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Case Report

Mesial temporal extraventricular neurocytoma (mtEVN): A case report and literature review

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ABSTRACT

We describe a case of mesial temporal extraventricular neurocytoma (mtEVN) in a 23-year-old male presenting with drug-resistant seizures and review the literature on this rare tumor.

A PubMed search was queried using the MeSH term "neurocytoma" and key search terms "extraventricular", "temporal", and "epilepsy". Titles and abstracts were screened for temporal neurocytomas. References were reviewed to identify further studies.

Twenty case reports were selected comparing the presentation, radiological, histopathological, and surgical outcomes of neocortex temporal EVNs (ntEVN) and mtEVNs.

Gross total resection of mtEVNs under intraoperative electrocorticography monitoring typically affords an excellent prognosis and successful seizure control.

1. Introduction

Drug-resistant focal impaired awareness seizures (FIAS) are most commonly associated with mesial temporal sclerosis [1]. Fortunately, epilepsy secondary to mesial temporal sclerosis is amenable to surgical treatment with satisfactory seizure control and improvement in life of quality. However, 20–35% of patients with temporal FIAS have an underlying brain tumor responsible [2]. Correctly identifying the etiology of FIAS is imperative to obtaining a successful outcome and seizure control [3]. Thus, the diagnostic dilemma of mesial temporal FIAS has been a challenge for epileptologists and epilepsy surgeons.

Extraventricular neurocytomas (EVN) have been reported and classified as a distinct entity that can cause drug-resistant seizures [4]. These benign tumors of contentious origin generally afflict children and young adults and can present in a variety of locations in the CNS [5]. In particular, EVNs arising in the temporal lobe most often present with FIAS. Temporally-located EVNs can occur in the neocortex or derive from the mesial temporal structures [6]. Mesial temporal extraventricular neurocytomas (mtEVN) are a subtype of temporal EVNs and have not been well documented in medical literature. It is important to highlight the individual characteristics of mtEVNs as these tumors differ from those of extratemporal EVNs and even neocortical temporal EVNs (ntEVN) in terms of their presentation, radiology, pathology, and surgical outcomes [6].

The authors present a case of mesial temporal extraventricular neurocytoma with drug-resistant seizures and review mesial temporal extraventricular neurocytoma in available literature to outline clinical characteristics and surgical outcomes.

2. Case report

A 23-year-old right-handed male presented to our institution with drug-resistant FIAS for five months. His typical attacks consisted of staring, lip smacking, drooling and clenching of his upper extremities and the episodes lasted from 30 s to almost 2 min. His seizures were poorly controlled despite adequate trials of phenobarbital and valproate. Neurological exam of the patient was normal. Brain magnetic resonance imaging (MRI) demonstrated a right mesial temporal volume

Abbreviations: FIAS, focal impaired awareness seizure; EVN, extraventricular neurocytoma; mtEVN, mesial temporal extraventricular neurocytoma; ntEVN, neocortical temporal extraventricular neurocytoma; MRI, magnetic resonance imaging; ADC, apparent diffusion coefficient; EEG, electroencephalogram; PLEDS, periodic lateralized epileptiform discharges; ECoG, intraoperative electrocorticography; NeuN, neuronal nuclei; MAP-2, microtubule associated protein 2; GFAP, glial fibrillary acidic protein; GTR, gross total resection; STR, subtotal resection.

