Unique Presentation of Occipital Condyle Giant Cell Tumor as Occipital Condyle Syndrome—A Review

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Abstract
Giant cell tumors (GCT) of the skull are rare and only a few case series with limited number of cases have been reported till date. In the cranium, GCT usually occurs in the sphenoid and temporal bone, and occipital condyle GCTs are very rare. We report a rare presentation of GCT of the occipital condyle manifested as occipital condyle syndrome. Despite gross total resection, they can recur aggressively; presence of cortical breach might be an indicator of aggressiveness prompting early postoperative imaging and adjuvant therapy.

Introduction
Giant cell tumors (GCTs) are locally aggressive, destructive bony lesions, usually found in the epiphysis of long bones.¹ GCTs of the skull are rare, with a predilection for sphenoid and temporal bone²; occipital condyle GCTs are extremely rare. Occipital condyle syndrome (OCS) is characterized by continuous unilateral occipital headache, associated with ipsilateral hypoglossal nerve paralysis. Though there are very few reported cases of GCTs involving the occipital condyle, its presentation solely as OCS has never been reported.

Case Summary
A 22-year-old girl presented to us with 3 months duration of insidious onset gradually progressive throbbing type of right suboccipital headache radiating to the neck and aggravated with neck movements. After a few days, she noticed slurring of speech and deviation of tongue to right side. Clinical examination was unremarkable except for right lower motor neuron hypoglossal palsy. Computed tomography (CT) of the skull showed an expansile lytic lesion involving the right occipital condyle with thinning and breach of the cortex. Magnetic resonance imaging (MRI) showed an intensely enhancing homogenous mass in the right occipital condyle, with restricted diffusion, encroaching onto the right hypoglossal canal and jugular foramen, suggesting an aggressive primary bony lesion. There was no soft tissue enhancement surrounding the lesion. She underwent far lateral approach and gross total decompression of the tumor along with occipitaoxial instrumented stabilization in view of potential instability caused by the tumor involving the articular surface of the occipital condyle. Histopathology revealed a tumor composed of mononuclear round cells.

Keywords
► occipital condyle
► giant cell tumor
► occipital condyle syndrome

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displaying moderate pleomorphism and few typical mitotic figures with several uniformly distributed osteoclast-like giant cells with reactive bone formation rendering a diagnosis of giant cell tumor.

Postoperatively patient had good relief of headache with static neurological deficit as preoperatively (Figs. 1–3).

At 3 months follow-up, the patient remained headache free, but a routine follow-up MRI showed evidence of large recurrent lesion extending to the clivus. The patient underwent adjuvant therapy with denosumab followed by radiation therapy. Follow-up MRI at 1 year showed stable residual lesion; patient remained asymptomatic except for residual right hypoglossal palsy (Fig. 4).

**Discussion**

GCTs are primary bone tumors that develop through enchondral ossification, constituting 5% of primary bone tumors. GCT in cranium and spine constitutes only less than 1%; sphenoid is the commonest followed by petrous temporal, parietal, and frontal bones. This variation is due to the fact that sphenoid and temporal bone develops through enchondral ossification. Occipital GCTs are extremely rare, with only 11 case reports available in literature (Table 1). Most authors have reported cases presenting with occipital headache and no physical findings. Optiz et al have reported an occipital GCT in a case of von Recklinghausen’s disease. Kajiwara and Takechi presented a case of occipital GCT with neck pain, dysphoria, and dysphagia, who was treated with denosumab. Motomochi et al reported a case involving the occipital condyle, with multiple cranial nerve palsies. Clinical data was not available in four cases. Our case of occipital condyle GCT has presented solely with OCS.

OCS, first described by Greenberg et al, is characterized by continuous occipital headache, with radiating neck pain aggravated by neck movements away from the side of pain and relieved by rotation toward the side of pain. Some patients may also have occipital tenderness. Usually, hypoglossal palsy manifests after the patient gets a headache.

Metastases and primary skull base tumors are commonly associated with OCS in up to half of the patients. Metastases usually originate from the breast, lung, thyroid, gastrointestinal tract, pharyngeal tumors, lymphomas, and prostate.

