International Journal of Scientific Reports
Ferdause J et al. Int J Sci Rep. 2023 Jul;9(7):220-226
http://www.sci-rep.com
pISSN 2454-2156 | eISSN 2454-2164
DOI: https://dx.doi.org/10.18203/issn.2454-2156.IntJSciRep20231762

Case Report

Giant cell tumor of clivus: a rare case report and review of literature

Jannatul Ferdause*, Rubama Karim, Anita Rahman Taposhi, Qamaruzzaman Chowdhury

Department of Radiation Oncology, Ahsania Mission Cancer and General Hospital, Dhaka, Bangladesh

Received: 06 February 2023
Revised: 24 May 2023
Accepted: 25 May 2023

***Correspondence:**
Dr. Jannatul Ferdause,
E-mail: taimur.jannatul@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Clival giant cell tumors (GCTs) are an extremely rare type of tumor, with only 13 cases reported to date. Despite being histologically considered benign, these tumors can be locally aggressive and have a high rate of local recurrence, as well as the potential for distant metastasis. Due to their rarity and the difficulty of treating them due to their critical location, the ideal treatment protocol for managing clival GCTs remains controversial. The present report describes a 22-year-old female who experienced ptosis on her right eye and visual disturbance for one month. Magnetic resonance imaging (MRI) revealed a large, heterogenous, lobulated mass lesion arising from the clivus, extending anteriorly and compressing the optic chiasm and optic tract, with both parasellar extension and extension into the sphenoid sinus. An endoscopic endonasal trans-sphenoidal procedure was performed to excise the lesion. Post-operative MRI revealed residual disease, so a revision surgery was done using a combined microscopic and endoscopic procedure. Following surgery, the patient was given Denosumab for one year as well as has been symptom-free for the past 18 months of follow-up. This report contributes to the limited literature on the GCTs involving the clivus.

Keywords: Giant cell tumor, Clivus, Denosumab

INTRODUCTION

Giant cell tumors (GCTs) or osteoclastomas, are locally aggressive benign tumors that typically affect the epiphysis of long bones such as distal femur, proximal tibia, distal radius and proximal humerus. These tumors are rare and tend to recur in the same area of the bone, characterized by proliferation of giant cells and osteoclast-like cells, which can cause destruction of the surrounding bone. Despite being benign, GCTs can cause significant morbidity due to their size and location, making appropriate treatment essential.[1,2] GCTs of bone constitute 3-7% of all bone tumors, with 2% of those occurring in the head and neck area, including the skull. In the head and neck region, GCTs occur primarily in the jaw bones.[3] Although rare, skull base GCTs primarily involve the sphenoid bone, followed by the petrous part of the temporal bone.[4] Primary GCTs of the clivus are extremely rare, with only 13 cases reported to date. Due to the small number of skull GCTs reported in the literature, standard treatments remain unclear, and the efficacy of surgery and adjuvant treatment remains uncertain. Herein, we present a case of a GCT in the clivus in a 22-year-old woman, who was treated with surgery followed by denosumab, and review the literature. Written informed consent was obtained from the patient.

CASE REPORT

A 22-year-old lady presented with a 1-month history of drooping of her right eyelid and visual disturbance. On examination, the right eye had reduced vision and partial ptosis. The remaining ophthalmological and neurological examinations were normal. She had a history of hypothyroidism for 4 years. The patient was evaluated

