ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

www.surgicalneurologyint.com

Surgical Neurology International

Editor-in-Chief: Nancy E. Epstein, MD, Clinical Professor of Neurological Surgery, School of Medicine, State U. of NY at Stony Brook.

SNI: Neuro-Oncology

Editor
Mitsutoshi Nakada, MD
Kanazawa University, Ishikawa, Japan

SNI
Open Access

Case Report

A rare diagnosis of an extraventricular neurocytoma

Claudia Gaggiotti[1], Giuseppe Roberto Giammalva[1], Marco Raimondi[2], Ada Maria Florena[2], Rosa Maria Gerardi[1], Francesca Graziano[1], Silvana Tumbiolo[3], Domenico Gerardo Iacopino[1], Rosario Maugeri[1]

[1]Department of Biomedicine Neurosciences and Advanced Diagnostics, School of Medicine, University of Palermo, [2]Department of Scienze per la Promozione della Salute e Materno Infantile, Pathology Unit, University of Palermo, [3]Department of Neurosciences and Emergency, Division of Neurosurgery, Villa Sofia Hospital, Palermo, Italy.

E-mail: Claudia Gaggiotti - claudia.gaggiotti92@gmail.com; *Giuseppe Roberto Giammalva - robertogiammalva@live.it; Marco Raimondi - marcorai26@gmail.com; Ada Maria Florena - adamaria.florena@unipa.it; Rosa Maria Gerardi - rosamariagerardimd@gmail.com; Francesca Graziano - fragraziano9@gmail.com; Silvana Tumbiolo - tumbiolosilvan@yahoo.it; Domenico Gerardo Iacopino - gerardo.iacopino@gmail.com; Rosario Maugeri - rosario.maugeri1977@gmail.com

***Corresponding author:**
Giuseppe Roberto Giammalva, Department of Biomedicine Neurosciences and Advanced Diagnostics, School of Medicine, University of Palermo, Palermo, Italy.

robertogiammalva@live.it

Received : 28 December 2020
Accepted : 09 February 2021
Published : 08 March 2021

DOI
10.25259/SNI_951_2020

Quick Response Code:

ABSTRACT

Background: Extraventricular neurocytoma (EVN) is an extremely rare neoplasm of the central nervous system. As reported, it arises in a variety of locations, but mainly within the cerebral hemispheres. Despite its histological similarity with central neurocytoma (CN), EVN occurs outside the ventricular system and, in 2007, was recognized by the World Health Organization as a separate entity.

Case Description: A 39-year-old man, with a ventriculoperitoneal shunt inserted for communicating hydrocephalus, was admitted at our Unit of Neurosurgery with a 1-month history of gait disturbance, postural instability, speech disorders, and occasional incontinence. Computed tomography scan and magnetic resonance imaging showed a mixed-density neoplasm in the left frontotemporal area, with anterior cerebral falx shift, and perilesional edema. The patient underwent surgical procedure; microsurgical excision of the lesion was performed through left pterional approach. Histopathological and immunohistochemical examination revealed monomorphic round cells of the neuronal lineage, with a percentage of Ki-67 positive nuclei <5% and no evidence of mitosis or necrotic areas. According to radiologic features, this pattern was compatible with the diagnosis of EVN. Patient had a favorable recovery and he is still in follow-up.

Conclusion: Because of their rarity, clinical, radiologic, and histopathological characteristics of EVNs are not yet well defined, as well as the optimal therapeutic management. Whereas EVNs are rarely described in literature, we aimed to share and discuss our experience along with a review of the published literature.

