

## Case Report

# Atypical Extraventricular Neurocytoma: A Rare Case Report and Review of Literature

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### Abstract

Extraventricular neurocytoma (EVN) is a rare brain tumor that poses diagnostic difficulty. Described herein is a case of atypical EVN arising in a 35-year-old man. A well circumscribed lesion in the right frontal lobe showed diffuse proliferation of monotonous tumor cells with perinuclear clearing and salt and pepper chromatin within a delicate fibrillary matrix. Tumor also showed vascular proliferation and high mitotic activity. Immunohistochemically, these tumor cells were strongly positive for synaptophysin and CD56 in the perinuclear cytoplasm, and negative for epithelial membrane antigen (EMA) and vimentin. Ki-67 labeling index was 25–30% in the most stained areas. These findings were compatible with those of atypical EVN. EVN should be considered as a candidate in the differential diagnosis of parenchymal brain tumor, especially oligodendroglioma.

**Keywords:** Atypical, extraventricular, immunohistochemistry, neurocytoma, synaptophysin

**Cite This Article:** Nagpal R, Ahuja A. Atypical Extraventricular Neurocytoma: A Rare Case Report and Review of Literature. *EJMO* 2020;4(1):94–97.

Neurocytoma arising outside the ventricular system are known as “extraventricular neurocytoma” and was first reported in 1989.<sup>[1]</sup> It shares similar biological and histopathological characteristics with central neurocytoma (CN). The World Health Organization (WHO) classification of brain tumors revised in 2007 includes EVN as a single pathological diagnosis and proposes an ICD-O code identical to that of central neurocytoma. The neurocytoma, which exhibits a MIB-1 labeling index of >2%, increased mitosis, focal necrosis and vascular proliferation is classified as atypical.<sup>[2,3]</sup> These tumors can pose diagnostic difficulty because of overlap of clinical and histological features with those of other brain tumors, especially oligodendroglioma.<sup>[4]</sup> Moreover, the clinical biology of EVN has not been fully characterized due to its rarity. We here report a case of atypical EVN of the right frontal lobe in a 35-year-old man, and immunohistochemically assess this tumor.

### Case Report

A 35-year-old male presented with a history of progressive holocranial headache, vomiting, diminution of vision, and one episode of generalised tonic-clonic seizures since past two months. On examination, the patient had altered sensorium, ptosis in right eye and left pronator drift. Ophthalmic examination revealed decreased vision, left lateral rectus palsy and bilateral papilledema. Non-contrast computed tomography (NCCT) head showed a heterogeneous hyperdense space occupying lesion (SOL) in the right frontal lobe with perifocal edema. Few coarse calcifications were seen involving both cortical and subcortical regions. Effacement of right lateral ventricle predominantly frontal horn and dilatation of contralesional left lateral ventricle was seen. There was evidence of midline shift towards left and effacement of bilateral ambient cisterns with uncal herniation (Fig.

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**Submitted Date:** September 10, 2019 **Accepted Date:** February 19, 2020 **Available Online Date:** March 12, 2020

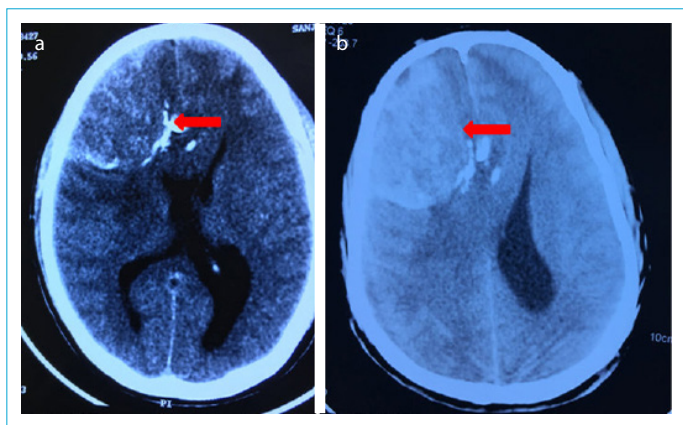
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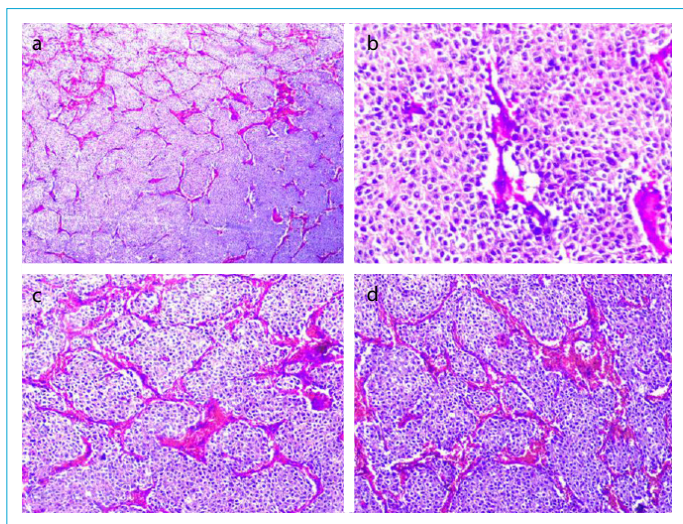


1a). Magnetic resonance imaging (MRI) T1 image revealed hyperintense lesion involving right frontal cortex and sub-cortical region with ipsilateral ventricular compression and contralateral ventricular dilatation (Fig. 1b). Because an extraventricular lesion was suggestive, en bloc tumor resection was performed under the diagnosis of meningioma.