with MRI of the brain, which showed a large lobulated, strongly enhancing lesion measuring approximately 4.1×2.4×2.5 cm in the basi-sphenoid area. The lesion extended anteriorly, compressing the optic chiasm and optic tract with both parasellar extension and inferiorly deepening into the sphenoid sinus. The mass was hypointense on T1WI and heterogeneously hyperintense on T2WI (Figure 1). The patient underwent endoscopic endonasal transsphenoidal removal of the tumor. The per-operative finding revealed that the tumor was hard to firm in consistency, moderately vascular, and firmly attached with the dura. Histopathology report showed the tumor was composed of numerous multinucleated osteoclast-like giant cells and spindle-shaped stromal cells, with rare mitoses; suggestive of a giant cell tumor of bone (Figure 2). Following surgery, the patient developed severe photophobia. After 20 days of the initial surgery, an magnetic resonance imaging confirmed a residual lesion measuring 2.4×2×2.3 cm (Figure 3). The patient was advised to undergo re-surgery, but it was unfortunately delayed for 3 months due to the COVID-19 pandemic. Just before her re-surgery, an MRI of the brain showed a large lobulated mass measuring 4.1×3×3.2 cm with intense enhancement at the clivus with right parasellar extension. The right cavernous sinus was encased (Figure 4). On a computed tomography (CT) scan of the base of the skull, gross bony erosion was present in the sphenoid bone (Figure 5). This time, surgery was done by a combined microscopic and endoscopic procedure (right pterional craniotomy was done, epidural trans-cavernous removal of parasellar tumor, intra-dural removal of supra-sellar portion of tumor and endoscopic removal of sellar portion of tumor). The histopathology report again showed features of a giant cell tumor. No evidence of malignancy was seen. Post-operatively, the patient's lateral rectus palsy improved gradually. One month following surgery, the patient underwent an MRI scan which showed a lobulated enhancing lesion measuring 2.5×1.6×2 cm in the sphenoid region with mild right parasellar extension and lateral extension into the right cavernous sinus encasing the right internal carotid artery (ICA). There was still mild compression of the optic chiasm and right optic nerve (Figure 6). Following the surgery, the patient was started on monthly Denosumab treatment. Three months later, a comparative magnetic resonance imaging study was done which showed partial regression of the disease (1.5×1.8 cm) at the site of the operation with further reduced compression on the optic chiasm and right optic nerve (Figure 7). Four months later, another magnetic resonance imaging scan was done which showed no significant change compared to the previous scan. The patient's parathyroid hormone (PTH) level was found to be 4 times greater than the upper limit of the normal range, so the treatment with denosumab was stopped for three months. A repeat magnetic resonance imaging revealed mild regression of the disease compared to the prior scan (Figure 8) and the patient's PTH level returned to normal. The patient is currently being monitored as well as is clinically asymptomatic.

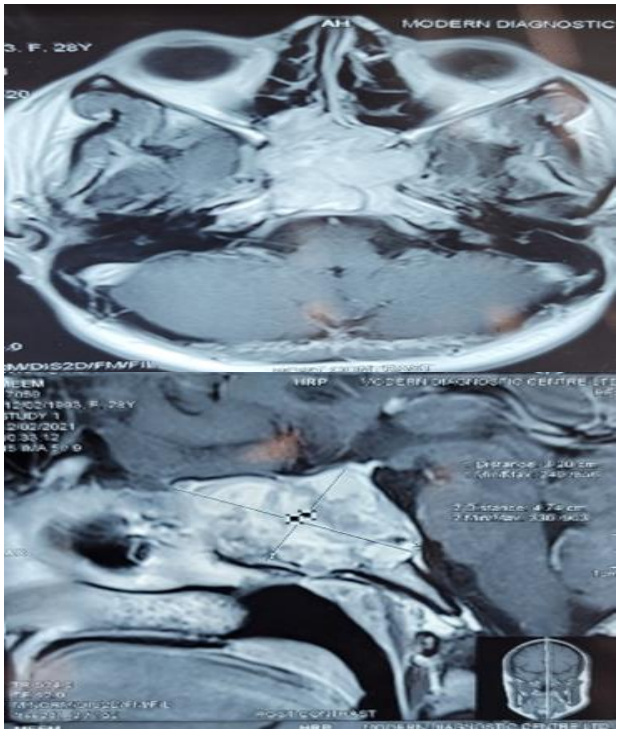

Figure 1: (MRI) of brain which showed there was a large lobulated strongly enhancing lesion measuring about 4.1×2.4×2.5 cm; in basi-sphenoid area, extending anteriorly and compressing the optic chisma and optic tract with both parasellar extension and inferiorly deepening into sphenoid sinus.