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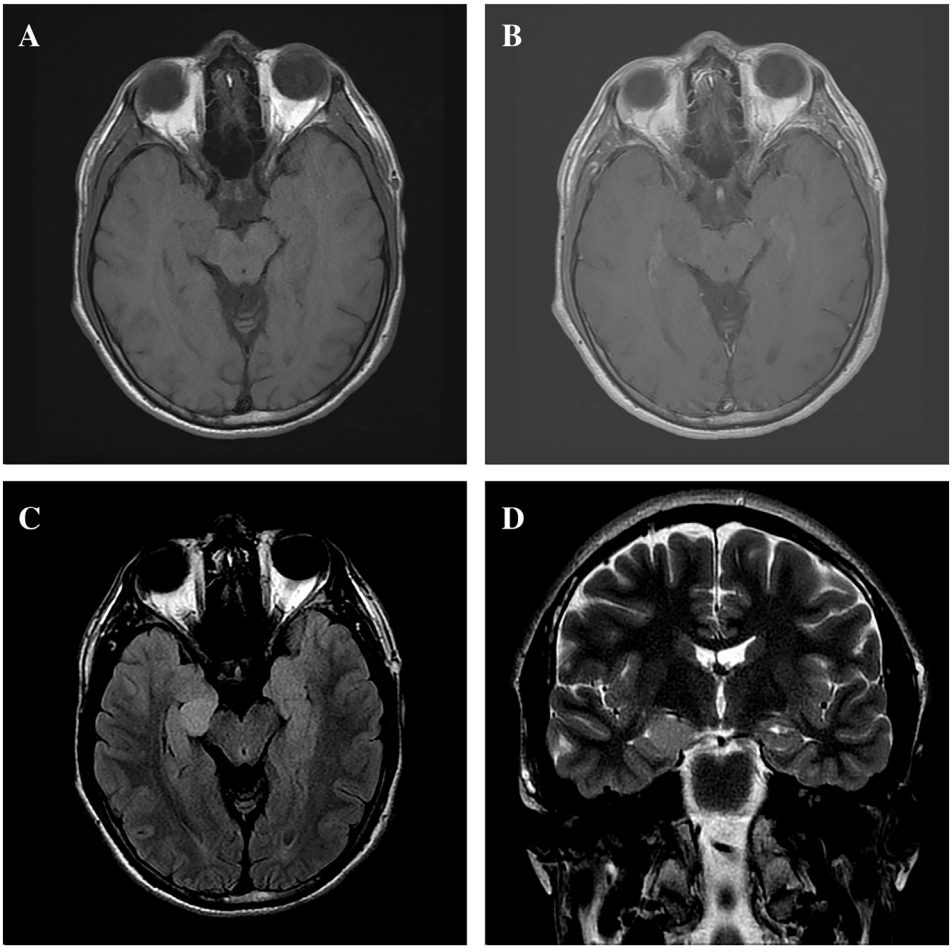

Fig. 1. Mass-like nonenhancing lesion present within the right hippocampal head measuring 1.9 × 1.6 × 1.2 cm. (A) Axial T1 pre-contrast. (B) Axial T1 post-contrast (C) Axial T2/FLAIR. (D) Coronal T2.

increase with no contrast enhancement, no cystic change, and no demonstration of facilitated diffusion on the ADC map (Fig. 1A–D). Long-term non-invasive video electroencephalogram (EEG) revealed frequent interictal epileptiform discharges in the right and left temporal lobes independently (Fig. 2). There were also three electrographic seizures originating from the right mesial temporal region evolving to bilateral tonic-clonic seizures. Neuropsychological evaluation showed average normal intellectual ability and cognitive function. In January 2017, the patient underwent right frontotemporal craniotomy for temporal lobectomy-amygdalohypocampectomy using intraoperative electrocorticography (ECoG). ECoG was performed by using 1 × 4 strips of electrodes recorded using a referential montage placed before and after the resection. Each run lasted at least 10 to 20 min. Before the resection, three strips were placed in anterior, middle and inferior temporal regions and two strips were placed in the lateral inferior and middle temporal cortical convexity. Intraoperative ECoG showed epileptiform discharges derived from the right mesial temporal region (Fig. 3A). Anterior temporal lobectomy-amygdalohypocampectomy was performed. Three electrode strips were then placed vertically in anterior, middle and posterior region at right temporal resection site. Epileptiform discharges on intraoperative ECoG disappeared after gross total tumor resection and mesial temporal resection compromising the right anterior temporal lobe, right amygdaloid, and right hippocampus (Fig. 3B). Postoperative recovery was uneventful and the patient was discharged home on postoperative day five (Engel Class Ia) with anti-seizure medication. Pathology reported extraventricular neurocytoma WHO grade II (Fig. 4A–B) with positive immunohistochemical staining for synaptophysin, NeuN, and MAP-2. Follow-up MRI at one year (Fig. 5A–B) showed stable postoperative changes with no sign of residual or recurrent tumor.

3. Methods

The PubMed database was queried from inception to June 16, 2018 using the MeSH term “neurocytoma” and the key search terms “extraventricular”, “tempor*”, and “epilepsy”. Titles and abstracts were screened for cases of temporal lobe neurocytomas. References were reviewed to identify further studies, which may have been excluded from the initial search. Non-English titles were included and translated with Google Translate (Google, Mountain View, California, USA) [7]. This has been recognized as an approach to potentially minimize language bias in literature reviews [8]. Articles not relevant to the aims of the review were excluded. Of the included articles, cases were stratified into either ntEVNs or mtEVNs.

