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Giant cell tumors of the clivus: Case report and literature review

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Abstract

Background: Clival giant cell tumors (GCTs) are extremely rare with only eight cases reported to date, and malignant transformation is quite rare. Herein, we report a case of an uncontrolled clival GCT, which was transformed malignant, and review the literature.

Case Description: A 25-year-old man experienced double vision for 1 month. Computed tomography and magnetic resonance imaging revealed a clival tumor. The endonasal endoscopic transsphenoidal approach (EEA) was used, and partial resection was performed because of massive bleeding. Histological examination showed a GCT. After radiation therapy, the tumor recurred; the EEA and the anterior transpetrosal approaches were used to perform second and third operations, respectively. The MIB-1 index increased from 4.2% to 26.3%.

Conclusions: GCTs are difficult to treat because of their location, vascularity, and the potential for malignant transformation.

Key Words: Clivus, giant cell tumor, malignant transformation

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INTRODUCTION

Giant cell tumors (GCTs) are generally benign, locally aggressive lesions that are typically located in the metaphysis of long bones. GCTs of the skull are rare and constitute <1% of all reported bone GCTs. These tumors preferentially involve the sphenoid and temporal bones.[11] Clival GCTs are rare with only eight cases reported to date. Furthermore, malignant clival GCT is quite rare and difficult to treat because of its location, high vascularity, and resistance to treatment.[10] Herein, we report an uncontrolled clival GCT despite repeated surgery and radiation, and review the literature, focusing on their treatment. Moreover, we first showed a high MIB-1 index, which implied malignant transformation of GCT.

CASE DESCRIPTION

A 25-year-old man experienced double vision for 1 month. He had no history of trauma or surgery. Physical examination revealed overall good health. Neurological examinations revealed right abducens nerve palsy. Motor and sensory examinations including cerebellar tests were normal with full cooperation and orientation. Results from laboratory tests conducted on admission, which included blood biochemical analysis, complete blood count, pituitary function, and tumor markers, were normal.

Computed tomography (CT) demonstrated a homogeneously enhanced mass (5.1 cm × 3.1 cm × 4.9 cm) in the clivus [Figure 1a and b]. The mass was isointense

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and hypointense on T1- and T2-weighted magnetic resonance imaging (MRI), respectively [Figure 1c and d]. Gadolinium-enhanced MRI revealed a homogeneously enhanced tumor extending into the brainstem [Figure 1e]. Three-dimensional (3D) CT angiography showed feeder arteries arising from the bilateral meningohypophyseal trunks (MHTs) [Figure 1f]. Preoperative embolization was not conducted owing to the risk of internal carotid artery (ICA) migration of embolic materials. A neuronavigation-guided operation was performed via the endonasal endoscopic transsphenoidal approach (EEA). The tumor was yellowish gray and bled profusely [Figure 2a and b]. Partial resection was performed because of massive intraoperative bleeding from the feeding artery (850 mL; [Figure 2b]). Histopathological analysis revealed a cellular tumor comprised of osteoclastic giant cells and stromal cells [Figure 2c]. Postoperative MRI showed partial resection [Figure 2d]. The MIB-1 index was 4.2%. One month after the operation, the patient received 3D conformal radiotherapy at a dose of 50 Gy delivered in 25 fractions. Two months after the initial surgery, MRI confirmed gradual postradiation tumor regrowth [Figure 2e]. The tumor gradually increased in size and eventually invaded the brainstem, leading to brainstem edema [Figure 2f]. Therefore, a second operation was planned; however, because of massive intraoperative bleeding during the previous operation, preoperative angiography was performed before surgery. Angiography revealed weak tumor staining, which may have been caused by radiotherapy [Figure 3a and b]. Seven months after the first surgery, we used the EEA for the epidural lesion. The tumor was fibrotic and there was slight intraoperative bleeding [Figure 3c]. Thereafter, 1 month after the second surgery, we performed the anterior transpetrosal approach (ATPA) for the subdural lesion [Figure 3d]. Although blood control was good owing to MHT interruption by this approach, the tumor was tightly adhered to the brainstem, and we performed a partial resection [Figure 3e]. Histopathological analysis revealed mitotic spindle cell proliferation [Figure 3f]. The MIB-1 index was 26.3%. Postoperatively, the patient had right hemiparesis and died 19 months after the second operation because of respiratory dysfunction due to tumor regrowth.