Keywords: Extraventricular neurocytoma, Neurocytoma, Neuronal tumors

INTRODUCTION

Extraventricular neurocytoma (EVN) is an extremely rare neuronal tumor with just approximately 100 reported cases in literature;[16] it has been considered for a long time as a variant of the central neurocytoma (CN), a rare tumor in itself with an estimated incidence of 0.25–0.50% of all primary brain tumors.[8,17,22,29]

In facts, neurocytic neoplasms generally arise within the lateral ventricles and they are occasionally located in the context of brain parenchyma, without any continuity to the ventricular system. Compared with CN, EVN shows similar histopathological characteristics but a wider

spectrum of locations and morphological features; both CN and EVN usually presents an indolent behavior, even though, since in 1989 Ferreol *et al*. described the first case of EVN, a higher rate of recurrence was observed in the latter.[7] Only in 2007 EVN was introduced as a separate entity in the World Health Organization (WHO) classification of tumors of the central nervous system.[19]

Apart from systematic reviews, published literature on EVNs consists of sporadic case reports and a few small case-series. In consideration of the low number of reports, we aim to share our experience and describe a case of a 39-year-old patient with a left frontotemporal EVN.

CASE DESCRIPTION

A 39-years-old man was admitted to the emergency room of our Institution for a 1-month history of gait disturbance, postural instability, speech disturbance, and episodes of incontinence. His history was remarkable for communicating hydrocephalus, which had been surgically treated at the age of 14 months with the placement of a ventriculoperitoneal shunt, followed by a distal shunt revision at the age of 16 years. At the admission, brain computed tomography (CT) scan was performed and it showed the presence of 5 cm mixed-density pseudonodular lesion. His neurological examination revealed temporospatial disorientation, absence of focal motor deficits and sensory alteration, normal and symmetrical osteotendinous reflexes, walk of little steps, and wide-based gait, several body oscillations during the Romberg's test. A contrast-enhanced brain CT study [Figure 1] confirmed the presence of an enhancing 57 mm left frontotemporal non-homogeneous neoformation, with several calcifications, hypodense colliquated areas, and perilesional edema. Preoperative magnetic resonance imaging (MRI) with gadolinium contrast medium, even though strongly fouled by motion artifacts due to poorly cooperative patient, showed a lesion with lobulated margins, non-homogeneous post contrast enhancement and heterogeneous signal intensity in relation to the presence of solid component mixed with necrotic-colliquative areas and calcifications. In particular, in the peripheral frontal portion, a small oval-shaped component was visible, surrounded by strongly hypointense peripheral border in FFE sequences, arguably due to hemosiderin deposition. The tumor presented a maximum diameter of 6.2 × 4.1 cm on the axial plane [Figure 2a], 6.3 × 3.5 cm on the sagittal plane [Figure 2b], and 3.6 × 3.3 cm on the coronal plane [Figure 2c], and it extended cranially to the knee of the corpus callosum, displacing the large falx to the right and causing a compressive effect on the frontal horn of the right lateral ventricle.

Surgical procedure was performed with the aid of optic neuronavigation, intraoperative monitoring and the resection was performed though a left pterional approach.[1,24]

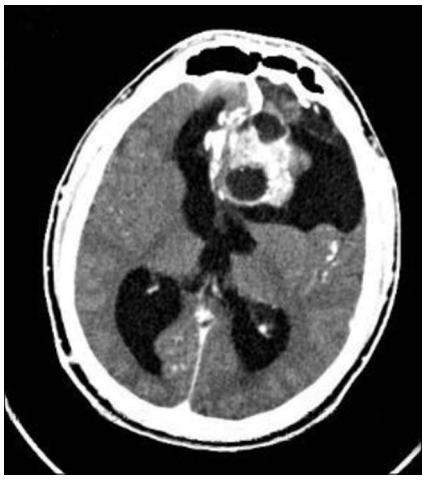

Figure 1: Preoperative contrast brain computed tomography scan showing the left frontotemporal non-homogeneous neoformation, with several calcifications, hypodense colliquated areas, and perilesional edema.

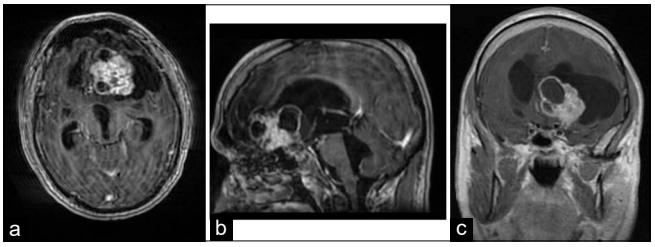

Figure 2: Preoperative contrast brain magnetic resonance imaging, showing the lesion with lobulated margins, non-homogeneous post contrast enhancement, solid component mixed with necrotic-colliquative areas and calcifications. (a) axial plane, (b) sagittal plane, (c) coronal plane.