4. Results

The initial search yielded 22 results. From this, 9 articles were deemed relevant and selected. After a review of references, an additional 6 articles were included, cumulating in a total of 15 studies, including this paper. Table 1 outlines the clinical, radiological, histopathological, and surgical outcomes of the 20 temporal EVN cases reviewed. Of these 20 cases, there were only 5 described cases of mtEVNs before this case report [6,9–11].

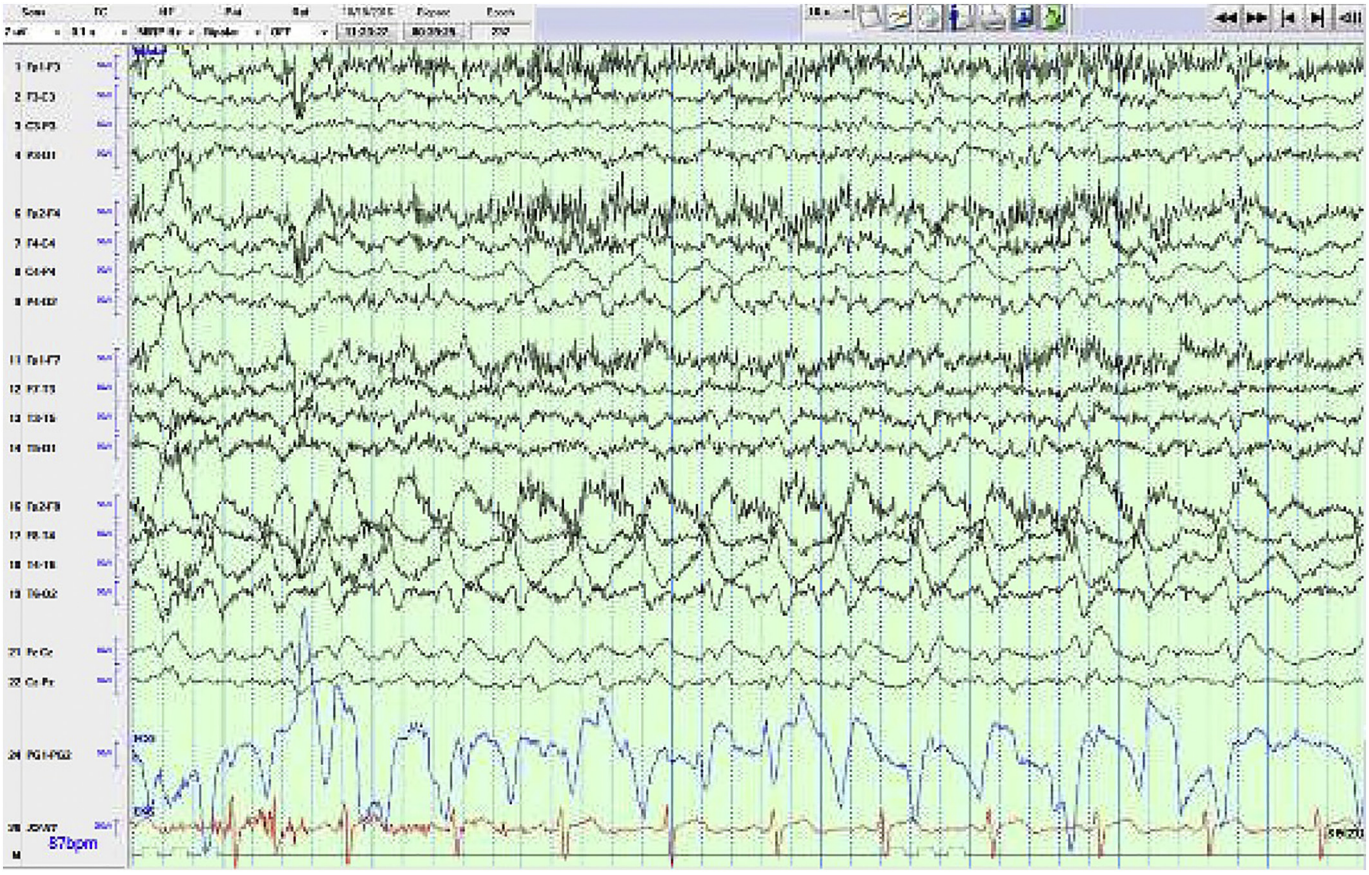

Fig. 2. Long-term continuous video EEG. The resting awake background consists of well-modulated, well-sustained, posterior dominant alpha rhythm at 9–10 Hz and 40–50 mV, which attenuated with eye opening and reoccurred with eye closure. There are frequent spike-and-slow waves with phase reversal at F8 and T4, along with intermittent slow waves at 4–5 Hz seen over the right temporal region. There are also independent sharp waves with phase reversal at T3 and T5. Frequent periodic lateralized discharges are seen in the right temporal region with phase reversal at F8 and T4. A focal onset seizure originating from the right mesial temporal region was captured lasting 37 s. This is seen on EEG as sharp waves which build up in the right temporal region before spreading to the right parasagittal region. On video, the patient was asleep. He woke up from sleep without any other clinical motor signs.

