Extraventricular Neurocytoma

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ABSTRACT

Extraventricular neurocytoma is a rare neuroepithelial tumor. Its propensity to occur in cerebral hemisphere is much higher. EVN has a histological resemblance to central neurocytoma but radiologically, it is more complex. Ganglionic differentiation is more common in EVN and tends to have more of a cystic component. Calcification is frequent but hemorrhage is only an occasional finding. Although it has been reported to occur in various regions, the propensity to occur in cerebral hemisphere is much higher. Herein, we report two cases which presented as a mass in the right frontal lobe and right parietal lobe. MRI showed hypointesity on T1, hyperintesity on T2-weighted images with moderate enhancement after contast injection. In short extraventricular neurocytoma should be considered indifferential diagnosis of complex intracranial masses.

Keywords: *central neurocytoma; computed tomography; xtraventricular neurocytoma; Magnetic Resonance Imaging.*

INTRODUCTION

Central neurocytoma (CN) is a rare brain tumor, typically found in supratentorial intraventricular system. CN have been reported occasionally in extraventricular locations, and are termed as extraventricular neurocytoma (EVN). CN comprises only 0.1–0.5% of all brain neoplasms,[1] EVNs are even rarer. EVN is primary neuroepithelial tumor of the central nervous system (CNS) included in 4th edition of World Health Organization and designated as WHO grade II.[2,3] Histologically and grade II immunohistochemically, it resembles to its counterpart intraventricular CN.[4] Even though EVN has been reported to be arising in varying locations, propensity of EVN to occur in cerebral hemisphere is higher. EVN is radiologically discrete, presenting as masses of complex density containing cystic lesions, calcification and occasional hemorrhage, with or without perilesional edema.

This paper reports two cases of EVN which we suspected to be glioma, and also presents a review of available literatures on radiological features of intracranial EVN.

CASE 1

A 59-years-old male complaining of headache and dizziness for two weeks, patient visited county hospital where CT showed space occupying lesion in right frontal lobe. He was referred to our hospital for surgical intervention. MR image obtained at our hospital by Magnetom 1.5 T (Siemens Healthcare, Germany) revealed a mass in the right frontal region measuring 8.6cm x 7.0cm x 6.0cm, containing solid and cystic components with surrounding perilesional edema. The Ipsilateral lateral ventricle was compressed causing supratentorial herniation and obstructive

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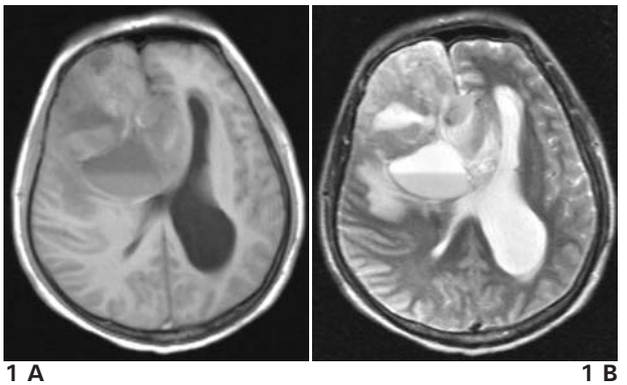
hydrocephalus. The mass was hypointense on T1 (TR = 400ms /TE = 14ms) (Figure 1A) and heterogeneously hyperintense in T2-weighted images (TR = 6000ms / TE = 76ms) (Figure 1B), following contrast injection solid portion of the mass showed mild heterogeneous enhancement (Figure 1C). Surgical resection of frontal lobe with tumor free margin was carried out. Pathological analysis of specimen on light microscopy showed oval to round cell with clear cytoplasm resembling to oligodendroglioma (Figure 1D). Immunohistochemistry revealed positive reaction to synaptophysin, neuron–specific enolase (NSE) and glial fibrillary acidic protein (GFAP). Since 3 years, he is on regular follow up, and remains asymptomatic and radiologically stable.

Right frontal lobe neurocytoma in a 59-years-old male.



1 A 1 B

Figure 1. A. T1 weighted image shows a large cystic mass compressing anterior horn of the ipsilateral lateral ventricle causing supratentorial herniation.

Figure 1. B. T2-weighted image shows heterogeneous high signal intensity with perilesional edema.