Informed consent was obtained from this patient.

DISCUSSION

Only 3–7% of all primary bone neoplasms manifest as GCTs, which are relatively rare.[3] They commonly originate in the epiphysis of long bones such as the distal femur, proximal tibia, and distal radius; they are rare in the cranium.[4] Cranial GCTs tend to occur in the skull, and tumors found at the skull base frequently involve the sphenoid bone.[5,13] Moreover, clival GCTs are extremely rare. Wolfe *et al*. first described a surgically treated clival GCT in 1983; only eight cases have been

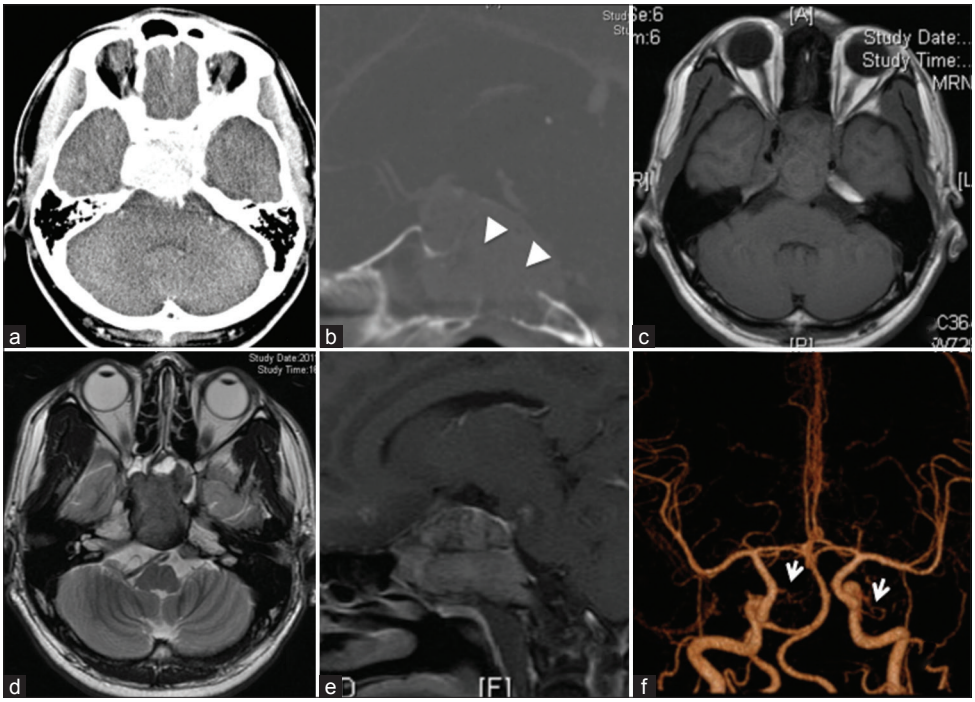

Figure 1: (a) Postcontrast head computed tomography scan revealing an enhanced mass in the clivus. (b) Postcontrast sagittal computed tomography showing clival erosion (arrowheads). T1-weighted (c) and T2-weighted (d) magnetic resonance images showing an iso- and hypo-intense mass, respectively. (e) Postcontrast sagittal T1-weighted magnetic resonance images revealing a homogeneously enhanced tumor. (f) Three-dimensional angiography showing both meningohypophyseal trunks (arrows)

