Ganglioglioneurocytoma of the Posterior Fossa

Ahmed M. Alkhani, Juan M. Bilbao, Paul Medline and Fadegbola A. Ogundimu

ABSTRACT: Objective and Importance: Ganglioglioneurocytoma is not yet a well defined clinical and histopathological entity; recent reports outline the histopathological features of this very rare trimorphic tumor, under different names with its basic components of gangliocytoma, neurocytoma and glioma. Four previous reports described this tumor in eleven patients. This is the first case report describing ganglioglioneurocytoma in the posterior fossa. Clinical Presentation and Intervention: A 31-year old male with midline posterior fossa ganglioglioneurocytoma is described, providing the neuroimages and histopathological studies. Conclusion: Ganglioglioneurocytoma is a rare mixed neuronal and glial tumor that can also occur in the posterior fossa.


Mixed cell tumors in the CNS containing both glial and neuronal elements are rare. Gangliogliomas account for about 1% of all brain neoplasms, which usually present with seizures in children. They have been reported in all levels of the neuroaxis, but were more common in the temporal lobe. The tumor contains a glial component usually astrocytic of variable cellularity and a ganglionic component of large often binucleated neurons scattered or in clusters that immunostain with synaptophysin and chromogranin. These tumors usually have a good prognosis following surgical resection.1

Central neurocytomas are rare tumors of the CNS, classically affect young adults, and arise in the lateral ventricles near the foramen of Monro. However, they have been reported away from the ventricles,2 in the cerebellum3 and in the spinal cord.4 The tumor consists of neurocytes; small round cells with perinuclear halo formation and stain with synaptophysin. Under the electron microscope, neurosecretory granules in the perinuclear cytoplasm and neurites are characteristic. This neoplasm is usually curable with total resection whenever possible. Glioneurocytomas are another mixed tumor with glial and neurocytic components. They have been reported with similar clinical and pathological findings.5

Nashio et al. in 1990 were the first to describe a tumor with well differentiated gangliocytes and neurocytes in the lateral ventricle.6 Since then, a total of eleven cases were reported describing tumors with such a morphology, usually associated with glial component of well differentiated astrocytes. In this paper we describe the 12th case, which to our knowledge is the first to be reported arising in the posterior fossa.

CASE REPORT

A 25-year-old previously healthy male presented with a one year history of progressive headache and blurring of vision. Physical exam showed papilledema and ataxic gait but normal cranial nerve function. CT scan images revealed a midline posterior fossa mass at the level of the fourth ventricle with a large dorsal cystic component and a smaller solid ventral component with calcification. The solid mass partially enhanced with IV contrast. It seemed to originate from the cerebellum and compressed the fourth ventricle causing obstructive hydrocephalus (Figure 1). The patient underwent surgery for gross total resection and had an uneventful recovery. Postoperative images showed only small residual calcifications. He had ventriculo-peritoneal shunt for hydro-
CT of the head showing the posterior fossa midline lesion without (left) and with contrast (right).

Figure 1: CT of the head showing the posterior fossa midline lesion without (left) and with contrast (right).

cæphalus. In an eighteen months post-operative follow up, he continued symptom free, with no radiological evidence of tumor recurrence.

**Histopathological studies:**

H&E staining of the paraffin sections showed the tumor to be composed of large mature-looking neurons often binucleated, scattered in the field in a pattern resembling gangliocytomas, and large aggregations of small round cells with perinuclear halos. There was a proliferation of moderately pleomorphic astrocytes with the formation of Rosenthal fibers (Figure 2). Mitotic activity was exceptional, microcystic changes and microcalcification were noted.

The immunostaining profile of the tumor was helpful in identifying the different cell types. Synaptophysin stained the larger binucleated ganglion cells and the small rounded neurocytes, with the typical immunostaining pattern on the cell surface as shown in Figure 3. Neuron specific enolase (NSE) and neurofilaments highlighted both gangliocytes and neurocytes. Only the large ganglion cells immunoreacted to chromogranin A (Figure 3). Glial fibrillary acidic protein (GFAP) stained the glial part of the tumor and only showed minor reaction in the background of the small cells population.