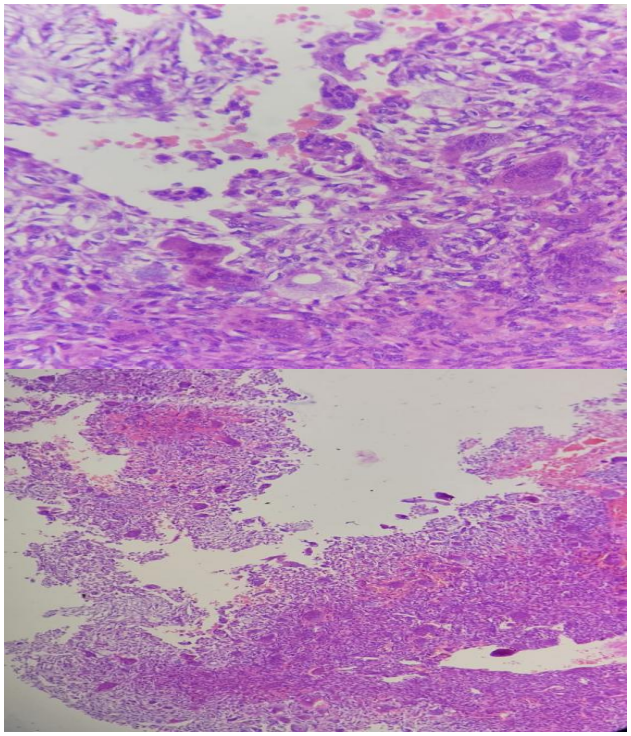

Figure 2: Histopathology report showed tumor made of numerous multinucleated osteoclast like giant cells and spindle shaped stromal cells and mitoses are rare; suggestive of giant cell tumor of bone.

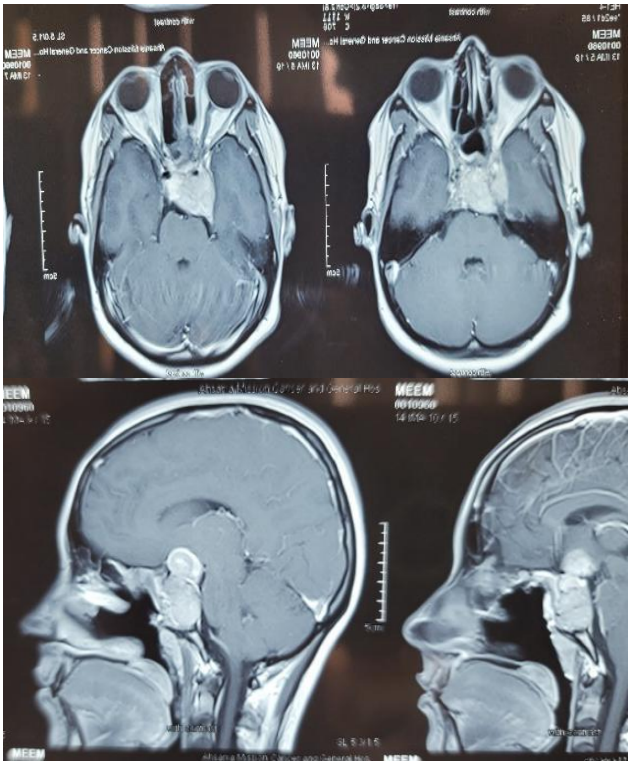

Figure 3: MRI of brain at 20th POD showing residual lesion measuring 2.4×2×2.3 cm.