MRI and CT are the imaging modalities of choice. However, radiological features alone are not sufficient to diagnose GCT. It is challenging to differentiate skull base GCTs from other benign lesions like brown tumors of hyperparathyroidism, giant cell reparative granuloma, cherubism, and aneurysmal bone cyst. Therefore, to avoid confusion, clinical, radiological, and pathological findings are to be correlated for the definite diagnosis of skull base GCT.

Campanacci et al had designed a staging system for GCT, with stage I tumors limited to bone but without cortical involvement; stage II tumors involving the cortex but without cortical breach; and stage III tumors that breach the cortex and extend into soft tissues. The treatment of choice for GCTs is en-bloc resection of the tumor whenever feasible. But skull base GCTs are often not amenable to complete resection owing to the proximity to critical neurovascular structures. Good local tumor control can be achieved by gross total resection. Recurrence rates are as high as 40 to 60% with subtotal resections. As most of these data are available from surgical series of long bone GCTs, it is doubtful whether this can be extrapolated to similar lesions of the skull base. Moreover, due to rarity of these cases, an optimal treatment strategy for skull base GCTs has not been described in literature.

Histological grading is a poor predictor of clinical outcome. The radiological staging system by Campanacci et al neither delivers reliable prognostic value regarding recurrence rates or functional outcomes nor helps in deciding upon the management options. Though some authors have reported Campanacci grade II/III tumor excision and soft tissue involvement as factors underlying increased recurrence rates, convincing evidence for the same could not be established. We assume that in our case cortical destruction is the probable underlying cause for this early aggressive recurrence despite the tumor being relatively small in size.
Adjuvant therapy can reduce the chances of recurrence. Also, many forms of radiation therapy and various chemotherapeutic agents were investigated in patients with unresectable tumors. Radiation therapy as a single agent was able to achieve control rates of up to 70 to 80%, but in the case of recurrent tumors, it was of limited response. There were

Fig. 2 (A) Preoperative magnetic resonance imaging T2 axial images showing hypointense right occipital condylar lesion. (B, C) Postcontrast images showing enhancing mass in right occipital condyle (axial and coronal, respectively). (D, E) Coronal and axial computed tomographic image showing the lesion. (F) Post operative CT scan showing the tumor cavity after excision of the lesion.
**Fig. 3** Tumor comprising mononuclear stromal cells interspersed with osteoclast-like giant cells (hematoxylin and eosin, original magnification 200X and scale bar 50 μm).

**Fig. 4** (A) Axial T2 magnetic resonance imaging showing large hypointense recurrence in right occipital condylar region. (B–D) Postcontrast magnetic resonance imaging showing moderately enhancing large recurrent lesion in axial, sagittal, and coronal planes, respectively.
concerns of malignant transformations with radiotherapy, but with newer highly conformal techniques of radiation, this seems to be insignificant.

Many chemotherapeutic agents like doxorubicin, cisplatin, methotrexate, zoledronate, and raloxifene have been tried. New target-based drugs are developed as the pathophysiology of GCT has been studied well. The neoplastic component of GCT is the stromal cell that overexpresses receptor activator of nuclear factor κB ligand (RANKL), while the osteoclast-like giant cells express RANK. RANKL is a member of the tumor necrosis factor-alpha family of molecules that binds to the RANK receptor. Denosumab is a human-derived monoclonal antibody against RANKL, which selectively binds human RANKL and inhibits osteoclast differentiation and osteoclast-mediated bone resorption. Results of a multicentric phase II trial regarding usage of denosumab for primary treatment as well as an adjunct in recurrent GCTs showed favorable risk-to-benefit ratio. Almost 99% of patients had a clinical benefit in either complete/partial reduction or nonprogression. Denosumab (120mg) is usually administered subcutaneously once every 4 weeks with additional loading doses on the 8th and 15th days. Three percent of patients developed osteonecrosis of the jaw on prolonged denosumab treatment. Further studies are required to identify the optimal duration and dosage for minimizing complications.