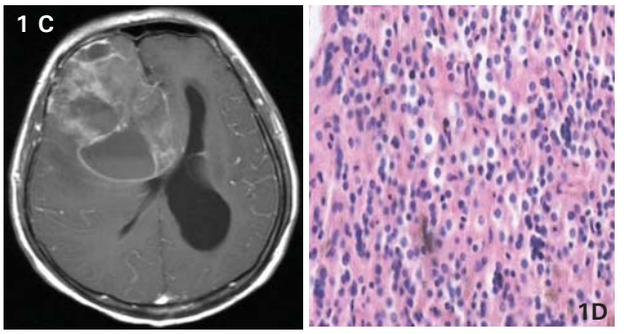


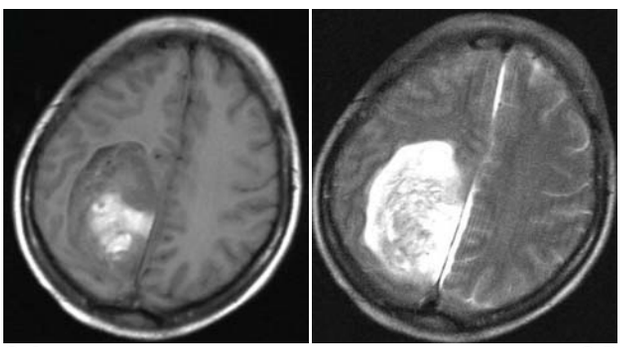
Figure 1. C. Contrast enhanced T1-weighted image shows heterogeneous enhancement of solid portion of the mass.

Figure 1. D. Pathological specimen H&E stain (x 400) showing oval to round tumor cells arrange in small groups with abundant translucent cytoplasm.

CASE 2

A 43-years-old female was referred from local county hospital with diagnosis of brain tumor. Her presenting complains were loss of consciousness with headache and dizziness. MR image was obtain in our hospital by Magnetom 1.5T (Siemens Healthcare, Germany) revealed a mass in right parietal lobe measuring 7.3cm x 4.9cm x 7.0cm, causing compression and 1.5 cm midline shift to left. On T1-weighted images (TR = 400ms /TE = 14ms) mass was hypointense with central area of ill defined hyperintensity suggesting intratumoral hemorrhage (Figure 2A). T2-weighted (TR = 6000ms / TE = 76ms) (Figure 2B) and fluid attenuated inversion recovery (FLAIR) (TR = 9000ms /TE = 110ms) (Figure 2C) images showed heterogeneous hyperintensity of the mass and adjacent flax with minimal perilesional edema. Moderate enhancement was noted after contrast injection (Figure 2D). Complete resection of mass with tumor free margin was carried out. Resected specimen on light microscopy showed oval to round cell with transparent cytoplasm, positive reaction to synaptophysin, NSE and GFAP was seen on immunohistochemistry. Follow-up MRI after 1 year of surgery revealed no disease recurrence.

Right parietal lobe neurocytoma in a 43-years-old female.



2 A 2 B

Figure 2. A. T1-weighted image shows low signal intensity space-occupying lesion with central area of ill-defined high signal intensity resembling hemorrhage. 2. B. heterogeneous high signal intensity of the mass and adjacent dura (arrow) with mild perilesional edema on T2-weighted image.

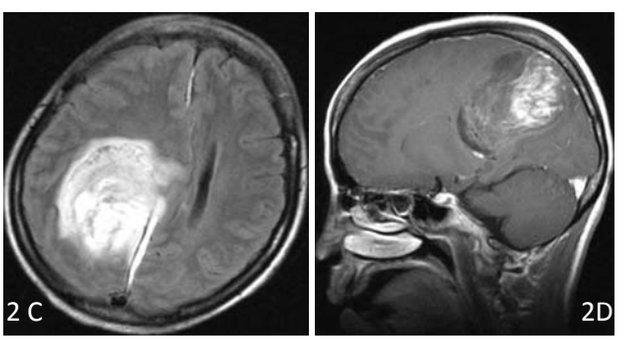


Figure 2.C. FLAIR. 2. D. Contrast nhanced T1-weighted image sagittal view shows heterogeneous mild enhancement.

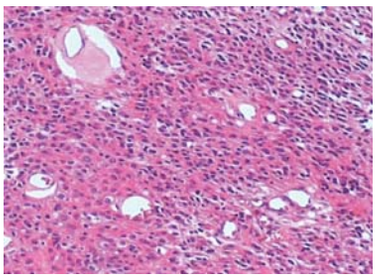


Figure 2. E. pathological specimen on H&E stain (x400) showing tumor cells with abundant cytoplasm in round to oval shape arranged in clusters.