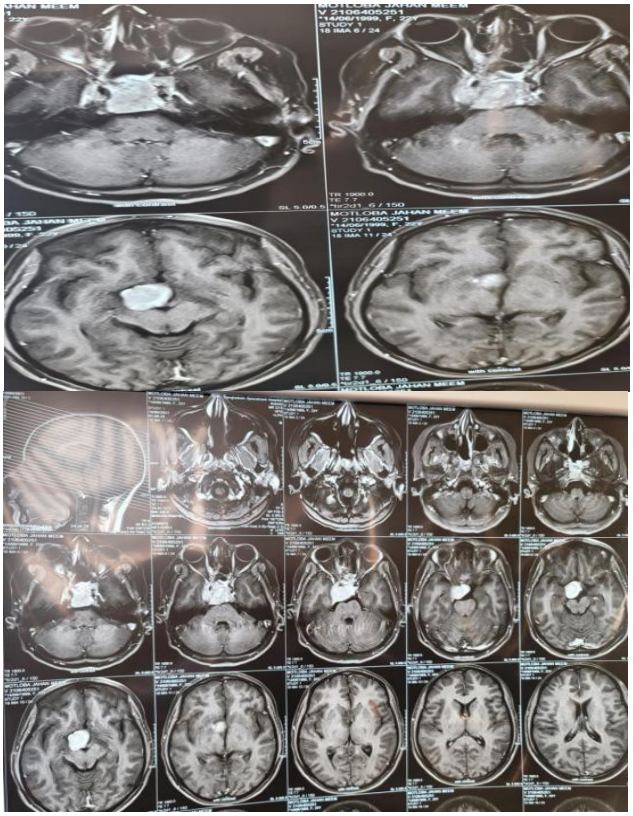

Figure 4: MRI brain showed large lobulated mass measuring 4.1×3×3.2 cm with intense enhancement at clivus with right parasellar extension, the right cavernous sinus was encased.

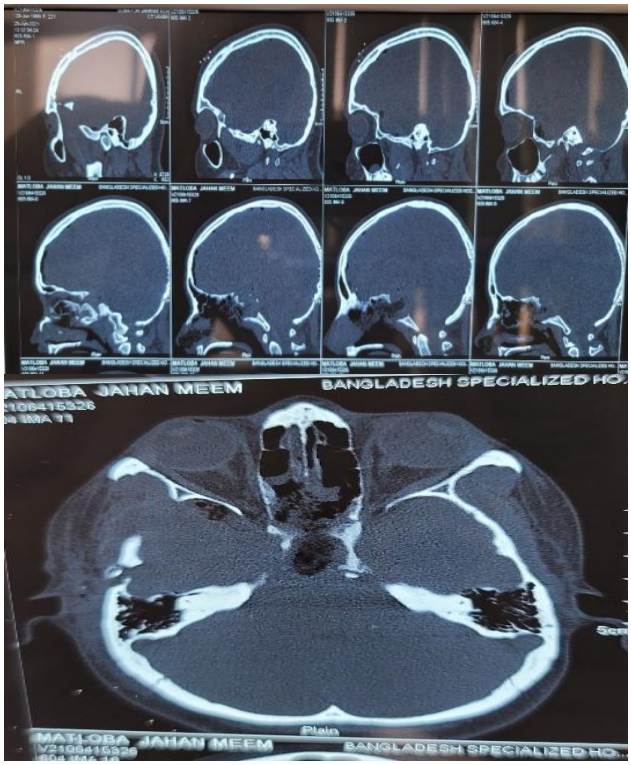

Figure 5: CT scan of base of skull, gross bony erosion was present in sphenoid bone.