5. Discussion

Central neurocytomas (CN) were first described by Hassoun et al. [12] in 1982, as a rare benign central nervous system (CNS) neoplasm located most often in the lateral ventricles near the foramen of Monro. In 1997, Giangaspero et al. [13] reported the first case of a tumor that mimicked CN but was situated in the brain parenchyma remote from ventricular system, subsequently called EVN. EVNs are associated with a more aggressive biological behavior as compared to CNs and in 2007, EVNs were recognized by the World Health Organization (WHO) as a distinct brain tumor entity [4]. To date, less than 100 case reports have been published on EVNs, with even less information reported on mtEVNs [14].

Although most temporal EVNs occur in the neocortex, they also occasionally derive from the mesial temporal structures. Feng et al. [6] was the first to focus on mtEVN as a distinct clinical entity as there are clear differences between mtEVNs and ntEVNs with regard to demographics, radiological features, and operative techniques. In terms of demographics, Feng et al. reported that patients with mtEVNs are significantly younger than patients with ntEVNs, with a predilection for males. Our updated review supports this age difference (average age of 19.7 vs. 35.5 years for mtEVN and ntEVN respectively, $p = 0.02$

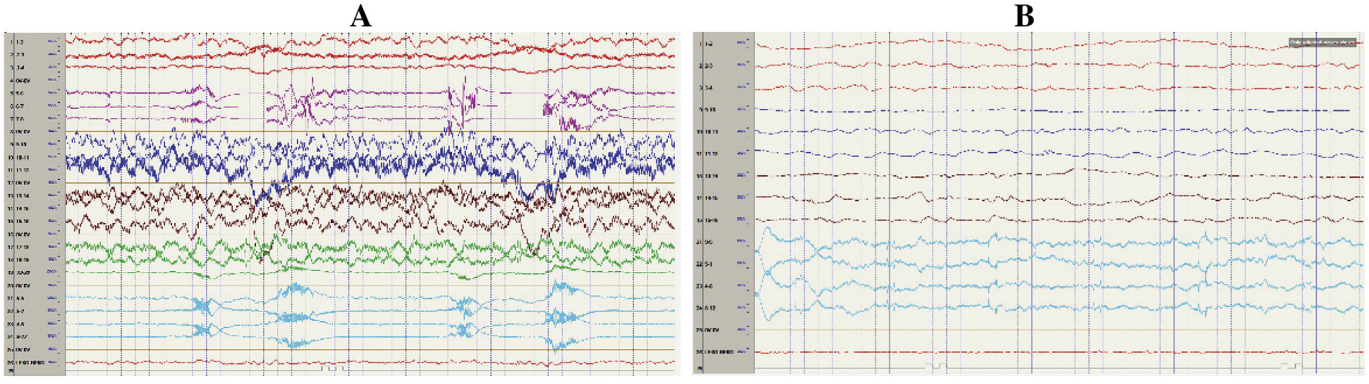

Fig. 3. Intraoperative ECoG (A) Before resection. Frequent high voltage epileptiform discharges from middle inferior temporal region. No epileptiform discharges seen in the temporal cortical convexity. (B) After resection. Epileptiform discharges decreased significantly. Very infrequent small sharp waves seen in the mid temporal region.

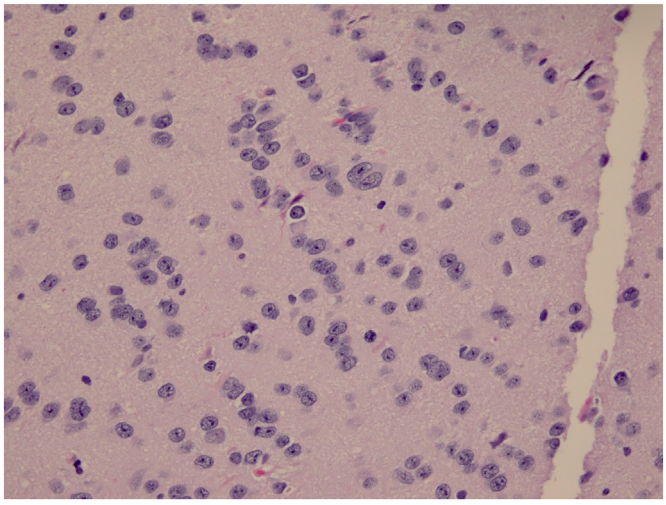

Fig. 4. Histopathologic features of mtEVN. Scattered GFAP-positive cells in a background of reactive astrocytes with rare neurofilament-positive gangliocytic cells.