Intraoperatively, the neoplasm appeared of soft and partly fibrous consistency, of reddish-grey color and with a fairly good cleavage plane from the adjacent cerebral parenchyma. With the aid of ultrasonic aspirator and microsurgical technique, macroscopical total resection of the exposed neoplastic lesion was carried out. Autologous fibrin glue was used to seal the dural plane.

Fragments of the lesion were sent for pathological examination, which revealed a population of neuronal lineage (Sinaptophysin+, neuron specific enolase+, glial fibrillary acid protein−) consisting of roundish monomorphic cells mixed with a proliferation of capillary vessels and the presence of widespread calcifications; the Ki-67 index was <5%, there was no evidence of mitosis or areas of necrosis. Histopathological and immunohistochemical pattern, according to radiological findings, was consistent with a diagnosis of EVN, classified by the WHO as a Grade II tumor [Figure 3a-c].

The postoperative course was uneventful and control CT scan [Figure 4] showed no complications. A further MRI

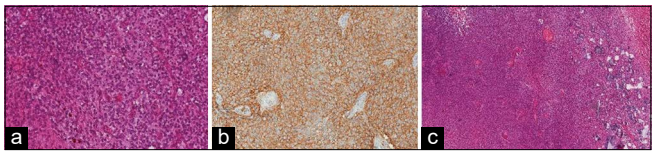

Figure 3: (a) On low power histopathological examination, sheets of monomorphic round cells interspersed by fine capillary channels and laminated concentric microcalcification, without evidence of ischemic necrosis or hemorrhage. (hematoxylin and eosin [H and E] ×40), (b) Higher magnification shows round cells with stippled chromatin arranged in a background of finely fibrillar neuropil cores (hematoxylin and eosin [H and E] ×250), (c) strong immunoreaction for synaptophysin expressed by tumor cells (avidin-biotin ×250).

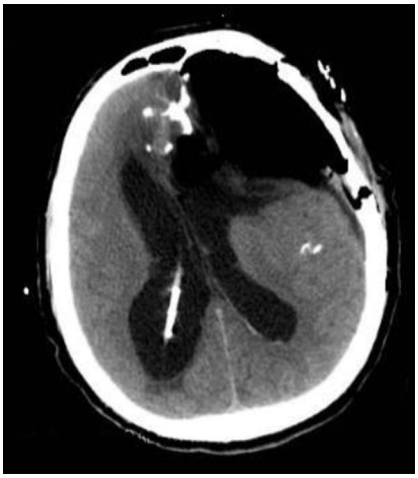

Figure 4: Postoperative brain computed tomography scan.

was performed [Figure 5a-c], which showed on the left frontal area, in correspondence of the surgical cavity, a large area of structural alteration, consisting predominantly of cerebrospinal fluid and a tissue portion with calcifications.

After the hospital discharge patient underwent at home neurorehabilitation with consistent improvement of his gait and speech. He also underwent adjuvant radiotherapy and at the present his follow-up is still ongoing.

DISCUSSION

Although the exact incidence is still not precisely defined, in a systematic review the incidence of cerebral EVN has been estimated to be 0.13% of approximately 7000 cases of intracranial tumors.[10] In a larger case series, among 868 patients with neurocytoma 19.3% showed an extra-ventricular location.[18] According to the literature, EVN exhibits no predilection for any particular sex, sometimes showing a slight predominance in males, and it seems to be distributed uniformly across all age groups.[2,4,10,13] Recently, it has been shown that EVN has a bimodal age distribution,