**Conclusion**

OCS may be the sole manifestation of GCTs of the occipital condyle, which is an extremely rare site for these locally

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**Table 1 Cases of GCT involving occipital bone reported till date**

<table>
<thead>
<tr>
<th>Study</th>
<th>Age/sex</th>
<th>Clinical features</th>
<th>Region</th>
<th>Extent of resection</th>
<th>Adjuvant therapy</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Troell²¹ 1930</td>
<td>20/M</td>
<td>NA</td>
<td>Occipital</td>
<td>PR</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td>Arseni et al¹⁹</td>
<td>8/F</td>
<td>NA</td>
<td>Occipital</td>
<td>STR</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td>Motomochi et al² 1985</td>
<td>53/M</td>
<td>Headache, dysphagia and dysarthria, 9,10,11, and 12 CN palsy</td>
<td>Occipital bone, condyle, hypoglossal canal, and clivus</td>
<td>STR</td>
<td>Yes (RT)</td>
<td>No (26 months)</td>
</tr>
<tr>
<td>Bertoni et al³ 1992</td>
<td>58/F</td>
<td>NA</td>
<td>Occipital</td>
<td>STR</td>
<td>No</td>
<td>Yes (died after 1.5 years)</td>
</tr>
<tr>
<td></td>
<td>24/F</td>
<td>NA</td>
<td>Occipital bone with petrous and sphenoid bone</td>
<td>STR</td>
<td>Yes (RT)</td>
<td>No (7 years)</td>
</tr>
<tr>
<td>Optiz et al⁵ 1996</td>
<td>NA</td>
<td>NA</td>
<td>Occipital condyle</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Lu et al⁵ 2011</td>
<td>19/F</td>
<td>Headache and vomiting</td>
<td>Left occipital bone with petromastoid and temporal bone</td>
<td>GTR</td>
<td>No</td>
<td>No (1 year)</td>
</tr>
<tr>
<td>Zhang et al⁷ 2013</td>
<td>19/F</td>
<td>Headache and vomiting</td>
<td>Occipital</td>
<td>GTR</td>
<td>No</td>
<td>No (31 months)</td>
</tr>
<tr>
<td>Harris et al⁶ 2004</td>
<td>24/F</td>
<td>Headache, tenderness, external swelling</td>
<td>Occipital bone, along with dural involvement</td>
<td>GTR</td>
<td>No</td>
<td>NA</td>
</tr>
<tr>
<td>Gonçahanedan uslu¹ 2014</td>
<td>22/F</td>
<td>Neck pain, headache</td>
<td>Occipital bone with dural sinus involvement</td>
<td>STR</td>
<td>Yes (RT)</td>
<td>No (20 months)</td>
</tr>
<tr>
<td>Kajiwara and Takeshi²⁰ 2019</td>
<td>56/M</td>
<td>Right neck pain, dysphoria, and dysphagia</td>
<td>Right occipital bone with condyle</td>
<td>Biopsy</td>
<td>Denosumab</td>
<td>No (5 years)</td>
</tr>
<tr>
<td>Our case</td>
<td>22/F</td>
<td>Right occipital headache, right hypoglossal palsy</td>
<td>Occipital condyle</td>
<td>GTR</td>
<td>Yes (RT and denosumab)</td>
<td>Yes (1 year)</td>
</tr>
</tbody>
</table>

*Abbreviations: CN, cranial nerves; F, female; GCT, giant cell tumor; GTR, gross total resection; M, male; NA, data not available; PR, partial resection; RT, radio therapy; STR, subtotal resection.*
aggressive lesions. A high index of suspicion and early imaging is necessary to detect these lesions before they produce cortical breach and encroach adjacent critical neurovascular structures. From our own experience and available literature data, we feel that cortical breach is a predictor of early recurrence in such lesions, despite gross total removal. However, despite large lesion size, adjuvant denosumab and radiation therapy may be helpful in maintaining symptomatic quiescency especially in regions where en-bloc resection is not feasible. Further long-term follow-up data from a sizeable number of such patients is required to develop a standard of care in skull base GCTs.

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Conflict of Interest
None declared.

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