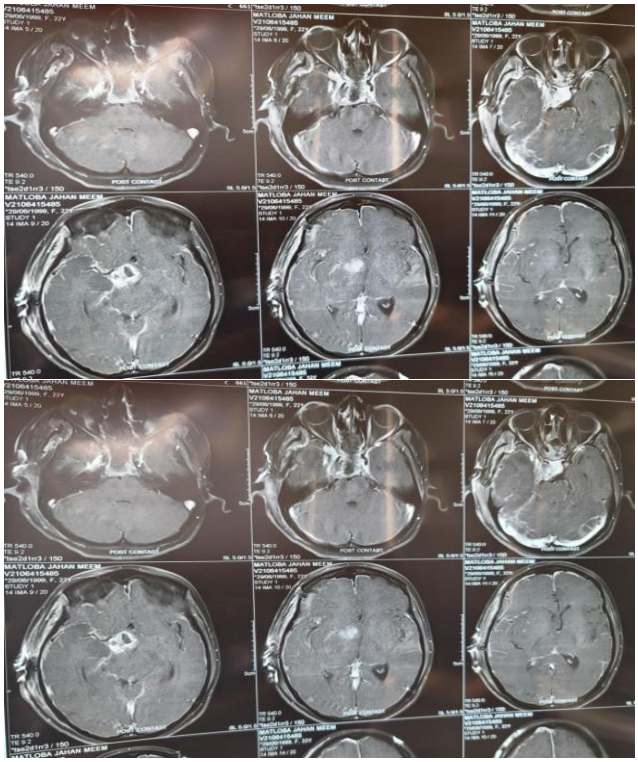

Figure 6: MRI showed lobulated enhancing lesion (2.5×1.6×2 cm) in the sphenoid region with mild right parasellar extension, laterally the lesion extends right cavernous sinus encasing right ICA; residual reduced as compared to previous scan. Mild compression of optic chiasma and right optic nerve was still present.

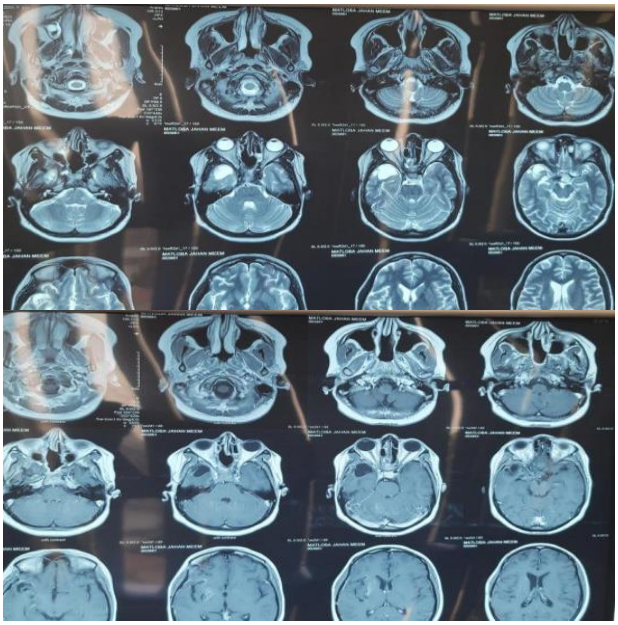

Figure 7: MRI comparative study was done which showed partial regression of disease compared to last scan and this time there was mild heterogeneously enhancing lesion (2.2×1.5×1.8 cm) at the site of operation with further reduced compression on optic chiasma and right optic nerve.

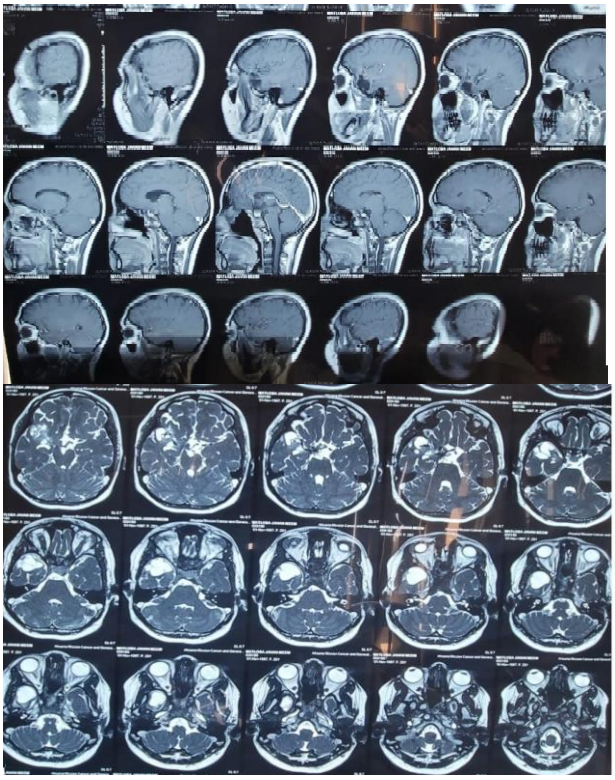

Figure 8: MRI comparative study was done which showed partial regression of disease compared to last scan and this time there was mild heterogeneously enhancing lesion (1.8×1.2×1.5 cm) at the site of operation with further reduced compression on optic chiasma and right optic nerve.

