

A Rare Tumor of Clivus Masquerading as Pituitary Adenoma

Abstract

Giant cell tumors (GCT) are generally benign, commonly affecting young adults, with a slight preponderance in females. They are locally aggressive with a high rate of local recurrence. Most of them are found in the epiphysis of long bones, making the base of the skull a rare site. We report the case of a 35-year-old female, who presented with neurological symptoms of headache and diplopia. On magnetic resonance imaging, a space-occupying lesion was discovered in the clivus. Histopathology was diagnostic of a GCT. GCT arising from the clivus is extremely uncommon, with about 15 cases published in the literature. The present case highlights the rarity of this tumor and contributes to the existing literature with analysis and evaluation of the management strategies and prognosis.

Keywords: *Clivus, giant cell tumor, skull base*

Introduction

Giant cell tumors (GCT) of bone are benign neoplasms, believed to arise from nonosteogenic stromal cells of the bone marrow near the epiphysis. Most of them are found in the epiphysis of long bones, whereas a small proportion occurs in the bones of the hand and foot, ribs, mandible, scapula, and vertebrae. GCT are very uncommon in the head and neck where they tend to show a predilection for the mandible and maxilla.^[1] Calvarial GCTs are rare accounting for 0.5% of all GCTs.^[2] We report a case of a primary GCT arising from the clivus, which is extremely uncommon, with about 15 cases published in the literature.^[3]

Case Report

A 35-year-old female presented to the neurosurgery department of our hospital complaining of intermittent headache and blurred vision for the past 6 months. She also complained of severe diplopia in the left lateral gaze. Her symptoms rapidly worsened over the past 3 months. On examination, visual acuity in bilateral eyes was 6/24. She also had left 6th cranial nerve palsy. Routine urine, stool, and blood analysis were normal. All her laboratory parameters including hormone profile were

within normal limits. Contrast magnetic resonance imaging (MRI) revealed a large clival-based homogeneously enhancing lesion involving the entire clivus and invading the sphenoid sinus, no calcification noted on MRI [Figure 1]. Based on preoperative radiology, a provisional diagnosis of pituitary adenoma, clival chordoma, and plasmacytoma was considered.

The patient underwent a standard extended endoscopic endonasal transsphenoidal surgery. The lesion was eroding into sphenoid sinus and there was destruction of the sellar floor with loss of midline landmarks. It was highly vascular, nonsuckable with gritty consistency and areas of calcification. In view of significant blood loss, the lesion was debulked and a subtotal resection could be performed. Hemostasis was achieved carefully using a hemostatic agent and packing by surgical. There was no intraoperative cerebrospinal fluid leak. The closure was done using Hadad flap and abdomen fat. The surgery was uneventful and the patient was discharged on postoperative day 3. Her symptoms improved significantly after surgery. The patient is on regular follow-up for the past 6 months and has received 2 cycles of radiotherapy (60 Gy/45 fr).

On gross examination, multiple gray white soft-tissue pieces were received.

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**Swati Singh,
Dipanker Singh
Mankotia¹,
Kepeemadam
Balasubramanyam
Shankar¹, Fouzia
Siraj**

*Department of Pathology,
ICMR-National Institute of
Pathology, ¹Department of
Neurosurgery, VMMC and
Safdarjung Hospital, New Delhi,
India*

Address for correspondence:

*Dr. Fouzia Siraj,
ICMR-National Institute of
Pathology, Safdarjung Hospital
Campus, New Delhi, India.
E-mail: fouziasiraj2009@gmail.
com*

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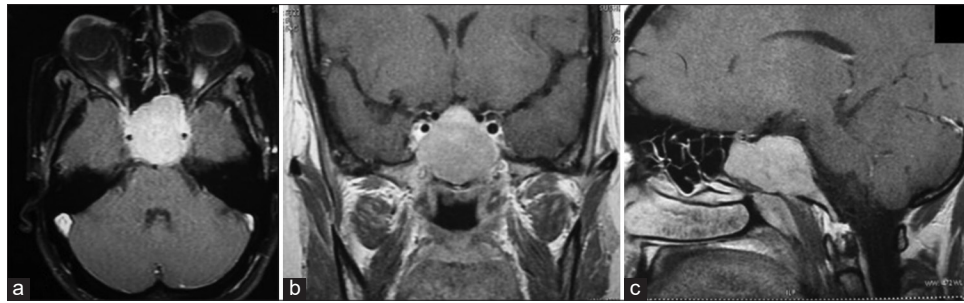