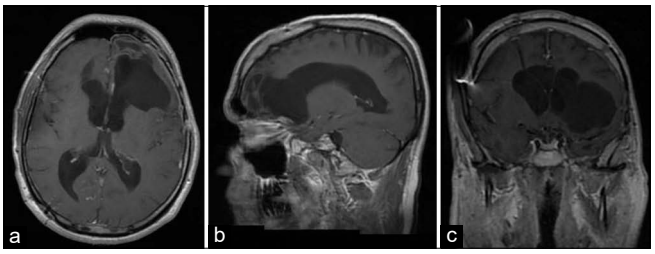

Figure 5: Postoperative brain magnetic resonance imaging showing large area of structural alteration, consisting predominantly of cerebrospinal fluid and a tissue portion with calcifications. (a) axial plane, (b) sagittal plane, (c) coronal plane.

with two distinct peaks of incidence in the second and fifth decades.[35]

EVNs may occur in various site outside the ventricular system; the most common location reported is the frontal lobe, followed by the parietal, temporal, and occipital lobes.[2] Less frequently involved regions are sellar region,[13,16] thalamus,[21] cerebellum,[5,15,27] and spine.[12,31] EVNs have also been described outside the context of central nervous system, in particular inside the pelvis,[9] adrenal gland,[6] and ovary.[11]

Clinical presentation of EVN is heterogeneous, non-specific and it varies depending on the location of the tumor and the mass effect exerted.[34] According to the literature, the main clinical manifestations comprehend headache, vomiting, seizures, and limb motor deficit. In addition, visual disturbance has been described as the first symptom of EVN of the sellar region.[16] Our patient complained, among other symptoms, urinary incontinence, which is an uncommon symptom that has been only once reported.[3]

In our case, the radiologic features of patient's lesion are consistent with the previous reports.[26] In fact, EVNs usually show focal cystic components and calcification; the solid portions of EVNs are often described as isodense or slightly hyperdense on CT, isointense or hypointense on T1WI, and isointense or hyperintense on T2WI. The lesion, in our patient, showed heterogeneous enhancement, a feature frequently noted in EVNs and other low-grade tumors. It also presented perilesional edema, which is described from 10% to more than 80% of EVNs cases.[13,37]

However, EVNs may exhibit a wealth of non-specific imaging features, leading to a difficult differential diagnosis mainly toward oligodendrogliomas and oligoastrocytomas with neurocytic differentiation, ganglioglioma, pilocytic astrocytoma, ependymoma, and dysembryoblastic neuroepithelial tumors.[32,36] As a consequence, the integration of radiological findings and histopathological examination is essential for definitive diagnosis.

Furthermore, CNs and EVNs exhibit a shared microscopic appearance. In facts, neurocytic neoplasms are mainly

composed of uniform roundish cells with neuronal differentiation, strongly immunoreactive for synaptophysin. EVN, however, has been described with a wider spectrum of proliferation rates and cellularity, showing tendency for ganglionic or glial differentiation; in 2001, Brat *et al*. proposed "atypical EVN," a variant associated with a higher recurrence rate.[4] The atypical histological features identified included increased mitotic activity, high Ki-67 proliferation index (>2%), focal necrosis, and vascular proliferation.[30] In our patient, histopathological examination revealed low Ki-67 index without evidence of mitotic activity or necrosis, while proliferation of capillary vessels was observed.

Age and atypical histological features have been suggested as negative prognostic factors associated with poorer outcomes.[14,23] Progression from typical to atypical EVN[3] and to neuroblastoma[28] is reported in the literature, although EVN usually shows non-aggressive behavior and has been classified by the WHO as a Grade II tumor since its introduction.[19,20]

The therapeutic management for EVNs is based on surgical removal, while radiotherapy or chemotherapy should be considered in cases of subtotal resection or as salvage for local recurrence after surgery. Compared with gross total resection, subtotal resection followed by radiotherapy may offer a reasonably good outcome with a similar overall survival.[14] The efficacy of postoperative chemotherapy is not clear and it is rarely employed; however, in two different case-reports EVN showed sensitivity to vincristine.[25,34]

Nevertheless, Dutta *et al*. recently investigated different patterns of care in a large cohort of patients with diagnosed neurocytomas, founding that tumor location and use of radiation were not predictive for improved survival.[4] Considering the usually benign nature of EVNs and the risks associated with adjuvant therapies, these should be administered to a selected subgroup of patients; the presence of unfavorable histopathological features should guide postoperative treatment decisions.

