Case Report

Extraventricular neurocytoma with ganglioid differentiation of the sellar and parasellar regions in an elderly patient: A case report

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ABSTRACT

Background: Extraventricular neurocytoma (EVN) is a rare variant of central neurocytoma which arises outside of the ventricular system. Diffuse ganglioid differentiation is a characteristic seen in a subset of these tumors which has an uncertain prognostic significance. Typically, EVN presents in children and young adults. Given the rarity of this tumor, the natural history and response to treatments remain unclear.

Case Description: We present a case of EVN with diffuse ganglioid differentiation in a 70-year-old male which arose in the midline parasellar region and extended into the third ventricle. This is the oldest such patient reported. Despite prior reports that extremes of age are associated with more aggressive behavior, the tumor in this case did not exhibit such an aggressive course.

Conclusion: In this report, we review the natural history and clinical course of this patient and summarize the literature regarding this rare pathological entity. Our patient responded well to therapy despite older age, ganglioid differentiation, and higher mitotic index.

Keywords: Extraventricular neurocytoma, ganglioid differentiation, ganglioneurocytoma, prognosis, suprasellar

INTRODUCTION

Central neurocytoma was first described by Hassoun et al. in 1982. It is typically located in the lateral ventricles near the foramen of Monro. Extraventricular neurocytoma (EVN) with ganglioid differentiation is a rare variant of central neurocytoma. It was first recognized as a distinct variant from central neurocytoma in 2007 WHO brain tumor classification. EVN predominantly occurs in children and young adults and is rarely found in elderly patients. EVN has been described in almost every location in the brain. In both central and extraventricular locations, neurocytoma tends to form cystic components.
EVN has the same histopathological features of central neurocytoma. These tumors are composed of uniform small cells or neurocytes with scant cytoplasm, round nuclei, and inconspicuous nucleoli.[6] Central neurocytoma sometimes has ganglioid differentiation. Of the two locations, the extraventricular site more commonly exhibits ganglioid differentiation.[2,9,17] Tumor cells are usually embedded in a neuropil-like fibrillary background and are immunoreactive to synaptophysin on immunochemistry.[3,12,16] EVN generally has a good prognosis, although more aggressive behavior and increased mitotic activity is seen in select cases.[15]

Herein, we present a case of a 70-year-old patient with an EVN with ganglioid differentiation located in the parasellar region and interpeduncular cistern with third ventricular extension. This would be the oldest patient reported in literature.

CASE REPORT

A 70-year-old man with hypertension initially presented with imbalance and dizziness and underwent magnetic resonance imaging (MRI), which demonstrated a 3.2 cm × 2.8 cm × 3.7 cm heterogeneously enhancing mass in the suprasellar region which extended to the posterior fossa resulting in mild mass effect on the midbrain and ventral pons and displacement of the optic chiasm [Figure 1]. An endonasal endoscopic approach was used for debulking of the mass. However, unbeknown to the surgical team, the patient had been on daily intranasal oxymetazoline for years, and as a result, excessive nasal cavity bleeding was encountered. Thus, only a biopsy was obtained.

The patient was diagnosed with EVN with ganglioid differentiation. Histopathological analysis showed a moderately hypercellular tumor marked by a proliferation of small cells with scant eosinophilic cytoplasm and generally rounded nuclei. These cells were intermixed with occasional large cells with large nuclei and prominent nucleoli resembling neurons or ganglioid cells [Figure 2]. The tumor demonstrated diffuse positive staining with antibodies to synaptophysin (prediluted; Biogenex; Fremont, CA) and occasionally NeuN (1:800 dilution; Millipore; St. Louis, MO). Tumor cells were negative for glial fibrillary acidic protein (GFAP) (1:600 dilution; DAKO; Carpinteria, CA) and isocitrate dehydrogenase 1 (NADP+) mutation (IDH-1 mutation). A Ki-67 (prediluted; Ventana; Indianapolis, IN) labeling index was 6–7%. FISH testing showed no evidence of 1p/19q codeletion.

He was followed with serial imaging due to the favorable prognosis of the tumor. 1 year later, the patient’s tumor subsequently progressed and the patient developed short-term memory impairment as well as obstructive hydrocephalus. A right modified orbitozygomatic craniotomy and placement of a left-sided external ventricular drain was performed. Most of the tumor in the interpeduncular cistern was resected with some residual tumor in the third ventricle that did not descend. The patient had third nerve palsy postoperatively; otherwise, he was doing well. Weaning him from the external ventricular drain was difficult due to persistent obstruction at the foramen of Monro. The patient then underwent a left frontal trans-sulcal transtubular transventricular debulking of the intraventricular tumor near the foramen of Monro with septum pellucidotomy. He was successfully weaned from his ventriculostomy.