Figure 1: Contrast magnetic resonance imaging (a-c) revealed a large clival-based homogeneously enhancing lesion involving the whole of clivus and invading the sphenoid sinus

Histopathological examination showed a tumor arranged in sheets with numerous scattered multinucleated giant cells. Sinonasal mucosal fragments were also noted adjacent to the tumor [Figure 2]. The giant cells were osteoclastic in nature and were surrounded by mononuclear spindle cells. No mitosis, necrosis, or significant cellular atypia was noted [Figure 3]. Few bony spicules were seen interspersed within the tumor stroma. The features were of a giant cell lesion. Other differential diagnoses of pituitary adenoma, plasmacytoma, and chordoma were ruled out on basis of clinical parameters, histology, and immunohistochemical features. A final diagnosis of Giant cell tumor was given.

Discussion

GCT represents about 3%–5% of all primary bone tumors in adults.^[4] It occurs mainly in the third decade of life with a slight preponderance in females. Less than 1% of GCTs occur in the skull, among which sphenoid and temporal bones are the most commonly involved.^[2]

Only 15 cases of clival GCT have been reported till date [Table 1], out of which eight patients were male and seven female.^[2,3] The average age among all the reported cases was 24.8 years. The most common symptoms were headache and diplopia. Our patient was a 35-year-old female, who presented with neurological symptoms which could be attributed to the anatomical location of the tumor.

GCTs of the bone are locally aggressive tumors which typically occur after the closure of the epiphyseal growth plate. However, occasionally, they may recur or metastasize. Few studies have implicated the role of radiation therapy in the sarcomatoid transformation of these tumors.^[5] Among the cases reported in the literature, two patients succumbed to metastatic GCT of the clivus.^[6,7] In the case reports by Scotto di Carlo *et al.*, one patient had an aggressive tumor which recurred after 1 month of the first surgery.

Recent studies have highlighted H3F3A mutations in GCT. The same mutation was identified in two cases of clival GCT in the study done by Scotto di Carlo *et al.*, establishing an identical pathogenesis as that of GCTs of other sites.^[2]

Radiologically, GCTs do not have a specific appearance. Usually, an expanding lytic and destructive lesion is seen

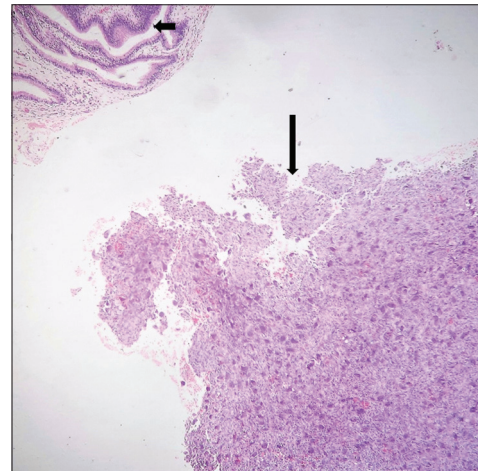


Figure 2: Photomicrograph showing pseudostratified columnar epithelium (short arrow) and an island of tumor cells (long arrow) (H and E, ×40)

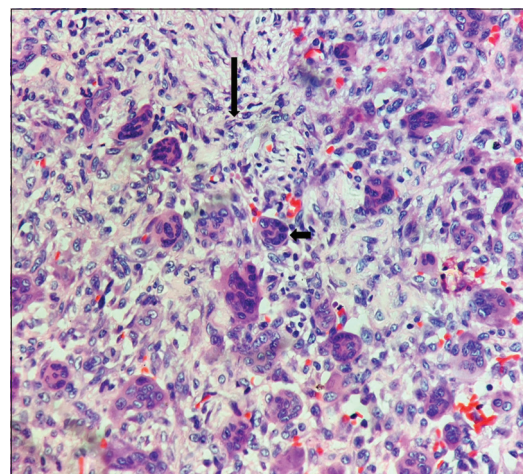


Figure 3: Photomicrograph showing tumor composed of multinucleated giant cells (short arrow) surrounded by round, mononuclear, and spindle cells (long arrow) (H and E, ×400)