**DISCUSSION**

Various dimorphic mosaics have been recognized arising from the three basic cells components: gangliocytes, neurocytes and astrocytes. These tumors are known as ganglioglioma, gangglioneurocytoma and glioneurocytoma. The presence of the three neoplastic elements in the same tumor is rare. We identified four reports in the literature describing a total of eleven cases, all with the essential histopathological features of ganglioglioneurocytoma (Table). In 1990 Nishio et al. were the first to describe a tumor with such morphology in a 30-year-old female with intraventricular tumor. The term ganglioglioneurocytoma was first used by Miller et al. in 1992 to describe four cases of a tumor demonstrating these features. Further illustration of these cases was published later. More recently Giangaspero et al. demonstrated the pathological findings in five cases from total of 11 with neurocytoma. At the same time Schweitzer and Davies
described a case of ganglioglioneurocytoma, hypothesizing its origin as a result of differentiation of a central neurocytoma into ganglioglioma with the trimorphic elements.9

Ganglioglioneurocytomas should be clearly distinguished from neuroblastomas with neuronal differentiation, or medulloblastomas with mixed neuronal and glial differentiation, as ganglioglioneurocytomas should have no primitive or anaplastic elements. Yamamoto et al. published a case of neurocytoma/ganglioglioma with leptomeningeal dissemination. This tumor has no glial component and as suggested by the authors it resembled neuroblastoma to some extent.10 It is also important to differentiate ganglioglioneurocytoma from the more common neurocytoma, where mature ganglion cells may get entrapped within the tumor as it infiltrates the native elements. The ganglion cells in this case would be surrounded by reactive astrocytes forming the so-called satellitosis phenomenon. This is why, with the exception of Nishio’s case, some recent reviewers would doubt that a tumor originating from gangliocytes and neurocytes does exist.11

Unless future structural and molecular studies provide more convincing evidence, we think it is unwise to include central neurocytoma under the umbrella name of ganglioglioneurocytoma.

Ganglioglioneurocytomas appear to affect children and young adults aged 5-30 years with no gender predilection. Radiologically, the tumor is well defined, with calcification and partial enhancement to intravenous contrast. The reported locations of the tumor include intraventricular, lobar, cerebellum (this case) and spinal cord. The histopathology of these tumors is characterized by the findings in the present case; large mature binucleated neurons stain with synaptophysin and chromogranin A, small round cells with perinuclear halo stain with synaptophysin and proliferation of pleomorphic astrocytes. The prognosis of ganglioglioneurocytoma seems to follow that of other tumors of neuronal origin; good outcome is reported following surgical resection. Post operative adjunctive radiotherapy was not instituted in our case and serial radiological follow up was planned.

Table: Summary of the published cases of ganglioglioneurocytoma.

<table>
<thead>
<tr>
<th>Authors</th>
<th>No. of cases</th>
<th>Tumor name</th>
<th>Sex</th>
<th>Age</th>
<th>Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nishio et al. 1990</td>
<td>1</td>
<td>Ganglioneurocytoma</td>
<td>F</td>
<td>30</td>
<td>Intraventricular</td>
</tr>
<tr>
<td>Miller et al. 1992</td>
<td>4</td>
<td>Ganglioglioneurocytoma</td>
<td>?</td>
<td>2 child</td>
<td>2 spinal</td>
</tr>
<tr>
<td>Giangaspero et al. 1997</td>
<td>5</td>
<td>Mixed Neuronal-astrocytic</td>
<td>3F</td>
<td>5-27</td>
<td>Lobar</td>
</tr>
<tr>
<td>Schweitzer et al. 1997</td>
<td>1</td>
<td>Neurocytoma &amp; Ganglioglioma</td>
<td>M</td>
<td>30</td>
<td>Intraventricular</td>
</tr>
<tr>
<td>Alkhani et al. 1999</td>
<td>1</td>
<td>Ganglioglioneurocytoma</td>
<td>M</td>
<td>25</td>
<td>Posterior fossa</td>
</tr>
</tbody>
</table>
Many theories have been proposed for the genesis of this neoplasm. A suggested mechanism is that these tumors arise from a hypothetical single precursor cell. In the course of the evolution of this tumor, the cell would either transdifferentiate to form the different cell lines, or simply differentiate directly into the three types of cells. A subependymal progenitor cell could be that single precursor, as it was shown to have the capacity for potential neuro-glial differentiation. Further studies aimed at establishing the mechanism of differentiation through chromosomal analysis may be helpful in determining whether a similar gene defect is present in all three cell lines. In summary, ganglioglioneurocytomas are rare primary CNS tumors. We reported a case that occurred in the posterior fossa. Their benign histological features seem to correlate with a good outcome after surgical resection.

REFERENCES