CONCLUSION

Since they are rare tumors, clinical, radiologic, and histopathological characteristics of EVNs are not yet well defined, as well as the optimal therapeutic management. Whereas EVNs are rarely described in the literature, we described our singular case of extra-ventricular neurocytoma, with our surgical management and an exhaustive review of the published literature.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Barone F, Alberio N, Iacopino D, Giammalva G, D'Arrigo C, Tagnese W, *et al*. Brain mapping as helpful tool in brain glioma surgical treatment-toward the "perfect surgery"? Brain Sci 2018;8:192.
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. Chen F, Jin R, Wu X, Dong Z, Chen D. Extraventricular neurocytoma in the left frontal lobe: A case report and literature review. World Neurosurg 2018;112:178-81.
4. Dutta SW, Kaleem TA, Muller DA, Peterson J, Harrell AC, Quinones-Hinojosa A, *et al*. Central neurocytoma: Clinical characteristics, patterns of care, and survival. J Clin Neurosci 2018;53:106-11.
5. Enam SA, Rosenblum ML, Ho KL. Neurocytoma in the cerebellum. Case report. J Neurosurg 1997;87:100-2.
6. Ersoz S, Kucuk H, Mungan S, Turgutalp H, Imamoglu M, Kosucu P. Neurocytoma arising in an adrenal gland mature teratoma. Fetal Pediatr Pathol 2011;30:275-9.
7. Ferreol E, Sawayal R, de Courten-Myers GM. Primary cerebral neuroblastoma (neurocytoma) in adults. J Neurooncol 1989;7:121-8.
8. Francaviglia N, Iacopino DG, Costantino G, Villa A, Impallaria P, Meli F, *et al*. Fluorescein for resection of high-grade gliomas: A safety study control in a single center and review of the literature. Surg Neurol Int 2017;8:145.
9. Friedrichs N, Vorreuther R, Fischer HP, Wiestler OD, Buettner R. Neurocytoma arising in the pelvis. Virchows Arch 2003;443:217-9.
10. Giammalva GR, Iacopino DG, Azzarello G, Gaggiotti C, Graziano F, Gulì C, *et al*. End-of-life care in high-grade glioma patients. The palliative and supportive perspective. Brain Sci 2018;8:125.
11. Hirschowitz L, Ansari A, Cahill DJ, Bamford DS, Love S. Central neurocytoma arising within a mature cystic teratoma of the ovary. Int J Gynecol Pathol 1997;16:176-9.
12. Hu JR, Li J, Lv GH, Deng YW, Zou MX. Extraventricular neurocytoma mimicking bone tumor in thoracic spinal column. Spine J 2015;15:e65-6.
13. Jiang M, Long L, Zeng J, Meng W, Zee CS. Imaging characteristics of cerebral extraventricular neurocytoma with pathological correlation. J Neurooncol 2018;140:289-96.
14. Kane AJ, Sughrue ME, Rutkowski MJ, Aranda D, Mills SA, Lehil M, *et al*. Atypia predicting prognosis for intracranial extraventricular neurocytomas. J Neurosurg 2012;116:349-54.
15. Kapoor N, Gandhi A, Chaurasia AK. Central neurocytoma in the vermis of the cerebellum. Indian J Pathol Microbiol 2009;52:108-9.