Microscopic examination of lesion revealed sheets of neoplastic cells with iso-morphous morphology (Fig. 2a) having moderate amount of cytoplasm, and round central nucleus with salt and pepper chromatin and perinuclear clearing (Fig. 2b). At places, capillary sized blood vessels were seen with arborizing pattern (Fig. 2c). However, focal areas showed microvascular proliferation (Fig. 2d). Mitotic



**Figure 1.** (a) NCCT head showing heterogenous hyperdense SOL in right frontal lobe with perifocal edema, effacement of right lateral ventricle and dilatation of contralateral left lateral ventricle. (b) MRI, T1 hyperintense lesion showing the similar findings.



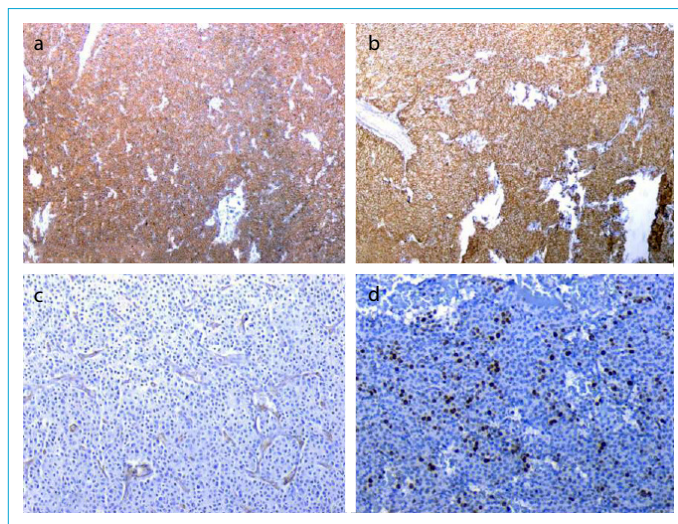
**Figure 2.** (a) Sheets of neoplastic cells with iso-morphous morphology (H&E stain, 4X). (b) Cells with round central nucleus, salt and pepper chromatin, perinuclear clearing and moderate amount of cytoplasm (H&E stain, 20X). (c) Capillary sized blood vessels with arborizing pattern (H&E stain, 20X). (d) Microvascular proliferation (H&E stain, 20X).

activity of 4-5/10 hpf was evident. Differential diagnoses of ependymoma, oligodendroglioma and extraventricular neurocytoma were considered and immunohistochemical (IHC) was ordered. IHC analysis of the neoplastic cells showed positive results with synaptophysin (Fig. 3a) and CD56 (Fig. 3b), while it returned negative for EMA (epithelial membrane antigen) (Fig. 3c) and vimentin. Ki-67 labeling index was approximately 25-30% in highest proliferating areas (Fig. 3d). The pathologic result was consistent with atypical extraventricular neurocytoma.

The patient was planned for radiotherapy with additional antiepileptic medications. However, he did not follow up the treatment.

## Discussion

CN was first described by Hassoun et al. in 1982 and was recognized as a distinct pathological entity in 1993.<sup>[5]</sup> It is classified as Grade II in the WHO classification of tumors of the central nervous system.<sup>[6]</sup> These tumors are most commonly diagnosed in the third decade of life. CNs are characteristically located in the supratentorial ventricular system in the region of the foramen of Monro, attached to the septum pellucidum, the walls of the lateral ventricles, the fornices, the corpus callosum, the roof of the third ventricle, or the choroid plexus and typically present with signs and symptoms of increased intracranial pressure, including headache, nausea and emesis, and papilledema. Visual disturbances including blurred vision, diplopia, decreased visual acuity, intermittent loss of vision, and photophobia, as well as mental disturbances including altered



**Figure 3.** Immunohistochemical (IHC) analysis of the neoplastic cells showed positive results with synaptophysin (a) and CD56 (b), negative immunoreaction for EMA (c). Ki-67 labeling index approximately 25-30% (d).

