Primary glioblastoma of the cerebellopontine angle in adults

Case report

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Glioblastomas represent 15%–20% of all intracranial tumors and account for approximately 50% of all gliomas in adults.10 These tumors are located most frequently in the cerebral hemispheres, basal ganglia, thalamus, and corpus callosum.18,21 Only rarely do they grow primarily within the posterior fossa in adults, and they infrequently exhibit exophytic growth patterns but usually protrude dorsally.7,8 Recently, Luetjens et al.16 reported on a 40-year-old man who presented with a large exophytic giant cell glioblastoma of the medulla oblongata located in the caudal fourth ventricle.

We recently encountered a glioblastoma in the CPA arising from CN VIII that was completely separated from the brainstem in a 60-year-old man. Although the findings were atypical, preoperative neuroimaging suggested that the tumor was a posterior petrous meningioma with a dural-tail sign. To our knowledge, our case seems to be the first report of an extraaxial primary glioblastoma of the CPA in an adult arising from the CN VIII complex. Overall, it represents the ninth report of primary glioma in the CPA (Table 1).1,2,6,9,13,17,20,25

Case Report

History and Examination. This 60-year-old man presented with progressive deafness in the left ear and left facial palsy lasting less than 2 months before admission. Two weeks later, he began to experience progressive dysarthria and dysphagia lasting 2 weeks. Preoperative neuroimaging suggested the diagnosis of CPA meningioma with “dural-tail” sign and involvement of the internal auditory canal. Serological examination showed an increase in the malignant markers of ferritin and neuron-specific enolase, which suggested underlying malignancy. The tumor was subtotally removed, and it was confirmed to be completely separated from the brainstem and cerebellum. Cranial nerves VII and VIII were destroyed and sacrificed. Transient severe bradycardia occurred during surgery due to entrapment of the caudal cranial nerve complex by the tumor in such an infiltrative way. The neuropathological examination revealed a glioblastoma. The patient underwent no further treatment and died of cachexia 2 months postoperatively. To the authors’ knowledge, this represents the first case of a primary glioblastoma in the CPA in an adult. A high index of suspicion along with reliance on clinical assessment, radiological findings, and serum detection of specific malignant markers is essential to diagnose such uncommon CPA lesions. (DOI: 10.3171/2010.12.JNS10912)

Key Words • glioblastoma • cerebellopontine angle • differential diagnosis

Abbreviations used in this paper: CN = cranial nerve; CNS = central nervous system; CPA = cerebellopontine angle; DTPA = diethylenetriamine pentaacetic acid; IAC = internal auditory canal; NSE = neuron-specific enolase.
**TABLE 1: Summary of reported cases of primary extraaxial glioma in the cisternal portion of the CPA**