in the temporal bone computed tomography. These tumors have vascular nature; therefore, they are mostly contrast enhancing. Magnetic resonance (MR) images generally demonstrate signal isointensity on T1-weighted images and signal hypointensity on both T2- and diffusion-weighted images.^[5] In the present review of the literature, the tumors were either expansile or lytic lesions. MRI findings

Table 1: Review of literature of giant cell tumor, clivus

Years	Age (years)/sex	Clinical features	Size (cm)	Duration of symptoms	MRI imaging T1/T2 findings	Vascularity	Surgery	RT	Outcome	Follow-up (months)
Wolfe et al., 1983	16/female	Headache, diplopia, visual disturbance	NA	4-7 weeks	NA	NA	STR	Yes	Alive with residual tumor	96
Kattner et al., 1998	9/female	Headache, diplopia	NA	1 month	Space-enhancing lesion T2-reveals hypo- and isointense mass of the sphenoid sinus	NA	Biopsy (TSS)	Yes	Alive with residual tumor	12
Sharma et al., 2002	18/female	Headache, progressive hearing loss, facial paresis	NA	6 months	Space-enhancing lesion, T1-isointense, T2-hyperintense	Moderately vascular	NTR	Yes	Alive	12
Sharma et al., 2002	12/female	Headache, right hearing loss, facial paresis, nasal regurgitation, nasal twang	NA	3 months	Space-enhancing lesion, T1-isointense, T2-hyperintense	Moderately vascular	GTR	Yes	Alive	12
Zorlu et al., 2006	14/female	Headache, diplopia	6×4 × 3.5	2.5 months	Space-enhancing lesion, demonstrated a lytic expansive mass lesion	NA	STR	Yes	Alive with residual tumor	24
Gupta et al., 2008	17/female	Headache, diplopia, amenorrhea, visual disturbance	7.6×5.4	6 months	Space-enhancing lesion	Moderately vascular	STR	Yes	Alive with residual tumor	24
Sasagawa et al., 2012	26/male	Headache, diplopia	3×3	NA	Space-enhancing lesion, T1-isointense, T2-hypointense	Highly vascular, massive bleeding	STR	Yes	Death	9
Locangeli et al., 2013	31/male	Headache, diplopia	NA	NA	Space-enhancing lesion, large giant cell tumor originating from the clivus and involving both cavernous sinuses	Highly vascular, ICA rupture	NTR	No	Alive with residual tumor	72
Roy et al., 2013	19/male	Headache, facial hyperesthesia	5.6×3.6×3.5	6 months	T1- large expansile mass, T2W-hyperintense	High vascularity	GTR	Yes	Alive with residual tumor	18
Agrawal et al., 2014	62/male	Headache, diplopia	NA	3 months	Space-enhancing lesion	NA	Endoscopic biopsy f/b STR	NA	No	NA
Shibao et al., 2015	25/male	Diplopia	5.1×3.1×4.9	1 month	Space-enhancing lesion, T1-isointense, T2-hypointense	Highly vascular, massive bleeding, brain stem invasion	STR	Yes	Death	31

Contd...

Table 1: Contd...