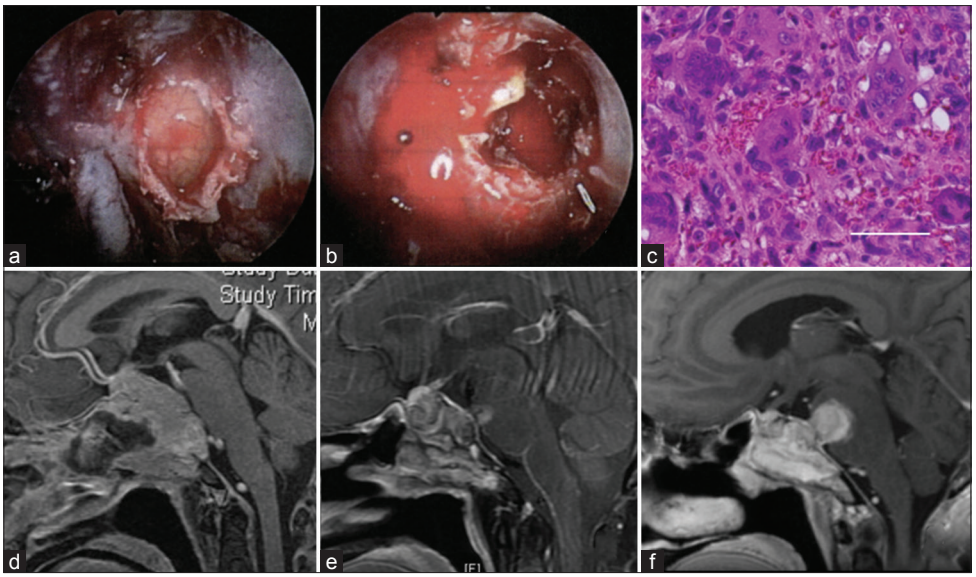

Figure 2: The first operation via an endoscopic endonasal transsphenoidal approach. An intraoperative image showing a yellowish gray tumor of the clivus (a), and profuse bleeding in the tumor (b). (c) A histological specimen showing numerous multinucleated giant cells with dense eosinophilic cytoplasm, scattered against a background of uniform mononuclear cells. Bar 50 μm. (d) Postcontrast sagittal T1-weighted magnetic resonance images revealing a partially resected tumor via the endoscopic endonasal transsphenoidal approach. Regrowth of the tumor after radiation (e) and showing an increase in recurrent tumor size (f)