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Age (yrs), Sex</th>
<th>CN of Origin</th>
<th>Signs &amp; Symptoms</th>
<th>Symptom Duration (mos)</th>
<th>MRI</th>
<th>Peritumoral Edema</th>
<th>IAC Involvement</th>
<th>Size (mm)</th>
<th>Treatment</th>
<th>Histological Findings</th>
<th>Follow-Up Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panse, 1904</td>
<td>adult</td>
<td>VIII</td>
<td>unk</td>
<td>unk</td>
<td>unk</td>
<td>unk</td>
<td>unk</td>
<td>unk</td>
<td>unk</td>
<td>fibrillary astrocytoma</td>
<td>unk</td>
</tr>
<tr>
<td>Cushing, 1917</td>
<td>adult</td>
<td>VIII</td>
<td>unk</td>
<td>unk</td>
<td>unk</td>
<td>unk</td>
<td>unk</td>
<td>unk</td>
<td>unk</td>
<td>fibrillary astrocytoma</td>
<td>unk</td>
</tr>
<tr>
<td>Kasantikul et al., 1980</td>
<td>adult</td>
<td>VIII</td>
<td>unk</td>
<td>unk</td>
<td>unk</td>
<td>unk</td>
<td>unk</td>
<td>unk</td>
<td>unk</td>
<td>fibrillary astrocytoma</td>
<td>unk</td>
</tr>
<tr>
<td>Forton et al., 1992</td>
<td>35, F</td>
<td>lt VIII</td>
<td>HD, GD</td>
<td>partial calcification</td>
<td>no</td>
<td>unk</td>
<td>unk</td>
<td>unk</td>
<td>fibrillary astrocytoma</td>
<td>unk</td>
<td></td>
</tr>
<tr>
<td>Beutler et al., 1995</td>
<td>58, M</td>
<td>lt VIII</td>
<td>HD, ataxia</td>
<td>24</td>
<td>T1, isointense; T2, hyperintense, no enhancement</td>
<td>no</td>
<td>yes</td>
<td>15 × 10 × 12</td>
<td>total resection w/ sacrifice of CN VIII</td>
<td>pilocytic astrocytoma</td>
<td>alive, no recurrence</td>
</tr>
<tr>
<td>Takada et al., 1999</td>
<td>8, F</td>
<td>rt VIII</td>
<td>HD, FP</td>
<td>solid-cystic, heterogeneous enhancement</td>
<td>no</td>
<td>yes</td>
<td>unspecified</td>
<td>unspecified</td>
<td>pilocytic astrocytoma</td>
<td>alive, no recurrence</td>
<td></td>
</tr>
<tr>
<td>Arnautovic et al., 2000</td>
<td>9, F</td>
<td>rt V</td>
<td>FNM, HA, ataxia</td>
<td>12</td>
<td>T1, hypointense; T2, hyperintense; diffuse enhancement</td>
<td>no</td>
<td>no</td>
<td>35 × 40 × 45</td>
<td>total resection w/ partial preservation of CN V</td>
<td>pilocytic astrocytoma</td>
<td>12 mos, no recurrence</td>
</tr>
<tr>
<td>Miron et al., 2009</td>
<td>12, M</td>
<td>rt VIII</td>
<td>HD, HA</td>
<td>36</td>
<td>T1, isointense in periphery &amp; hypointense in center; T2, hypointense; slightly heterogeneous enhancement</td>
<td>no</td>
<td>yes</td>
<td>21.8 × 22.3 × 23.7</td>
<td>total resection w/ sacrifice of CN VIII</td>
<td>pilocytic astrocytoma</td>
<td>6 mos, no recurrence</td>
</tr>
<tr>
<td>present case</td>
<td>60, M</td>
<td>lt VIII</td>
<td>HD, FP, FNM, HS, DA, DP</td>
<td>2</td>
<td>T1, predominantly hypointense; T2, iso- to hyperintense; significantly heterogeneous ringlike enhancement w/ dural tail sign</td>
<td>yes</td>
<td>yes</td>
<td>36 × 35 × 33</td>
<td>subtotal resection w/ sacrifice of CNs VII &amp; VIII</td>
<td>glioblastoma</td>
<td>2 mos, dead</td>
</tr>
</tbody>
</table>

* DA = dysarthria; DP = dysphagia; FNM = facial numbness; FP = facial palsy; GD = gait disturbance; HA = headache; HD = hearing disturbance; HS = hoarseness; unk = unknown.
Pure-tone audiometry showed a sensorineural hearing loss in the left ear. The auditory brainstem evoked response on the left side showed no identifiable waves, even when the stimulus intensity to the left ear was increased to 90 dB.

Computed tomography scanning of the head revealed a predominantly hyperdense lesion with mixed densities in the left CPA with modest enlargement of the IAC (Fig. 1). Computed tomography scanning of the chest and abdomen revealed normal findings.

Magnetic resonance imaging showed a well-defined, extraxial solid mass (3.6 × 3.5 × 3.3 cm) in the left CPA with extensive peritumoral edema involving the brainstem and cerebellum. The mass compressed the brainstem and cerebellum and extended into the IAC, widening the meatus. The mass was predominantly hypointense on T1-weighted and iso- to hyperintense on T2-weighted MR imaging. After administration of Gd-DTPA, the mass showed a significantly heterogeneous ringlike enhancement in the CPA and a triangular enhancing enlargement in the left IAC, with its attachment to the petrous bone markedly enhanced as a dural-tail sign (Fig. 2).

The serum concentration of NSE was measured by radioimmunoassay and was abnormally high (56.35 ng/ml; reference value < 20 ng/ml). Again, serum ferritin measured by radioimmunoassay reached 670.75 ng/ml, which is above the reference value (range 21.81–274.66 ng/ml).

Operation. At surgery, a gray-white, gelatinous, moderately vascularized mass was encountered in the CPA adherent to the dura of the posterior surface of the petrous bone. On macroscopic examination, there was no obvious infiltration of the tumor into the brainstem and cerebellum parenchyma, which were easily separated from the tumor. However, the tumor clearly invaded the proximal part of the left CN VII and VIII complex next to its point of exit from the brainstem, as well as the distal part in the IAC. Cranial nerves VII and VIII could not be identified in the tumor and were sacrificed during tumor removal. The trigeminal nerve and caudal cranial nerve complex (CNs IX–XII) were all entrapped in the tumor. The former was successfully preserved in structure, and the surrounding tumor was removed. However, severe transient bradycardia occurred when trying to dissect the tumor from CNs IX–XII. Considering that the tumor might have infiltrated into the caudal CN complex, radical excision was impossible and the tumor was subtotally resected. Intraoperative frozen section biopsy was performed and yielded a diagnosis of malignant glioma; therefore, there was no need to obtain a dural specimen.

