

# Mesial temporal extraventricular neurocytoma: a rare cause of refractory complex partial seizure

Rui Feng<sup>1</sup>, Jie Hu<sup>1,2</sup>, Jinsong Wu<sup>1</sup>, Liqin Lang<sup>1,2</sup>, Bei Wang<sup>3</sup>, Haixia Bi<sup>4</sup>, Xin Gu<sup>2</sup>, Jun Guo<sup>2</sup>, Li Pan<sup>1</sup>

<sup>1</sup> Department of Neurosurgery, Huashan Hospital

<sup>2</sup> Department of Neurosurgery, Jing'an Branch of Huashan Hospital

<sup>3</sup> Department of Neurology, Jing'an Branch of Huashan Hospital

<sup>4</sup> Department of Neuropathology, Jing'an Branch of Huashan Hospital, Shanghai Medical College, Fudan University, Shanghai 200040, China

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**ABSTRACT** – *Aim.* Mesial temporal extraventricular neurocytoma (mtEVN) is a rare cause of refractory complex focal seizures. The characteristics of this clinical entity are discussed in this article. *Methods.* We report two cases of mtEVN and review the related literature, with particular emphasis on radiological characteristics, clinical features, and operative techniques. *Results.* After successful surgery, our two cases of mtEVN achieved excellent outcome. Including the cases presented here, a total of three cases of mtEVNs and 11 of neocortical temporal extraventricular neurocytoma (ntEVNs) are reported in the literature. mtEVNs are distinct from ntEVNs with regards to demographics, aetiology, radiological features, and operative techniques. *Conclusion.* mtEVNs and ntEVNs exhibit distinguishing features. Under electrocorticographic monitoring, tailored resection of the neocortical epileptogenic focus, as well as the entire tumour and mesial temporal structures, can yield excellent outcome and satisfactory seizure control.

**Key words:** mesial temporal extraventricular neurocytoma (mtEVN), neocortical temporal extraventricular neurocytoma (ntEVN), refractory/intractable epilepsy, complex partial seizure, surgical treatment

## Correspondence:

Jie Hu or Jinsong Wu  
12 Wulumuqi Zhong Road,  
Department of Neurosurgery,  
Huashan Hospital,  
Shanghai Medical College,  
Fudan University,  
Shanghai 200040, China  
<jiehu68@yahoo.com>  
<wjssongc@126.com>

For neurologists and epilepsy surgeons, the most common explanation for complex partial seizures (CPS) is mesial temporal sclerosis (MTS) (Pascual, 2007). However, for the presurgical evaluation of CPS, differential diagnosis with regards to tumours should be considered, since tumours constitute approxi-

mately 20-35% of temporal epilepsy pathology (Rabinowicz *et al.*, 1995). Among them, mesial temporal extraventricular neurocytoma (mtEVN) is extremely rare, but should be considered in the differential diagnosis. Neurocytoma usually occurs in the ventricular system and was first noticed by Hassoun *et al.* (1982).

However, several studies of extraventricular neurocytomas (EVNs) have been reported and many of these appear to be associated with intractable epilepsy, and were reclassified as a distinct entity in 2007 (Louis *et al.*, 2007). Although temporal EVNs mostly occur in the neocortex, they also rarely derive from mesial temporal structures. Here, we present two cases of mtEVNs based on our surgical experience and review all temporal EVNs in the literature. There is only

one other case of mtEVN reported by Giulioni *et al.* (2011) and seven cases of neocortical temporal EVNs (ntEVNs) (see *table 1*) in the literature. We discuss the clinical and radiological characteristics, surgical treatment, and outcome of this rare entity. To our knowledge, this is the first report to focus on mtEVN as a distinct clinical entity, as well as a first description of positron emission tomography (PET) of EVNs.

**Table 1.** Temporal Extra-Ventricular Neurocytomas (EVNs) in the literature.

	Publication	Age at OP (years) /sex	Seizure type & History	Lateralisation	Surgical condition	Outcome / Months of follow-up	Adjuvant therapy
ntEVNs	Nishio <i>et al.</i> , 1992	41/M	GTCS & CPS for 30 years; 1st OP at 33 years	R	1st cyst resection, 2nd STR	AWD, reduced seizures/8 months	none
	Rabinowicz <i>et al.</i> , 1995	42/M	CPS for 7 years	R	GTR	NED, seizure control/4 months	NM
	Kim <i>et al.</i> , 1997	25/M	unconsciousness & GTCS once	R	GTR	NED/5 months	NM
	Giangaspero <i>et al.</i> , 1997*	18/F	epileptic seizures for 7 years	L	GTR	NED/6 months	none
	Tortori-Donati <i>et al.</i> , 1999	9/F	CPS for 2.5 years	R	radical excision	NED, seizure control/6 months	NM
	Morioka <i>et al.</i> , 2000	12/F	CPS & GTCS for 6 years; 1st OP at 8 years	R	1st partial, 2nd GTR	NED, seizure free/72 months	none
	Brat <i>et al.</i> , 2001	37/M	NM	L	GTR	NED/12 months	none
	(multi-centre study)	61/F	NM	L	STR	AWD/34 months	yes
		11/M	NM	R	STR	AWD/18 months	yes
		76/F	NM	R	STR	AWD/14 months	yes
mtEVNs		39/F	NM	R	NM	NM	NM
	Giulioni <i>et al.</i> , 2011	17/M	CPS for 8 years	L	GTR	NED, seizure-free/4 months	none
	Feng <i>et al.</i> , 2014 (Case 1)	22/M	CPS for 4 years	L	GTR	NED, seizure-free/8 months	none
	Feng <i>et al.</i> , 2014 (Case 2)	25/M	CPS for 2 years	R	GTR	NED, seizure-free/6 months	none