DISCUSSION

GCT is a solitary lucent lesion with osteoclast like giant cells and stromal cells. The exact etiology of the GCT is unknown but presumed to be due to PTH related protein, increased receptor activator of nuclear factor-Kappa B ligand (RANKL) expression by stromal cells of GCT of bone, which in turn causes resorption of bone.[5]

GCTs most frequently occurs in long bones, but rarely in the skull, accounting for <1% of all bone GCTs, where it is usually located in sphenoid and temporal bone.[6] However, in present case, tumor arises from clivus with parasellar extension. Till date only thirteen cases of primary clival GCTs have been reported. We summarize 14 clival GCTs including our case (Table 1).

Patients in study ranging in age from 9-62 years old, with 7 each female, male patients. Major symptoms included headache, possibly due to raised intracranial pressure, and diplopia caused by 6th cranial nerve palsy. These symptoms lasted for anywhere from 1-6 months. Our specific case, patient had presented with visual disturbance and drooping of right eyelid for a period of 1 month. Size of tumors in the study ranged from 30-76 mm. In most cases, including patient, there was gross bony erosion present and homogenously enhanced tumor observed on CT and gadolinium enhanced MRI scans.

Radical surgical extirpation is considered the treatment of choice for cranial GCTs, requiring the complete removal of the diseased bone. However, this may not always be possible due to the anatomical location and involvement of vital structures, as was the case for our patient where the lesion extended to the right cavernous sinus encasing the right internal carotid artery. Therefore, a minimally intralesional approach was taken. Various techniques, such as endonasal endoscopic transsphenoidal approach (EEA), frontal craniotomy, and transsphenoidal approach, have been utilized for treating clival GCTs. In our case, we performed an EEA during 1st surgery and a combined microscopic and endoscopic procedure in second surgery.

Of 11 cases in study, radiotherapy was performed on, 2 cases showed malignant transformation, leading to resistance to radiotherapy.

Chemotherapy has not commonly been performed for clival GCT and has been rarely evaluated in another skull base GCTs. However, Yamamoto et al study 2 cranial base case GCT reported responded well to chemotherapy showing regression on periodic CT scans.[17]

Denosumab, a fully human monoclonal antibody against RANKL, effective for treating extracranial GCTs.[18] First report describing beneficial effects of skull base GCT published by Inoue and colleagues, describing a 16 years old male with relapsed GCT of skull base treated with Denosumab after failure of surgery, resulting in marked reduction in tumor size.[19]

Table 1: Clinical characteristics and outcome of clival giant cell tumor cases reported in English literature.

Authors	Age (Year)/ sex	Symptoms	Duration of symptoms	Size (cm)	CT	MRI	Angiography	Treatment	RT	Outcome of last follow up	Follow up (months)
Wolfe[6]	16/F	HA, D, visual disturbance	4-7 weeks	NA	NA	NA	NA	STR (Transseptal biopsy and de-compression)	Yes (DNA)	Alive with residual tumor	96
Kattner[7]	9/F	HA, D	1 months	NA	Bone erosion+	Enhance ment +	NA	Biopsy (TSS) fb subtotal excision	57.6 Gy/32F	Alive with residual tumor	12
Sharma[8]	18/F	HA, progressive hearing loss, facial paresis, swallowing difficulty, nasal regurgitation, gait ataxia	6 months	NA	Bone erosion+	Enhance ment +	NA	NTR (left RMSO approach)	Yes (DNA)	Alive	12
Sharma[8]	12/F	HA, right hearing loss, facial paresis, nasal regurgitation and nasal twang	3 months	NA	Bone erosion+	Enhance ment +	NA	GTR (left RMSO approach)	Yes (DNA)	Alive	12
Zorlu[4]	14/F	HA, D	2.5 months	6×4×3.5	NA	Enhance ment +	NA	STR (TSS) fbredo surgery at 3 months for recurrent tumor (TSS)	60 Gy/30F	Alive with tumor	24
Gupta[9]	17/F	HA, D, amenorrhea, visual disturbance	6 months	7.6×5.4	Bone erosion+	Enhance ment +	NA	STS (Le Fort I)	45 Gy/25F	Alive with tumor	24
Sasagawa[10]	26/M	HA, D	NA	3×3	Bone erosion+	Enhance ment +, cystic	NA	STR (TSS) fb redo surgery for recurrent tumor STR (biopsy, osteo-sarcoma) fb chemo-therapy (adriamycin, CDDP)	50 Gy/25 F	Death (metastasis to lung)	9