Years	Age (years)/sex	Clinical features	Size (cm)	Duration of symptoms	MRI imaging T1/ T2 findings	Vascularity	Surgery	RT	Outcome	Follow-up (months)
Patibandla et al., 2017	20/male	Left hemicranial headache, vomiting, drooping of left eyelid	NA	6 weeks	T1/T2- isointense	NA	STR	Yes	Alive with residual tumor	3
Satapathy et al., 2018	24/male	Headache, diplopia, diminished vision	5.7×4.5×5.7	4 months	Space-enhancing lesion, large mass centered on clivus	Moderately vascular	GTR	Yes	Alive	8
Di carlo et al., 2018	55/female	Headache, vomiting	5×2.8×3.8	NA	Space-enhancing lesion, revealed a lobulated mass originating from the clivus and extending into the sella and the epistropheus	NA	suboccipital approach f/b redosurgery	Yes	Alive	36
Di carlo et al., 2018	A/M	Headache, diplopia	NA	NA	Space-enhancing lesion, lobulated mass	NA	Endoscopic endonasal approach	No	Alive	72
Present case	35/female	Headache, diplopia, blurred vision	4×2.5×0.5	6 months	Space-enhancing lesion, homogenously enhancing space-occupying lesion	Highly vascular	Endoscopic endonasal transsphenoidal subtotal resection	Yes (60 gy/45 fr)	Alive with residual tumor	6

f/b – Followed by; fr – Fraction, gy – Grays, GTR – Gross total resection, ICA – Internal carotid artery, MRI – Magnetic resonance imaging; NTR – Near-total resection; NA – Not available; STR – Subtotal resection; TSS – Transsphenoidal sinus surgery; RT – Radiotherapy

showed mostly contrast enhancing and isointense masses on T1-weighted images. The intensity was variable in T2-weighted images. Moderate to high vascularity was noted in majority of cases [Table 1].

Radiological features overlap with those of pituitary adenoma and the two entities are difficult to distinguish at times. MR for pituitary adenoma exhibits isointensity to gray matter on both T1- and T2-weighted images. However, larger lesions are often heterogenous and vary in signal due to areas of cystic change, necrosis, or hemorrhage. Calcification is rare. In contrast, chordoma shows intermediate to low signal intensity with small foci of hyperintensity (intratumoral hemorrhage or a mucus pool) on T1-weighted images. On T2, most exhibit a very high signal, thus distinguishing it from GCT which is usually isointense.

Histologically, these tumors consist of three cell types: osteoclast-like multinucleated giant cells; round mononuclear cells resembling monocytes; and spindle-shaped, fibroblast-like stromal cells. In our case, there were no atypical features histologically; however, a lack of these features does not predict the subsequent course of the disease.^[3] Therefore, regular follow-up is mandatory.

On histopathology, the differential diagnosis consists of giant cell-rich tumors, namely giant cell reparative granuloma, chordoma, chondrosarcoma, osteoblastoma, chondroblastoma, brown cell tumor of the parathyroid gland, ossifying fibroma, fibrous dysplasia, or aneurysmal bone cyst.^[8] In our case, possibilities of plasmacytoma and chordoma were ruled out on histology as well as negative IHC staining for CD138 (ruling out plasmacytoma), CK, and S100 (excluding chordoma). Clinical, histological, and laboratory parameters were evaluated to rule out pituitary adenoma.

Treatment modalities include gross total resection (GTR), curettage, curettage and adjuvant chemotherapy, or radiotherapy. GTR is associated with the lowest recurrence rate and should be the goal of treatment. However, the location and highly vascular nature of these tumors render complete resection difficult. This was evident in the review of literature as only three out of fifteen patients underwent GTR [Table 1]. Many surgical approaches including the EEA, frontal craniotomy, and transmaxillary approach have been utilized for treating clival GCTs. In our case, endoscopic endonasal transsphenoidal surgery with subtotal resection was performed in view of significant blood loss.

If GTR cannot be achieved, the combination of subtotal resection and radiation results in a similar recurrence rate.^[9] The role of adjuvant radiotherapy in treatment is still controversial with some authors reporting that radiotherapy may trigger the sarcomatous transformation of GCT.^[5] It is, therefore, reserved for tumors that are not amenable to complete resection. In the present review, ten patients were given radiotherapy following subtotal resection. With the advent of denosumab, there is now a role for chemotherapy in the treatment of GCT.^[10]

Conclusion

GCT are generally benign tumors which can be locally aggressive and mimic malignant tumors clinically and radiologically. The exact diagnosis can only be made on histopathology. GCT at the skull base, especially centered over the clivus remains a management challenge for the surgical fraternity because of their location and vascularity. Despite advances in microsurgical and radiation techniques, long-term control is still not achieved.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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