www.surgicalneurologyint.com

Surgical Neurology International

Editor-in-Chief: Nancy E. Epstein, MD, NYU Winthrop Hospital, Mineola, NY, USA.

SNI: Skull Base

Editor
Ekkehard Kasper, MD
McMaster University Faculty of Health Sciences, Hamilton, Ontario, Canada

ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

SNI
Open Access

Case Report

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

Shahed Tish[1], Ghaith Habboub[2], Richard A. Prayson[3], Troy D. Woodard[1,4], Varun R. Kshettry[1,2], Pablo F. Recinos[1,2,4]

[1]Minimally-Invasive Cranial Base and Pituitary Surgery Program, Rose Ella Burkhardt Brain Tumor and Neuro-oncology Center, Cleveland Clinic Section of Skull Base Surgery, [2]Section of Skull Base Surgery, Department of Neurological Surgery, Cleveland Clinic, [3]Department of Anatomic Pathology, Cleveland Clinic, [4]Section of Rhinology, Sinus, and Skull Base Surgery, Head and Neck Institute, Cleveland Clinic, Cleveland, Ohio, United States.

E-mail: Shahed Tish - tishs@ccf.org; Ghaith Habboub - habboug@ccf.org; Richard A. Prayson - praysor@ccf.org; Troy D. Woodard - woodart@ccf.org; Varun R. Kshettry - kshettv@ccf.org; *Pablo F. Recinos - recinop@ccf.org

***Corresponding author:**
Pablo Recinos,
Department of Brain Tumor and Neuro-Oncology Center, Cleveland Clinic, 9500 Euclid Avenue, CA-51, Cleveland, Ohio 44195, United States.

recinop@ccf.org

Received : 02 November 18
Accepted : 21 January 19
Published : 10 May 19

DOI
10.25259/SNI-30-2019

Quick Response Code:

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.[8] Extraventricular neurocytoma (EVN) with ganglioid differentiation is a rare variant of central neurocytoma.[4,5] It was first recognized as a distinct variant from central neurocytoma in 2007 WHO brain tumor classification.[10] 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.[13] In both central and extraventricular locations, neurocytoma tends to form cystic components.[2,7,16]

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

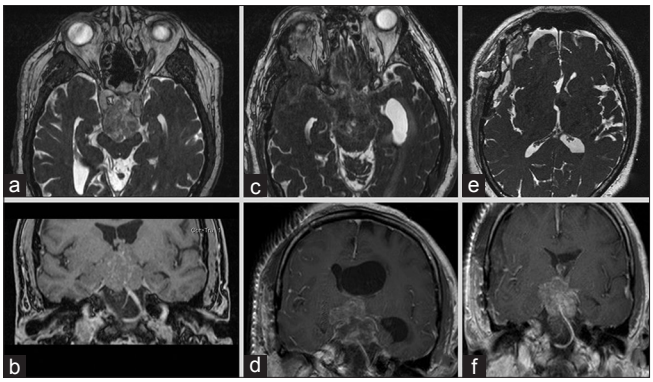

Figure 1: Constructive interference in steady state axial and T1 - post-contrast coronal magnetic resonance imaging sequences showing pre-craniotomy (a, b), post-craniotomy (c, d), and following debulking of the third ventricular portion of the tumor and septostomy (e, f).

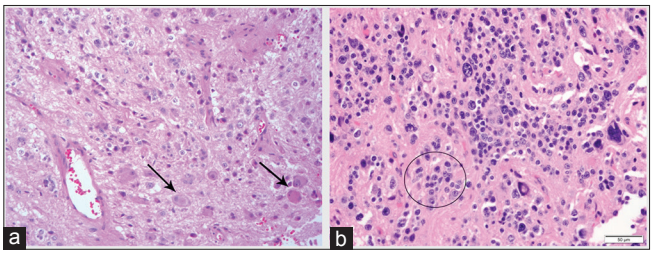

Figure 2: (a) Ganglioid differentiation of the tumor. Arrows are pointing at ganglion cells. (b) Neurocytes (small round cells with round nucleus) with surrounding capillaries. The circle is showing an example of neurocytes.

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

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

Age	Gender	Location	Pathology	Immunostaining positive for	Cellular growth	Reference
1 year 7 month	Male	Frontal lobe	Small to large anomalous neurons and glial cells	Synaptophysin, GFAP, S100	MIB-12%	K. Yako 2005[20]
27 year	Male	Left parietal	Oligodendroglial-like cells, neoplastic cells with abundant eosinophilic cytoplasm	Synaptophysin, Neurofilament	Ki-67 3%	Nabavizadeh *et al*. 2014[11]
11 year	Female	Frontal lobe	Oligodendroglioma-like cells among small round cells	NSE, Synaptophysin, S100, GFAP, NF-200kD mAb, MAP-2	MIB-1 0.5%	Funato *et al*. 1997[7]
37 year	Female	Septum pellucidum, corpus callosum, right frontal lobe	Large cell with ganglioid differentiation and small cells with a round nucleus and a scant cytoplasm	Neurofilament protein (210 KD)	N/A	Nishio *et al*. 1990[12]
23 year	Male	Left parietal lobe	Ganglion cells among small round cells	Synaptophysin, GFAP	N/A	Shin *et al*. 2002[17]
14 year	Female	Right temporal lobe	Midsized cells identified as abnormal ganglion cells, small tumor cells surrounding the vessels	Immunostains confirmed that the tumor had neuronal and astrocytic characteristics	N/A	Chan *et al*. 2001[4]
12 year	Male	Left frontal lobe	A pleomorphic ganglion cell tumor with necrosis, and endothelial proliferation	N/A	N/A	Biernat *et al* 2000[1]
70 year	Male	Suprasellar, interpeduncular cisterns, and third ventricle	Hypercellular tumor, cells with generally rounded nuclei intermixed with occasional ganglioid cells	Synaptophysin, NeuN, Neurofilament	Ki-67 6-7%	This report