EVN: extraventricular neurocytoma; ntEVNs: neocortical temporal EVNs; mtEVNs: mesial temporal EVNs; NM: not mentioned; CPS: complex partial seizures; GTCS: generalised tonic-clonic seizure; NED, no evidence of disease; AWD, alive with disease; GTR: gross total resection; STR: subtotal resection; OP: operation.

\*This case presented with mixed neuronal-astrocytic tumours with neurocytoma features.

## Case studies

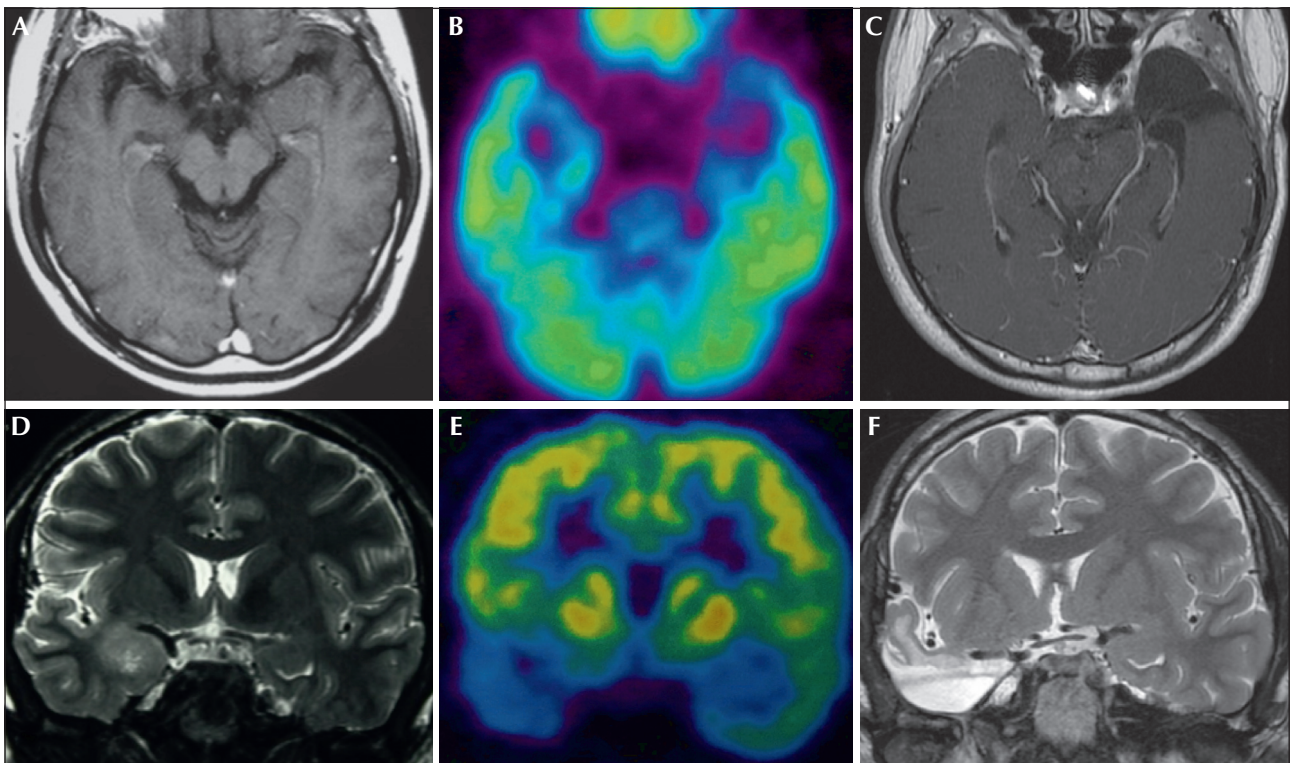
### Case 1

A 22-year-old, right-handed male suffered from intermittent CPS attacks with an aura of olfactory hallucination for four years. Medication with multiple antiepileptic drugs (AEDs) yielded poor control of these epileptic attacks. He was admitted to our department in July 2012. Magnetic resonance imaging (MRI) demonstrated a lesion located in the left mesial temporal lobe, with barely any enhancement (*figure 1*). Computed tomography (CT) showed no obvious calcification of the tumour. A preoperative diagnosis of low-grade glioma was highly suspected. A PET study revealed hypometabolism of the tumour itself, as well as the surrounding temporal parenchyma (*figure 1*). Ictal EEG recording of an aura (olfactory hallucination) revealed an onset of epileptic discharges derived from the left temporal region (*figure 2*). Neuropsychological evaluation revealed average intellectual ability and cognitive functions. Clinical psychological examination showed depression and increased anxiety. Surgery was performed by pterional approach craniotomy. Intraoperative electro-