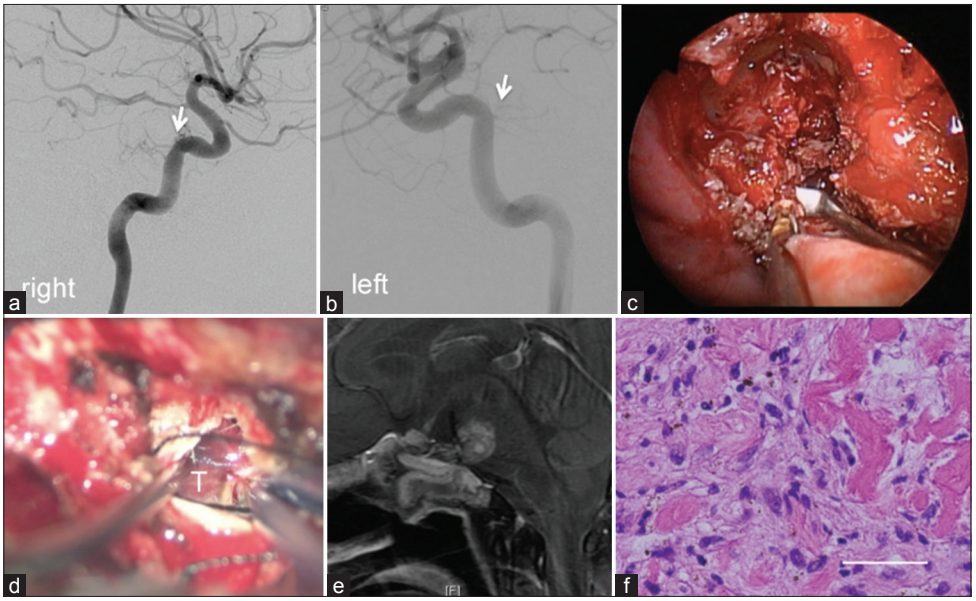

Figure 3: Angiography showing weak tumor staining from meningohypophyseal trunks (arrows). Right side (a), and left side is (b). The second (c) and the third operations (d): An intraoperative image showing a fibrous tumor via the endoscopic endonasal transsphenoidal approach (c), and the anterior transpetrosal approach (d), respectively. (e) Postcontrast sagittal T1-weighted magnetic resonance images revealing partial resection after surgery. (f) A histological specimen showing spindle cell proliferation, with scattered giant cells, pigmentation, and hyalinization. Bar 50 μm

reported since. We summarize 9 clival GCTs including our case [Tables 1 and 2].[1,5-7,9-11,13] The patients' age at diagnosis ranged from 9 to 62 years, with 5 male and 4 female patients. Major symptoms included headaches owing to high intracranial pressure and diplopia caused by abducens nerve palsy. The symptoms lasted for 1–6 months. The tumor size (maximum diameter) ranged from 30 to 76 mm leading to elevated intracranial pressure. In most cases, including ours, clival erosion, and a homogeneously enhanced tumor were observed on CT and Gadolinium-enhanced MRI, respectively. Although feeding arteries were not described in previous reports, we observed that the MHT arteries supplied the tumor.

Some papers reported that total resection could enable a reduction in GCT recurrence.[5] However, because of

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

Author, year	Age (years), sex	Location	Symptoms	Duration	Neurology	Size (cm)	CT	MRI	BSA	Angiography
Wolfe *et al.*, 1983[11]	16, female	Clivus	Headache, diplopia, visual disturbance	4-7 weeks	NA	NA	NA	NA	NA	NA
Kattner *et al.*, 1998[7]	9, female	Clivus	Headache, diplopia	1 month	CN VI palsy	NA	Bone erosion	Enhanced	–	NA
Zorlu *et al.*, 2006[13]	14, female	Clivus	Headache, diplopia	2.5 months	None	6×4×3.5	NA	Enhanced	–	NA
Gupta *et al.*, 2008[5]	17, female	Clivus	Headache, diplopia, amenorrhea, visual disturbance	6 months	CN II atrophy, CN VI palsy, CN V disturbance	7.6×5.4	Bone erosion	Enhanced	–	NA
Sasagawa *et al.*, 2012[10]	26, male	Clivus	Headache, diplopia	NA	CN VI palsy	3×3	Bone erosion	Enhanced, cystic	+	NA
Iacoangeli *et al.*, 2013[6]	31, male	Clivus	Headache, diplopia	NA*	CN VI palsy	NA	Bone erosion	Enhanced	–	ICA dislocated
Roy *et al.*, 2013[9]	19, male	Clivus	Headache, facial hypesthesia	6 months	CN V disturbance	5.6×3.6×3.5	Bone erosion	NA	–	NA
Agrawal *et al.*, 2014[1]	62, male	Clivus	Headache, diplopia	3 months	CN VI palsy	NA	NA	Enhanced	–	NA
Present case	25, male	Clivus	Diplopia	1 month	CN VI palsy	5.1×3.1×4.9	Bone erosion	Enhanced	+	Feeding artery (MHT)

*Progressive. CT: Computed tomography, MRI: Magnetic resonance imaging, BSA: Brainstem adhesion, CN: Cranial nerve, NA: Not available, ICA: Internal carotid artery, MHT: Meningohypophyseal trunk

Table 2: Surgical outcomes of clival giant cell tumor cases reported in English literature