Brat *et al*. reported 35 cases of which 66% had ganglioid differentiation. However, no clinical information can be discerned.[2]

GFAP: Glial fibrillary acidic protein

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.[18] 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.[18] 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.[9] 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.[5,7,11] 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.[9] 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.[14,19]

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. Ganglioid cells stained positively for chromogranin.[2]

EVNs with ganglioid differentiation tends to exhibit a favorable prognosis but in some cases can behave more aggressively.[2] 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.[13] 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

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.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Biernat W, Zakrzewski K, Liberski PP. January 2000: 12 year old boy with recent onset seizures. Brain Pathol 2000;10:313-4, 319.
2. Brat DJ, Scheithauer BW, Eberhart CG, Burger PC. Extraventricular neurocytomas: Pathologic features and clinical outcome. Am J Surg Pathol 2001;25:1252-60.
3. Buhl R, Huang H, Hugo HH, Mehdorn HM. Ganglioneurocytoma of the third ventricle. J Neurooncol 2004;66:341-4.
4. Chan A, McAbee G, Queenan J, Manning A. Ganglioneurocytoma mimicking a malignant tumor: Case report with a literature review of the MRI appearance of neurocytomas and gangliogliomas. J Neuroimaging 2001;11:47-50.
5. Choudhri O, Razavi SM, Vogel H, Li G. Atypical and rare variants of central neurocytomas. Neurosurg Clin N Am 2015;26:91-8.
6. Dagcinar A, Hilmi Kaya A, Ali Taşdemir H, Kuruoglu E, Sabancilar Z, Sav A, *et al*. A fourth ventricular ganglioneurocytoma representing with cerebellar epilepsy: A case report and review of the literature. Eur J Paediatr Neurol 2007;11:257-60.
7. Funato H, Inoshita N, Okeda R, Yamamoto S, Aoyagi M. Cystic ganglioneurocytoma outside the ventricular region. Acta Neuropathol 1997;94:95-8.
8. Hassoun J, Gambarelli D, Grisoli F, Pellet W, Salamon G, Pellissier JF, *et al*. Central neurocytoma. An electron-microscopic study of two cases. Acta Neuropathol 1982;56:151-6.
9. International Agency for Research on Cancer. WHO Classification of Tumours of the Central Nervous System (IARC WHO Classification of Tumours). 4th ed. Lyon: International Agency for Research on Cancer; 2016
10. Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, Burger PC, Jouvet A, *et al*. The 2007 WHO classification of tumours of the central nervous system. Acta Neuropathol 2007;114:97-109.
11. Nabavizadeh SA, Chawla S, Baccon J, Zhang PJ, Poptani H, Melhem ER, *et al*. Extraventricular neurocytoma and ganglioneurocytoma: Advanced MR imaging, histopathological, and chromosomal findings. J Neuroimaging 2014;24:613-6.
12. Nishio S, Takeshita I, Fukui M. Primary cerebral ganglioneurocytoma in an adult. Cancer 1990;66:358-62.
13. Patil AS, Menon G, Easwer HV, Nair S. Extraventricular neurocytoma, a comprehensive review. Acta Neurochir (Wien) 2014;156:349-54.
14. Perry A, Burton SS, Fuller GN, Robinson CA, Palmer CA, Resch L, *et al*. Oligodendroglial neoplasms with ganglioglioma-like maturation: A diagnostic pitfall. Acta Neuropathol 2010;120:237-52.
15. Rusiecki D, Lach B, Manoranjan B, Fleming A, Ajani O, Singh SK, *et al*. Progression of atypical extraventricular neurocytoma to anaplastic ganglioglioma. Hum Pathol 2017;59:125-30.
16. Sabatino G, Della Pepa GM, Albanese A, Lauriola L, Marchese E. Cystic ganglioneurocytoma of the lateral ventricles. Br J Neurosurg 2014;28:688-90.
17. Shin JH, Lee HK, Lee JK, Khang SK, Choi CG, Suh DC, *et al*. MR imaging and histopathologic findings of a case of cerebral ganglioneurocytoma. Korean J Radiol 2002;3:214-7.
18. Wang J, Song DL, Deng L, Sun SY, Liu C, Gong DS, *et al*. Extraventricular neurocytoma of the sellar region: Case report and literature review. Springerplus 2016;5:987.
19. Wesseling P, van den Bent M, Perry A. Oligodendroglioma: Pathology, molecular mechanisms and markers. Acta Neuropathol 2015;129:809-27.
20. Yako K, Nakazato Y, Hirato J, Tosaka M, Ohtani T, Ishiuchi S, *et al*. Dysplastic ganglioneurocytoma with increased glucose metabolism: A heterotopia with unique histopathology. Clin Neuropathol 2005;24:267-70.

How to cite this article: Tish S, Woodard TD, Habboub G, Prayson RA, Kshettry VR, Recinos PF. Extraventricular neurocytoma with ganglioid differentiation of the sellar and parasellar regions in an elderly patient: A case report. Surg Neurol Int 2019;10:82.