DISCUSSION

EVN is a primary tumor of the brain parenchyma which is devoid of any ventricular connection and is definitely among the rarest CNS tumors. The age of clinical manifestation ranges from 5 to 76 years (mean 40.5) but 70% are diagnosed in between 20 to 40 years with equal sex distribution.[5] EVN have been reported to occur in cerebral hemisphere, thalamus, cerebellum, pons, amygdale, retina, spinal cord,[1,2,6-8] and is also been observed outside the CNS, for instance in pelvic cavity and ovary.[1,7,8] Even atypical and malignant cases have been reported previously with pathological findings of atypical cells and mitotic behavior.[8,9] Sign and symptoms of EVN vary according to location and mass effect to the surrounding structures. But headache and seizure seems to be more common presentations following previous literatures. EVN generally is a large circumscribed complex mass, often partly or mainly cystic accompanied by frequent calcification (10%) and sporadic intratumoral hemorrhage with or without peritumoral edema.[10] Ganglionic differentiation is more common in EVN, and tends to have more of a cystic components and heterogeneous enhancement.[7,10] These tumors can pose diagnostic difficulty because of overlap of imaging and histological features with those of other brain tumors, particularly oligodendroglioma. Characteristic MRI findings show hypo signal intensity in T1-weighted images and hyper signal intensity in T2-weighted images. Contrast enhancement is mild and occasionally shows rim-like appearance. CT can better delineate calcification but imaging features vary according to the cellularity, degree of calcification and associated hemorrhage.[8,10-12]

Since its first report in 1989 by Ferreol et al,[13] in 1989 our MEDLINE search for EVN yielded 43 literatures, however, most unfolding pathological features. We collected literatures focusing on radiological characteristics (Table 1).

Table 1. **Reported cases of EVN with imaging features.**

S.N	First Author (Year)	Age/sex	Symptoms	Location	Nature of lesion	CT	MRI			
							T1WI	T2WI	Contrast	Other
1	Figureueiredo EG et al (2010)	26y/F	Seizure	Right frontal lobe	Solid	-	-	-	Intense enhancement	-
2	Ghosal N et al (2011)	9y/M	Headache	Left fronto-parietal region	Solid & cystic with edema	Calcification	Hetero SI	Hetero intensity	Hetero enhancement	-
3	Donati PT et al (1999)	9y/F	Seizure & precocious puberty	Right temporal lobe	Solid & cystic	Isodense lesion with multiple calcification	Solid part high SI	Hetero high SI	No enhancement	-
4.	Yang GF et al (2008)	24y/F	Headache	Left parietal lobe	Solid & cystic with edema	Hetro with calcification	Low SI	Solid part low SI	Intense enhancement	-
		2y/M	Right side hemiparesis	Left fronto-parietal region	Solid & cystic with edema	Hetro with calcification	Solid part iso SI	Solid part low SI	Extensive hetero enhancement	-
		46y/F	Visual impairment	Sellar and parasellar region	Solid	Isodense with calcification	Iso SI	Variable intensity	Intense enhancement	DWI –high SI
5.	Ayse A et al (2009)	45y/M	Left extremity weakness	Right temporo-parietal region	Solid	Hypodense	-	Variable intensity	No enhancement	CT perfusion - reduced rCBF and rCBV with prolonged MTT
6.	Soontornniyomkij Vet al (1996)	18y/M	Diplopia and right tochlear nerve palsy	Pons	Solid	-	Iso SI	High SI	Enhanced	-
7.	Swinson BM et al (2006)	58y/M	Headache and left sided paresthesia	Pons	Cystic	Calcification	Low SI	High SI	Ring enhancement	-

8.	Mark RE et al (2004)	54y/F	Intermittent right face numbness & tingling	Right insular lobe	Solid	-	-	-	No enhancement	FLAIR – high SI
9.	Buccoliero AM et al (2002)	20y/F	Seizure	Right parietal lobe	Cystic with small peripheral solid mass and scanty edema	Hypodense	-	Hetero high SI	Solid nodule heterogeneous enhancement	-
10.	Möller-Hartmann W et al. (2002)	16y/F	Headache	Right parieto-occipital region	Solid & cyst	Hyperdense, rim like calcification	Solid portion iso SI	High SI	Hetero enhancement	MR spectroscopy - Complete absence of NAA, mild elevation of cr and significant elevation of cho, no resonance for lactate and lipids
11.	Moriguchi S et al (2006)	54y/F	Numbness of face and left upper limb	Right parietal lobe	Solid	-	Low SI	High SI	Homo enhancement	-
12.	Ueda F et al (2007)	34y/M	Seizure	Left frontal lobe	Solid	-	-	-	Hetero enhancement	MR spectroscopy - NAA, lactate and lipids were not detected, cr was detected, cho was elevated
13.	Giulioni M et al (2010)	17y/M	Seizure	Left temporal lobe	Solid	-	Low SI	High SI	No enhancement	FLAIR – high SI
14.	Brown DM et al (2001)	76y/F	Retroorbital headache	Left sphenoid wing	Solid	No calcification	-	-	Hetero enhancement	-