Continued.

Author/ year	Age (Year)/ sex	Symptoms	Duration of symptoms	Size (cm)	CT	MRI	Angiography	Treatment	RT	Outcome of last follow up	Follow up (months)
Iacoangeli[11]	31/M	HA, D	NA	NA	Bone erosion+	Enhancement +	ICA displacement	NTR (TSS)	No	Alive with tumor	72
Roy[12]	19/M	HA, facial hypesthesia	6 months	5.6×3.6×3.5	Bone erosion+	NA	NA	GTR (Le Fort I)	45 Gy	Alive with tumor	18
Agrawal[13]	62/M	HA, D	3 months	NA	NA	Enhancement +	NA	Endoscopic biopsy fb STR (bifrontal approach)	NA	NA	NA
Shibao[14]	25/M	D	1 month	5.1×3.1×4.9	Bone erosion+	Enhancement +	Feeding artery (MHT)	STR (TSS) fb redo surgery for the recurrent tumor re-growth: STR (TSS + anterior trans-petrosal approach)	Yes (DNA)	Death	31
Patibandla[15]	20/M	Left hemi-cranial HA, vomiting, drooping of the left eye lid	6 weeks	NA	Bone erosion+	NA	NA	STR (TSS)	IMRT	Alive with tumor	3
Satapathy[16]	24/M	HA, D. diminished vision	4 months	5.7×4.5×5.7	Bone erosion+	Enhancement +	NA	GTR (Extended bifrontal craniotomy)	60 GY	Alive	8
Present case	22/F	drooping of right eye lid, diminished vision	1 month	4.1×2.4×2.5	Bone erosion+	Enhancement +	NA	STR (EEA) fb redo surgery at 3 month: frontal craniotomy as well as trans-sphenoidal approach) fb denosumab	NO	Alive	12

Cm=Centimeter; CT=Computed tomography; D=Diplopia; DNA=Details not available; EBRT=External beam radiotherapy; fb=Followed by; F= Female; Fr= fraction; GTR= Gross total resection; HA= Headache; ICA= Internal cerebral artery; IMRT=Intensity modulated radiotherapy; M= Male; MRI=Magnetis resonance imaging; NA=Not available; NTR= Near total resection; RT=Radiotherapy; STR=Subtotal resection; TSS=Trans sphenoidal sinus surgery; Y=Year.

In our case, the patient had undergone two surgeries for the treatment of clival GCT. After the second surgery, the plan was to begin adjuvant radiotherapy, but due to the worsening COVID-19 pandemic situation, it was not possible. Instead, the patient was given monthly doses of Denosumab and there was a good response to the treatment. The disease process gradually regressed, but after one year, the patient's PTH levels had risen four times above the normal range. Upon discontinuing the Denosumab treatment, the PTH levels returned to normal and the disease process also regressed to some extent. The patient is now clinically asymptomatic. However, the possibility of radiotherapy was kept as an option in case of any future disease progression. It is important to note that long-term use of denosumab may not be the ideal therapeutic option as it can cause side effects, such as hypocalcemia, hypophosphatemia, increased bone mineral density, and an increased risk of fracture and osteonecrosis.[18,20] However, denosumab has an important role in the management of clival GCT.