Histopathological Examination. Histopathological examination of the surgical specimen showed a highly cellular tumor comprising atypical glial tumor cells with frequent mitotic activity and a high nuclear/cytoplasm ratio (Fig. 3A). Marked coagulation necrosis and microvascular proliferation were present throughout the tumor (Fig. 3B). However, there was no appearance of psammomatous necrosis. Immunoreactivity showed that the tumor cells were diffusely positive for GFAP and p53 (Fig. 3C and D), but not for S100 protein, cytokeratin, epithelial membrane antigen, CD20, CD3, and CD45. The proliferation rate determined by Ki 67 immunohistochemical analysis was 40%–50%. According to the 2007 WHO classification and grading criteria, the diagnosis of a glioblastoma, WHO Grade IV, was made.

Postoperative Course. The postoperative period was uneventful without additional neurological deficits. However, the neurological dysfunction of involved CNs remained the same, especially that of the caudal CNs, which posed a problem for feeding and in part precipitated the patient’s death. Because of the high malignancy associated with poor prognosis, the patient refused further medical intervention and follow-up MR imaging. He was discharged from the hospital 10 days after surgery with a gastric tube for nasal feeding. The administration of eye protection lubricants was continued. Unfortunately, the patient died of cachexia 2 months postoperatively.

Discussion

Cerebellopontine gliomas are very rare, and most of them appear to be a secondary exophytic extension of a primary brainstem or cerebellar tumor. To our knowledge,
8 cases of primary extraaxial CPA gliomas have been reported in the literature (Table 1). Each tumor was completely separate from the brainstem. On the basis of the currently available data, our case appears to be the first report of a primary extraaxial CPA glioblastoma.

In our case, the clinical manifestation was characterized by the unilaterally multiple CN (V–XII)-related neurological impairment over a short duration of symptoms (< 2 months), in the absence of brainstem and cerebellar symptoms. The preoperative neuroimaging findings, even if they were atypical, suggested a posterior petrous meningioma with IAC enlargement. However, the rapidly progressive clinical course did not favor such a diagnosis. Subsequently, the detection of malignant markers in serum showed surprisingly increased levels of ferritin and NSE, suggesting a diagnosis of malignancy. At surgery, a clear tissue interface between the brainstem, cerebellum, and tumor capsule was identified, with interruption only at the point at which CN VIII emerged from the brainstem. Histopathologically, the tumor demonstrated high cellularity, mitosis, notable microvascular proliferation, and coagulation necrosis but without a pseudopalisading pattern, which is a characteristic feature of glioblastoma.

The immunostaining studies showed that tumor, with...
marked proliferative activity (Ki 67, 40%-50%), was diffusely positive for GFAP and p53, but not for S100, cytokeratin, epithelial membrane antigen, CD20, CD3, and CD45, thus verifying the tumor’s glial origin. According to the 2007 WHO classification, for Grade IV tumors, necrosis may be of any type and perinecrotic palisading need not be present.15

A glioblastoma is a morphologically diverse neoplasm, but vascular hyperproliferation and necrosis are essential diagnostic features that distinguish glioblastoma from lower-grade gliomas.12 Taken together, the diagnosis of glioblastoma should be valid. The tumor in our case seemed to be a strictly extraxial CPA glioblastoma originating in the proximal segment of CN VIII and extending along the course of adjacent CNs in an infiltrative and destructive fashion. It is less likely for a brainstem glioblastoma to involve the considerably distal portion of a CN in the IAC without involving the brainstem itself.

The diffuse labeling for GFAP contrasted with the absence of immunoreactivity for S100 in the present glioblastoma. Although a glia-associated protein, S100 does not serve as specific an instrument as GFAP for glial tumor qualitative diagnosis. According to the literature we reviewed, all the gliomas were exclusively immunoreactive for GFAP, but inconsistently for S100.24

Glioblastoma may develop through 2 distinct pathways of neoplastic progression. Tumors that progress from less malignant astrocytomas, termed secondary glioblastomas, develop in younger patients (mean age 45 years) and typically display both well- and poorly differentiated foci. The mean time to progression from anaplastic glioma to glioblastoma was approximately 2 years, and that from low-grade gloma to glioblastoma was approximately 5 years. In contrast, primary glioblastomas affect older patients (mean age 62 years), have short clinical histories (<3 months), and develop de novo without clinical or histological evidence of a less malignant precursor lesion.19 Due to the short symptom duration (2 months), older age, and uniformly poor differentiation in our case, the tumor appeared to be a primary glioblastoma. Reifenberger et al.22 reported a rare primary glioblastoma of the oculomotor nerve in a 70-year-old woman with a 1-month history of transient diplopia. Our report is the second to describe glioblastoma arising from CNs other than the optic and olfactory nerves. Histologically, the optic and olfactory nerves differ from the other CNs in that they are direct extensions of the CNS and have no peripheral segments.