At the 6 weeks postoperative follow-up, the third nerve palsy resolved. His short-term memory and balance were significantly improved. He underwent radiation therapy with a dose of 5400 cGy in 27 fractions 5 months following surgery to treat his residual tumor. His last follow-up was at 1 year after surgery, and he continued to improve. MRI showed a slight decrease in the size of the residual tumor as compared to his preradiation MRI.

DISCUSSION

EVN with ganglioid differentiation is a rare central nervous system tumor. There are <50 documented cases and the available literature is limited to sparse case reports and case series. It has a tendency to occur in children and young adults. The mean age of presentation is 25 years with ages ranging from 2 to 70 years [Table 1]. Despite the fact that EVN with ganglioid differentiation...
is typically a disease of adolescents and young adults, it should be considered in the differential diagnosis for an intracranial mass in an elderly patient, as presented in this case.

Sellar and parasellar EVN was previously reported. The main clinical manifestations were visual field defects, headache, and dizziness. Almost all cases were managed with a transsphenoidal approach and adjunct postoperative radiotherapy which showed a good response. In our case, the bulk of the tumor was in the suprasellar cistern and interpeduncular cistern. A smaller portion of the tumor penetrated the floor of the third ventricle, suggesting an extraventricular suprasellar origin [Figure 1]. Similarly, partial debulking through multiple approaches followed by radiation offered good tumor control.

Ganglioneurocytoma is a term used to describe EVN with diffuse and convincing ganglioid differentiation. The histopathologic criteria include clinical aspects consistent with neurocytoma, transition between neurocytoma and ganglion cells, and ganglion cells distributed throughout the tumor rather than focal ganglioid differentiation, However, the degree of ganglioid differentiation varies between cases, and it is difficult to conclude whether it is a component of the tumor or reactive gliosis. Neurocytomas may show some histological resemblance to oligodendroglioma by creating a honeycomb appearance. The absence of IDH-1 mutations and 1p/19q codeletion, which is typical findings in oligodendroglioma, favored the diagnosis of EVN with ganglioid differentiation.

EVN with diffuse ganglioid differentiation may arise from any location in the brain including but not limited to frontal, temporal, and parietal lobes. All patients were children and young adults, with the exception of one case of a 37-year-old female. These tumors had low proliferative indexes and shared the same histopathological features consisting of neurocytes and ganglionic components. Almost all tumors were positive for synaptophysin. Positive staining for NSE, NeuN, neurofilament, S-100, and GFAP was described [Table 1]. In a series of 35 patients with EVN, Brat et al. reported either focal or diffuse ganglioid differentiation in 66% of cases. Diffuse ganglioid differentiation was present in 37% of all 35 cases. Ganglion cells stained positively for chromogranin.

EVNs with ganglioid differentiation tends to exhibit a favorable prognosis but in some cases can behave more aggressively. It is unusual for these tumors to present in an elderly patient. Prior reports have suggested that extremes of age may be a risk factor for poor prognosis in EVNs. Our patient, despite the older age, the higher proliferative marker, and the ganglioid differentiation, still responded well to surgery, and radiation at 1 year and continued to improve clinically and radiologically. Longer follow-up, however, is needed to truly assess tumor growth and long-term prognosis.

**CONCLUSION**

EVN is a rare intracranial tumor most commonly seen in younger populations. Nevertheless, it should be considered in the

| Age | Gender | Location | Pathology | Cellular growth | Reference |
|-----|--------|----------|-----------|----------------|-----------|
| 1 year | Female | Frontal lobe | Small cell with large nucleus and prominent nucleoli | Ki-67 0.5% | Funato et al. 2001 |
| 2 year | Female | Frontal lobe | Small cell with a round nucleus and a scant cytoplasm | Ki-67 6-7% | Funato et al. 2001 |
| 3 year | Female | Frontal lobe | Large cell with ganglioid differentiation and small cells with a round nucleus and a scant cytoplasm | N/A | Funato et al. 2001 |
| 3 year | Female | Frontal lobe | Ganglion cells among small round cells | N/A | Funato et al. 2001 |
| 12 year | Male | Left frontal lobe | Ganglioneuroma tumor with neuronal and astrocytic characteristics | N/A | Biernat et al. 2009 |

**Table 1:** Summary of the patients with extraventricular neurocytoma with diffuse ganglioid differentiation listed in the literature.

**CONCLUSION**

EVN is a rare intracranial tumor most commonly seen in younger populations. Nevertheless, it should be considered in the
differential diagnosis of an extraventricular tumor in older adults. Our patient responded well to therapy despite older age, ganglioid differentiation, and higher mitotic index, but the impact of these variables as prognostic factors remains unclear. With a growing body of literature, the natural history of EVN will be further clarified to better direct care for these patients.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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