Table 1
Clinical and pathological features of neocortical and mesial temporal EVNs in the literature.

		n	ntEVNs	n	mtEVNs
Demographics	Age (mean)	14	35.5 years	6	19.7 years
	Female		50%		17%
	Male		50%		83%
Tumor lateralization	Right	14	64%	6	50%
	Left		36%		50%
Radiographic features	Cystic changes	12	33%	6	0%
	Mass effect		33%		33%
	Perilesional edema		11%		0%
	Hypointense on T1		44%		50%
	Hyperintense on T2		100%		100%
	Contrast enhancing		56%		17%
Histology	Hypervascular	9	33%	2	0%
	Hypovascular		11%		100%
	Calcifications	5	80%	3	0%
	Mitoses (≥1/HPF)	8	100%	1	0%
	Necrosis		0%		0%
Immunohistochemistry	Syn (+)	12	100%	5	100%
	GFAP (+)	6	83%	3	67%
	NF	2	50%	1	100%
	NSE	2	100%	No studies	
	NeuN	No studies		3	100%
	MAP-2	1	100%	1	100%
Surgical condition	STR	13	31%	4	0%
	GTR		69%		100%
Adjuvant therapy	Radiation	9	33%	4	0%
Outcome	Length of follow-up (mean)	13	22.4 months	5	11.2 months
	NED		77%		100%

EVN: extraventricular neurocytoma; mtEVN: mesial temporal extraventricular neurocytoma; ntEVN: neocortical temporal extraventricular neurocytoma; HPF: high-powered field; Syn: synuclein; GFAP: glial fibrillary acidic protein; NF: neurofilament; NSE: neuro-specific enolase; MAP-2: microtubule associated protein 2; STR: subtotal resection; GTR: gross total resection; NED: no evidence of disease.

[2-tailed t-test]) but found no significant gender preference in either group ($p = 0.10$ [χ^2, 2, $n = 6$] and $p = 0.78$ [χ^2, 2, $n = 13$] for mtEVN and ntEVN, respectively). Five of the mtEVN cases presented with a history of drug-resistant FIAS ranging from 5months to 8years; one case did not mention clinical presentation. Our case is the first to report on the semiology of FIAS seizures associated with a mtEVN. No prior mtEVN case described the nature of the presenting semiology. Of the prior ntEVN cases, only Rabinowicz et al. [15] described seizure character. Their patient was a 42-year-old man who presented with FIAS consisting of foul gustatory and olfactory hallucinations, oral automatisms, and gastric rising sensation. Phenobarbital and phenytoin had been ineffective and the patient continued to have seizures despite therapeutic trials of carbamazepine and valproate. Similar to our case, intraoperative ECoG was performed and resection was performed over the entire epileptogenic zone, including total gross tumor resection. Postoperatively, seizures were controlled with medication at four months follow-up.

On imaging, temporal EVNs generally appear hypo- to isointense on T1-weighted images and hyperintense on T2-weighted images. However, there are notable radiological differences between ntEVNs and mtEVNs. On imaging, ntEVNs tended to be more well-defined, contain both solid and cystic components [2,14,16], contain frequent calcifications [2,16–19], and vary in terms of contrast-enhancement, with the majority enhancing [14,16,19–21]. In contrast, mtEVNs are less clearly demarcated from the surrounding mesial structures, distinctly lack calcifications, and express no enhancement after contrast administration in any of the 6 cases. These differences have important implications for both the diagnosis and treatment of mtEVNs. EVNs encompass a large differential, including glial and glioneuronal neoplasms like oligodendrocytomas, ependyomas, and dysembryoplastic neuroepithelial tumors [22]. The current literature says that helpful diagnostic aids in identifying EVNs include the presence of well-defined margins, focal calcifications, cystic changes, and contrast-enhancement [20,21]. These radiologic indicators are conspicuously missing in mtEVNs, illustrating the wide morphological spectrum of EVNs. Ill-defined margins present a separate challenge as the goal of treatment is to maximize the amount of tumor that can be

