114:185-9.
14. Tse LF, Wong KC, Kumta SM, Huang L, Chow TC, Griffith JF. Bisphosphonates reduce local recurrence in extremity giant cell tumor of bone: A case-control study. Bone 2008;42:68-73.
15. Zwolak P, Manivel JC, Jasinski P, Kirstein MN, Dudek AZ, Fisher J, *et al*. Cytotoxic effect of zoledronic acid-loaded bone cement on giant cell tumor, multiple myeloma, and renal cell carcinoma cell lines. J Bone Joint Surg Am 2010;92:162-8.
16. Thomas D, Henshaw R, Skubitz K, Chawla S, Staddon A, Blay JY, *et al*. Denosumab in patients with giant-cell tumour of bone: An open-label, phase 2 study. Lancet Oncol 2010;11:275-80.
17. Gupta R, Mohindra S, Mahore A, Mathuriya SN, Radotra BD. Giant cell tumour of the clivus. Br J Neurosurg 2008;22:447-9.
18. Kattner KA, Stroink A, Gupta K, Fukushima T, Li C. Giant cell tumor of the sphenoid bone. Skull Base Surg 1998;8:93-7.