consciousness, memory loss and disorientation can also be seen. Computed tomographic (CT) scans usually show a well-circumscribed, isodense to hyperdense lesion with areas of calcification, enhances postcontrast.<sup>[5]</sup> CN-like tumors have been reported in a variety of locations outside the supratentorial ventricular system, including cerebral hemisphere, insular cortex, thalamus, hypothalamus, cerebellum, pons, spinal cord, cauda equina and retina.<sup>[5,7]</sup> These neoplasms have been termed EVNs and are classified as distinct entity in 2007 WHO classification of tumors of the nervous system.<sup>[6,8]</sup> EVN rarely occurs in young people.<sup>[3]</sup> Cortical based EVNs may not cause symptoms until they are much larger in size and may be in closer proximity to critical neurovascular structures.<sup>[8]</sup> Presenting symptoms vary depending on the location of the tumor. EVNs of the cerebral hemispheres, which seem to be the most common site for EVN tumorigenesis, often present with seizures. The appearance of EVNs on neuroimaging studies is similar to that of CNs.<sup>[5]</sup>

The defining histologic features of neurocytoma are sheet-like monotonous population of neoplastic cells with round, regular nuclei surrounded by fibrillary matrix.<sup>[2,4]</sup> These cells also form pseudorosettes surrounding small islands of fibrillary neuropil-like material.<sup>[4]</sup> Nuclei are round or oval with finely speckled salt and pepper chromatin and a sometimes prominent nucleolus.<sup>[3]</sup> Perinuclear halos are present, giving the neoplasm a honeycomb appearance similar to that of an oligodendroglioma.<sup>[2,5]</sup> Some cases also show focal or diffuse ganglion cell differentiation, which is far higher than in central neurocytoma.<sup>[3]</sup> In our case, sheets of iso-morphous neoplastic cells having moderate amount of cytoplasm, round central nucleus, salt and pepper chromatin and focal areas with microvascular proliferation were seen. Mitotic activity of 4-5/10 hpf was also noted.

The IHC profile is peculiar with diffuse synaptophysin immunoreactivity both within the cytoplasm and in the neuropil. The GFAP shows immunoreactivity in entrapped non-neoplastic astrocytes and focal cytoplasmic staining in tumor cells.<sup>[4]</sup> The EVN usually show a MIB-1 labeling index of less than 2%. Tumors with indices greater than 2% have been referred to as "atypical neurocytomas". The atypical ones also show atypical histological features, increased mitosis, focal necrosis and vascular proliferation.<sup>[3]</sup> Ki-67 labeling index in our case was approximately 25-30% in highest proliferating areas.

Differential diagnoses include oligodendroglioma, ependymoma and cerebral neuroblastoma. Oligodendroglioma has round, regular nuclei with clear cytoplasm, but no fibrillary background. Fine granular nuclei with nucleoli, and diffuse or focal ganglion cell differentiation is not seen.

The clear cell variant of ependymoma gives an oligodendroglioma-like appearance. Perivascular pseudorosettes of ependymoma are similar to perivascular fibrillary zone of neurocytoma. In contrast to EVN, oligodendroglioma and ependymoma show no reactivity with synaptophysin. Ependymoma frequently expresses EMA. Olig2, a recently identified transcription factor, is expressed in the oligodendroglial lineage. Because CN does not express this protein, combined usage of Olig2 with neuronal markers is helpful in differentiating neurocytoma. Cerebral neuroblastoma is mainly a pediatric tumor and is composed of cytologically malignant, poorly differentiated neuroectodermal cells and accompanied by necrosis.<sup>[4]</sup> In our case the cells show immunoreactivity with synaptophysin and CD56 whereas no reactivity was seen with EMA and vimentin. However Ki-67 labelling index was approximately 25-30% in highest proliferating regions. Thus the final diagnosis of atypical extraventricular neurocytoma was rendered.

The treatment of atypical neurocytoma is not well established. Rades et al.<sup>[9]</sup> have documented that complete resection would provide better local control and survival rates than incomplete resection and that local control and survival rates are improved with postoperative radiation therapy in cases of incomplete resection. In our case, en bloc resection was performed under the diagnosis of meningioma. Patient was planned for radiotherapy and anti-epileptic treatment but he did not follow up the treatment.

Kane et al. reported higher rates of recurrence and mortality in both CNs and EVNs with atypical features i.e 40% recurrence and 20% mortality in atypical CN compared with 68% recurrence and 44% mortality, respectively, in atypical EVNs. However, most of the reported cases of atypical EVN were adults and tend to be older than those of typical EVN.<sup>[8]</sup>

## Conclusion

EVN should be considered in the differential diagnosis of parenchymal brain tumor. The presence of delicate fibrillary matrix similar to neuropil and combined usage of immunohistochemistry with neuronal markers is helpful for the diagnosis of EVN.

## Disclosures

**Informed consent:** Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

**Authorship Contributions:** Concept – A.A.; Design – R.N.; Supervision – A.A.; Materials – A.A.; Data collection &/or processing – R.N.; Analysis and/or interpretation – A.A.; Literature search – R.N.; Writing – R.N.; Critical review – A.A.



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