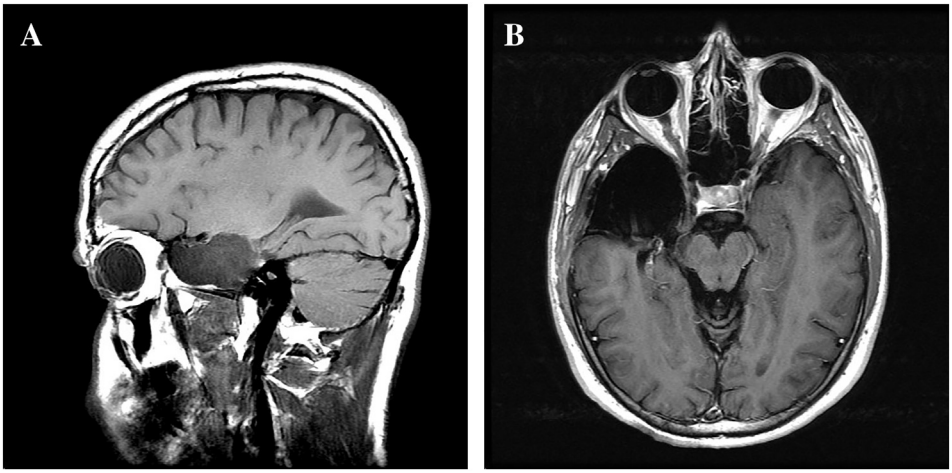

Fig. 5. Follow-up MRI at 1-year post-resection. (A) Sagittal T1. (B) Axial T1.

resected safely since radial resection is critical in preventing disease reoccurrence [18]. Although no visible perilesional edema was present around any of the mtEVNs, there was considerable mass effect in all six of the reported cases. In contrast to mesial temporal sclerosis, mtEVNs typically demonstrate displacement of the mesial temporal lobe and ventricular horn, without obvious cystic change [6,11].

Given the equivocal radiographic findings of mtEVNs, the vast majority will be diagnosed by histopathology and immunohistochemistry. Strong synaptophysin staining has been recognized as the most suitable and reliable diagnostic marker for EVNs [5]. Our case report also noted strong anti-NeuN immunoreactivity, which has been similarly reported by two previous mtEVN cases [9,10]. Our case is the first to report MAP2 immunoreactivity in a mtEVN, which previously has been only described by a ntEVN case study [16]. Unlike interventricular neurocytomas which originate from the ventricles, many EVNs exhibited a high degree of ganglionic differentiation and a strong focal GFAP reactivity in the tumor cells [20]. Three EVNs were designated as "atypical' based on the presence of necrosis, vascular proliferation, or increased mitotic activity (rate ≥ 3 mitoses/10 high power fields) [17,20]. All three atypical cases were ntEVNs. Of the limited data subset, mtEVNs generally demonstrated hypovascularity and low mitotic activity.

Successful tailored resection of the entire mtEVN under ECoG monitoring affords an excellent prognosis and successful seizure control [6]. Limitations in achieving a complete resection or gross total resection (GTR) may be due to eloquence of the surrounding structures or invasion of the surrounding periventricular parenchyma [23]. Subtotal resection (STR) is associated with atypical EVNs and consequently a poorer prognosis. Adjuvant radiotherapy with STR may offer better tumor control but has not appeared to increase overall survival [13]. Prior reports suggest that extremes of age may also be associated with less favorable outcomes, as patients over 50 years may be at higher risk for tumor recurrence and patients under 18 years at higher risk for atypical disease [5]. Despite the younger ages of the mtEVN patients in our review (2/6 patients were under 18 years old), all of the mtEVN cases underwent successful gross total resection, demonstrated typical EVN histopathology, and showed no evidence of recurrent seizures at follow-up which ranged from 6 months to 1 year.

6. Conclusion

MtEVN is a distinct clinical entity with unique radiographic, pathologic, and demographic characteristics. Compared to ntEVNs, mtEVNS tend to present in younger patients and are less well-demarcated, nonenhancing, noncalcified, and lack a cystic component. Our case is the first to our knowledge to report on the semiology of FIAS seizures associated with mtEVNs and also the strong MAP2 immunoreactivity in a mtEVN. Successful gross total resection of mtEVNs under ECoG monitoring affords an excellent prognosis and successful seizure control.

Conflict of interest

The authors have no conflicts of interest, financial or otherwise, associated with this work.

Ethical statement

The work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki).

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