16. Kawaji H, Saito O, Amano S, Kasahara M, Baba S, Namba H. Extraventricular neurocytoma of the sellar region with spinal dissemination. Brain Tumor Pathol 2014;31:51-6.
17. la Torre D, Maugeri R, Angileri FF, Pezzino G, Conti A, Cardali SM, *et al*. Human leukocyte antigen frequency in human high-grade gliomas: A case-control study in Sicily. Neurosurgery 2009;64:1082-8; discussion 1088-9.
18. Liu K, Wen G, Lv XF, Deng YJ, Deng YJ, Hou GQ, *et al*. MR imaging of cerebral extraventricular neurocytoma: A report of 9 cases. Am J Neuroradiol 2013;34:541-6.
19. 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.
20. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, *et al*. The 2016 World Health Organization classification of tumors of the central nervous system: A summary. Acta Neuropathol 2016;131:803-20.
21. Mallick S, Benson R, Rath G. Patterns of care and survival outcomes in patients with an extraventricular neurocytoma: An individual patient data analysis of 201 cases. Neurol India 2018;66:362-7.
22. Maugeri R, Villa A, Pino M, Imperato A, Giammalva GR, Costantino G, *et al*. With a little help from my friends: The role of intraoperative fluorescent dyes in the surgical management of high-grade gliomas. Brain Sci 2018;8:31.
23. Patil AS, Menon G, Easwer HV, Nair S. Extraventricular neurocytoma, a comprehensive review. Acta Neurochir (Wien) 2014;156:349-54.
24. Pino MA, Imperato A, Musca I, Maugeri R, Giammalva GR, Costantino G, *et al*. New hope in brain glioma surgery: The role of intraoperative ultrasound. A review. Brain Sci 2018;8:202.
25. Raja AI, Yeaney GA, Jakacki RI, Hamilton RL, Pollack IF. Extraventricular neurocytoma in neurofibromatosis Type 1: Case report. J Neurosurg Pediatr 2008;2:63-7.
26. Romano N, Federici M, Castaldi A. Imaging of extraventricular neurocytoma: A systematic literature review. Radiol Med 2020;125:961-70.
27. Rusiecki D, Lach B, Manoranjan B, Fleming A, Ajani O, Singh SK. Progression of atypical extraventricular neurocytoma to anaplastic ganglioglioma. Hum Pathol 2017;59:125-30.
28. Sakurada K, Akasaka M, Kuchiki H, Saino M, Mori W, Sato S, *et al*. A rare case of extraventricular neurocytoma. Brain Tumor Pathol 2007;24:19-23.
29. Sharma MC, Deb P, Sharma S, Sarkar C. Neurocytoma: A comprehensive review. Neurosurg Rev 2006;29:270-85.
30. Singh A, Chand K, Singh H, Sarkar C, Sharma MC. Atypical neurocytoma of the spinal cord in a young child. Childs Nerv Syst 2007;23:207-11.
31. Tsai CY, Tsai TH, Lin CH, Cheng YH, Lieu AS. Unusual exophytic neurocytoma of thoracic spine mimicking meningioma: A case report and review of the literature. Eur Spine J 2011;20 Suppl 2:S239-42.
32. Umana GE, Alberio N, Amico P, Lavecchia A, Fagone S, Fricia M, *et al*. Giant Cystic Brain Metastasis from Ovarian Papillary Serous Adenocarcinoma: Case Report and Review of the Literature, Interdisciplinary Neurosurgery: Advanced Techniques and Case Management; 2020.
33. Umana GE, Raudino G, Alberio N, Inserra F, Giovinazzo G, Fricia M, *et al*. Slit-like hypertensive hydrocephalus: Report of a late, complex, and multifactorial complication in an oncologic patient. Surg Neurol Int 2020;11:219.
34. von Koch CS, Schmidt MH, Uyehara-Lock JH, Berger MS, Chang SM. The role of PCV chemotherapy in the treatment of central neurocytoma: Illustration of a case and review of the literature. Surg Neurol 2003;60:560-5.
35. Wang YY, Kearney T, du Plessis D, Gnanalingham KK. Extraventricular neurocytoma of the sellar region. Br J Neurosurg 2012;26:420-2.
36. Xiong Z, Zhang J, Li Z, Jiang J, Han Q, Sun S, *et al*. A comparative study of intraventricular central neurocytomas and extraventricular neurocytomas. J Neurooncol 2015;121:521-9.
37. Yi KS, Sohn CH, Yun TJ, Choi SH, Kim JH, Han MH, *et al*. MR imaging findings of extraventricular neurocytoma: A series of ten patients confirmed by immunohistochemistry of IDH1 gene mutation. Acta Neurochir (Wien) 2012;154:1973-9.

How to cite this article: Gaggiotti C, Giammalva GR, Raimondi M, Florena AM, Gerardi RM, Graziano F, *et al*. A Rare diagnosis of an extraventricular neurocytoma. Surg Neurol Int 2021;12:88.