Author, year	Treatment (approach)	Intraoperative finding	Recurrence	Outcome	Follow-up (months)	MIB1
Wolfe *et al.*, 1983[11]	Partial (transseptal biopsy and decompression) → postoperative radiation	NA	–	Alive with tumor	96	NA
Kattner *et al.*, 1998[7]	Biopsy (transsphenoidal approach) → subtotal (transsphenoidal approach) → postoperative radiation (57.6 CGE/32 Fr)	NA	–	Alive with tumor	12	NA
Zorlu *et al.*, 2006[13]	Subtotal (transsphenoidal approach) → recurrence (3 months) → EBRT (60 Gy/30 Fr) → nasal bleeding → removal of intranasal tumor	NA	+	Alive with tumor	24	NA
Gupta *et al.*, 2008[5]	Subtotal (Le Fort I) → postoperative radiation (45 Gy/25 Fr)	Moderate vascularity	–	Alive with tumor	24	NA
Sasagawa *et al.*, 2012[10]	Subtotal (transsphenoidal approach) → postoperative radiation (50 Gy/25 Fr) → recurrence → subtotal (osteosarcoma) → adriamycin, CDDP → embolization → lung metastasis	High vascularity	+	Death	9	10%
Iacoangeli *et al.*, 2013[6]	Total (EEA)	ICA rupture	–	Alive without tumor	72	NA
Roy *et al.*, 2013[9]	Total (Le Fort I) → radiotherapy (45 Gy)	High vascularity	–	Alive with tumor	18	NA
Agrawal *et al.*, 2014[1]	Subtotal (bifrontal approach)	NA	NA	NA	NA	NA
Present case	Subtotal (EEA) → postoperative radiation → regrowth → subtotal (EEA, ATPA)	High vascularity, brainstem invasion	+	Death	31	4.2% → 26.3%

ATPA: Anterior transpetrosal approach, CDDP: Cisplatin, EBRT: External beam radiotherapy, EEA: Endonasal endoscopic transsphenoidal approach, ICA: Internal carotid artery, NA: Not available, MHT: Meningohypophyseal trunk

extensive intraoperative bleeding during the clival GCT surgeries, complete resection was considered difficult (complete resection 22.2%, 2/9). Moreover, in our case, radical resection was hindered by massive bleeding from the feeding artery, which originated from the ICA. Many surgical approaches, including the EEA, frontal craniotomy, and transmaxillary approach, have been utilized for treating clival GCTs. We performed the EEA during the first and second surgeries and the ATPA for the third surgery. Partial resection was achieved via EEA,

because of massive intraoperative bleeding; therefore, postoperative radiation therapy was performed. During the ATPA, we could ligate the feeding artery from the MHT and control intraoperative bleeding. Based on this fact, we believe that bleeding control could have been more effective by performing the ATPA before the EEA. Although we were able to observe the prepontine cistern via the ATPA, the tumor was tightly adhered to the brainstem and could only be resected partially. Only two cases, including ours, have shown brainstem adhesion.

Radiation therapy has been performed for seven residual tumors. In most cases, the tumor was stable for >1 year. However, two cases including ours showed malignant transformation, leading to resistance to radiation therapy. Sasagawa *et al*. reported a secondary malignant clival GCT with an MIB-1 index of 10%.[10] In our case, the MIB-1 index increased from 4.2% to 26.3% at recurrence. Although other reports have not analyzed the MIB-1 index, it might be an indicator for malignant transformation. This would be natural history, not induced by radiation because of its short duration of 7 months in our case. Whereas <2% of extracranial GCTs become malignant, the malignant transformation of intracranial GCTs is exceptionally rare.[8]

Chemotherapy has not been performed for clival GCTs and has rarely been evaluated in other skull base GCTs. Yamamoto *et al*. reported two cases of cranial base GCTs that responded well to chemotherapy and showed regression on periodic CT scans.[12] Denosumab, a fully human monoclonal antibody against RANKL, was effective for treating extracranial GCTs.[2] Such chemotherapeutic agents should be considered for the treatment of malignant clival tumors, where radical resection is complicated.

CONCLUSIONS

It is challenging to treat clival tumors because of their location, vascularity, and potential malignant transformation. Angiographic assessment is important in order to control intraoperative bleeding. Pathological assessments such as the MIB-1 index are required for further investigation of the biological properties of clival GCTs.

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Conflicts of interest
There are no conflicts of interest.

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