CONCLUSION

It is challenging to treat clival GCTs due to its critical location and the treatment protocol is not yet well established due to rarity of disease. Surgery followed by adjuvant radiotherapy has pivotal role. However, Denosumab has useful role in management of clival GCTs following incomplete surgery.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Pai SB, Lalitha RM, Prasad K, Saraswathi GR, Harish K. Giant cell tumor of the temporal bone-a case report. BMC Ear, Nose and Throat Disorders. 2005;5(1):8.
2. Leonard J, Gökden M, Kyriakos M, Derdeyn CP, Rich KM. Malignant giant-cell tumor of the parietal bone: case report and review of the literature. Neurosurgery. 2001;48(2):424-9.
3. 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(4):163-73.
4. 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(2):149-52.
5. Cowan RW, Singh G, Ghert M. PTHrP increases RANKL expression by stromal cells from giant cell tumor of bone. J Orthop Res. 2012;30(6):877-84.
6. Wolfe JT 3rd, Scheithauer BW, Dahlin DC. Giant-cell tumor of the sphenoid bone. Review of 10 cases. J Neurosurg. 1983;59(2):322-7.
7. Kattner KA. Giant cell tumor of the sphenoid bone. Skull Base Surg. 1998;8(2):93-7.
8. Sharma RR. Craniospinal giant cell tumors: clinicoradiological analysis in a series of 11 cases. J Clin Neurosci. 2002;9(1):41-50.
9. Gupta R, Mohindra S, Mahore A, Mathuriya SN, Radotra BD. Giant cell tumour of the clivus. Br J Neurosurg. 2008;22(3):447-9.
10. Sasagawa Y, Tachibana O, Shiraga S, Takata H, Kinoshita E, Nojima T et al. Secondary malignant giant cell tumor of the clivus: case report. Clin Neurol Neurosurg. 2012;114(6):786-8.
11. Iacoangeli M. Endoscopic endonasal approach for the treatment of a large clival giant cell tumor complicated by an intraoperative internal carotid artery rupture. Cancer Manag Res. 2013;5:21-4.
12. Roy S, Joshi NP, Sigamani E, Malik A, Sharma MC, Mohanti BK et al. Clival giant cell tumor presenting with isolated trigeminal nerve involvement. Eur Arch Otorhinolaryngol. 2013;270(3):1167-71.
13. Agrawal, A., et al., Giant cell tumor of the clivus with presence of epithelioid histiocytes. Asian J Neurosurg. 2014;9(1):48-9.
14. Shibao S, Toda M, Yoshida K. Giant cell tumors of the clivus: Case report and literature review. Surgical Neurol Int. 2015;6(25):S623-7.
15. Patibandla MR, Thotakura MK. Clival giant cell tumor-A rare case report and review of literature with respect to current line of management. Asian J Neurosurg. 2017;12(1):78-81.
16. Satapathy A. Giant cell tumor at the clivus: Not an area 51. Neurol India. 2018;66(3):861-4.
17. Yamamoto M. Giant cell tumor of the sphenoid bone: long-term follow-up of two cases after chemotherapy. Surg Neurol. 1998;49(5):547-52.
18. Chawla S. Safety and efficacy of denosumab for adults and skeletally mature adolescents with giant cell tumour of bone: interim analysis of an open-label, parallel-group, phase 2 study. Lancet Oncol. 2013;14(9):901-8.
19. Inoue A. Role of Denosumab in Endoscopic Endonasal Treatment for Juvenile Clival Giant Cell Tumor: A Case Report and Review of the Literature. World Neurosurg. 2016;91:674.e1-6.
20. Thomas D. Denosumab in patients with giant-cell tumour of bone: an open-label, phase 2 study. Lancet Oncol. 2010;11(3):275-80.

Cite this article as: Ferdause J, Karim R, Taposhi AR, Chowdhury Q. Giant cell tumor of clivus: a rare case report and review of literature. Int J Sci Rep 2023;9(7):220-6.