Regarding the origin of primary gliomas in the CPA, several authors have previously documented the possible mechanisms in detail.1,17,22 In summary, the first hypothesis is that the tumor arose primarily from CNS tissue that lay within the proximal parts of the CN itself. Central nervous system tissue may extend well into the CN, and isolated islands of CNS tissue may even be found within the CN at a considerable distance from its exit point. The second hypothesis is that the tumor originated as primary in the heterotopic neuroglial cell nests in the leptomeninges covering the proximal CN or the adjacent brainstem. Such heterotopias may occur in any part of the CNS but show a certain predilection for the leptomeninges of the medulla oblongata, the lumbar spinal cord, and the pons. We assume that the tumor in our case, analogous to the previously reported cases, most likely originated from glial cells either within the proximal nerve itself or in the adjacent leptomeninges.

There are no characteristic radiological features available to distinguish a primary extraaxial glioma in the CPA from the much more common extraaxial neuroma and meningioma. Enlargement of the acoustic meatus can be found in patients with such tumors arising from CN VIII,17,25 including our case which assumed a dural tail sign as well. The 3D CISS (3D constructive interference in steady state) sequence proved to be superior to other sequences in identifying the site of origin, which is critical to the preoperative diagnosis for such an unusual CPA lesion.26 In addition, the data from diffusion- and perfusion-weighted MR imaging or MR spectroscopy, when available, are very helpful in diagnosing glioblastoma.

Accurate serum tumor markers available for malignant glioma could either facilitate the differential diagnosis or monitor the postoperative course. In our patient, elevated serum levels of ferritin and NSE were found. However, neither marker is specific to the diagnosis of glioma.5,23 Recently, Jung et al.11 observed significantly elevated serum GFAP levels in patients with glioblastoma, as well as a significant correlation between tumor volume, tumor necrosis volume, and serum GFAP level. Brommel and et al.1 reached a similar conclusion and proposed that serum GFAP seems to be a reliable biomarker in patients with high-grade gliomas.

In summary, the useful clues for the preoperative diagnosis of primary CPA glioblastoma may be as follows: 1) a rapidly progressive course of disease with the neurological deficits predominantly associated with unilateral multiple CNs (There are few, if any, cerebellar and brainstem long tract signs, and signs of raised intracranial pressure are rarely present); 2) neuroimaging features such as mixed density or signal intensity (presence of hemorrhage), prominent heterogeneous and ringlike enhancement (suggestive of necrosis),14 a well-defined margin, and peritumoral edema disproportional to the size of extraaxial lesions extending into the IAC; 3) increased combined detection of multiple malignancy markers such as NSE, S100B, and GFAP, especially the serum GFAP level; and 4) no evidence of metastasis from an intracerebral glioblastoma or extracranial malignancy. However, histological examination is sometimes the only way to arrive at the definitive diagnosis.

The current standard treatment for glioblastoma includes maximum resection of the tumor (>95%), followed by concurrent radiation therapy and chemotherapy with the novel alkylating drug temozolomide. Yet this aggressive therapy has only a modest effect on survival, with most patients surviving about 1 year after diagnosis.12 Because of the severe transient bradycardia related to the tumor involvement of CNs IX–XII, subtotal tumor resection was performed in our case, and it was not followed by radio- or chemotherapy. A high Ki 67 labeling index may be predictive of a poor clinical outcome. The patient died of malnutrition 2 months postoperatively, which, we supposed, played an important role in the deterioration of caudal CN function due to the aggressive tumor progression.
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Conclusions

We have presented the first known example of a glioblastoma occupying the CPA and originating from glial cells either within the proximal CN VIII itself or in the adjacent leptomeninges. We believe that even if this is a rare occurrence, glioblastoma and, generally, gliomas should be included in the differential diagnosis of atypical CPA lesions in adults. Improvement of neuroradiological techniques and specific serum tumor markers will be helpful in obtaining a correct preoperative diagnosis for CPA lesions.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Wu. Drafting the article: Wu. Critically revising the article: all authors. Reviewed final version of the manuscript and approved it for submission: all authors.

References


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