Hetero = heterogeneous, SI = signal intensity, Homo = homogeneous, DWI = diffusion weighted imaging, rCBF = regional cerebral blood flow, rCBV = regional cerebral blood volume, MTT = mean transit time, FLAIR = Fluid-attenuated inversion-recovery, homo = homogeneous, NAA = N-acetylaspartate, cr = creatine, cho = choline

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Most of the lesions were mixed containing solid and cystic component. Calcification on CT was one of the distinctive findings but as our patients were referred from local hospital CT pictures were not available in hospital record, although signal intensity suggestive of calcification in MRI was apparent on second case. On MRI most lesions were low SI on T1WI and high SI on T2WI showing mild to moderate enhancement following contrast injection. CT perfusion reported by Ayse A et al.[14] showed reduced regional cerebral blood flow (rCBF) and regional cerebral blood volume, (rCBV) with prolong mean transit time (MMT). Diffusion weighted image (DWI) performed in one case by yang et al.[10] displayed restricted diffusion. MR spectroscopy done by Hartmann WM et al,[11] and Ueda F et al,[15] demonstrated decrease of N-acetylaspartate (NAA) peak, mild elevation of creatine and significant increase of choline peak, with no resonance for lactate and lipids.

In our both cases, cystic areas were evident but right frontal lobe lesion showed relatively huge cyst. The lesion in right parietal lobe demonstrated hemorrhage, however, both lesions showed distinctive MRI signal intensity in T1WI and T2WI with mild heterogeneous enhancement. Despite the characteristic neuroimaging findings, radiologists are reluctant to give EVN as a first possible diagnosis due to rarity and variable radiological presentations. As in our cases both were diagnosed as glioma before surgical intervention.

Neuropathologically EVN resembles central neurocytoma by presence of small uniformed round cells with a clear cytoplasm surrounded by a fine fibrillary matrix. The nuclei are round or oval with finely speckled "salt and pepper" chromatin. Perinuclear halos are present, giving the neoplasm a honeycomb appearance similar to that of an oligodendroglioma.[5,8] On immunohistochemical studies, a positive reaction to the neuronal marker proteins such as, neuron specific enolase (NSE) and synaptophysin is seen. Glial Fibrillary acidic protein (GFAP) is only positive if some scattered reactive astrocytes are present within the periphery of the tumors.[7,9,16,17] Ultrastructural evaluation with Electron microscope is most reliable, it shows numerous well formed synapses containing parallel bundle of microtubules which are specific for neuronal differentiation.[7]

The assessment of proliferative potential of a neurocytoma is done by immunolabeling with MIB-1, a monoclonal antibody directed against the nuclear antigen Ki-67. Typically EVNs have low MIB-1 LI less then $<2\%$, which denote the benign disease process and good prognosis, MIB-1 LI $\geq 2\%$ is associated with aggressive behavior and poor prognosis.[8] The treatment best accepted is gross total resection, adjuvant modality includes radiation therapy, chemotherapy.[1,4,8,9]

In differential diagnosis, EVN must be differentiated from oligodendroglioma which is a tumor of middle age, mostly arise in the fronto-temporal region showing cystic change and calcification anywhere within the tumor and is larger than EVN, It can erode inner table of the calvarium which is the distinguishing feature. Typical MR imaging features of oligodendroglioma include T1-hypointensity and T2-hyperintensity compared to gray matter, with ill-defined enhancement in 15% to 20% of cases.[10,14] Primitive neuroectodermal tumor (PNET) occurs before five years of age, with the frontal and parietal lobes being the preferred sites. The tumor is usually huge and the solid portion of the PNET may have a low or high-attenuation appearance, with cystic degeneration, hemorrhage, and calcification. Calcification can be discrete or mass like. PNETs may display complex MR signal intensity and heterogeneous enhancement.[10,14] High-grade astrocytoma occurs in 40 to 50 years of age. A complex mass with isointensity or hypointensity on T1-weighted images, and isointensity or hyperintensity on T2-weighted images may be seen; however, calcification within astrocytomas is less common than in EVNs. Gangliocytoma and ganglioglioma are usually tumors of children and young adults. They frequently show cystic change and calcification, surrounding edema is usually low or even absent. The temporal lobe is the preferred site. Its typical imaging findings are a large cystic mass with a calcified mural nodule.

In conclusion, high degree of suspicion and diagnosis by exclusion is necessary for differentiating EVN from other parenchymal brain tumors.

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