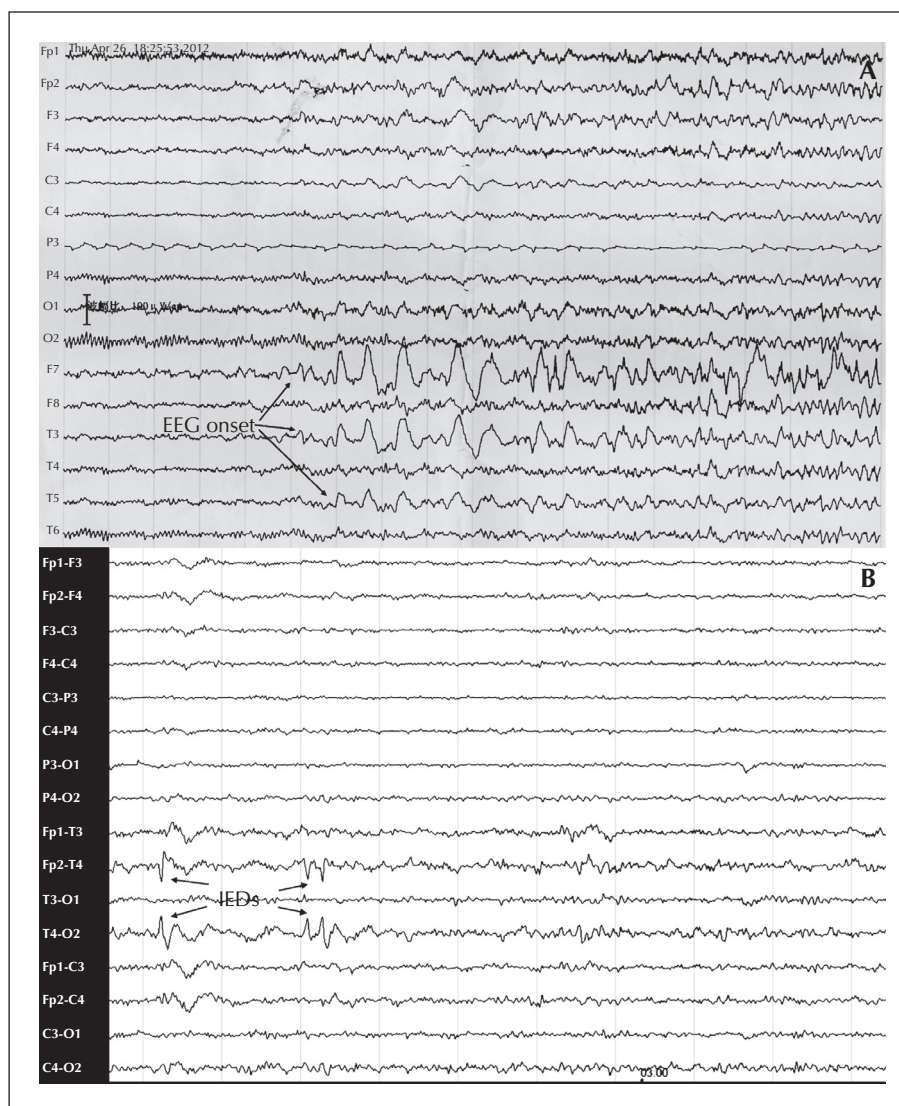
corticography (EcoG) on the temporal cortex showed obvious abnormal discharges, possibly derived from the anterior and mesial temporal lobe. After completing a standard anterior temporal lobectomy (sATL), which consisted of resection of the temporal neocortex (4 cm from the temporal pole), the entire tumour, uncus-amygdala area, anterior hippocampus, and neighbouring parahippocampal gyrus, the epileptic discharges on EcoG disappeared. Histopathological studies confirmed the diagnosis of mtEVN (*figure 3*). The post-operative period was uneventful, and the patient was discharged eight days later. He has since achieved complete seizure freedom (Engel class Ia) with medication. Thirteen months later, the MRI follow-up showed no sign of recurrence (*figure 1*). Neuropsychological follow-up at nine months, post-operatively, showed a similar level of intellectual ability and cognitive functions, while depressive symptoms and anxiety disappeared.

### Case 2

A 25-year-old, right-handed male suffered from intractable CPS attacks for two years while taking multiple AEDs. MRI showed a lesion located in the



**Figure 1.** Patient 1: axial enhanced MR (A) and PET (B) show a left mesial temporal tumour with barely any enhancement and significantly decreased FDG uptake; postoperative enhanced MRI (C) demonstrates total removal of the tumour and no sign of recurrence. Patient 2: coronal MR image of T2WI (D) shows enlarged right mesial temporal structures with hyperintensity; coronal PET (E) shows the tumour and ipsilateral mesial temporal lobe with decreased FDG uptake; postoperative MRI (F) demonstrates total removal of the tumour and no sign of recurrence. The imaging features in both cases were similar.

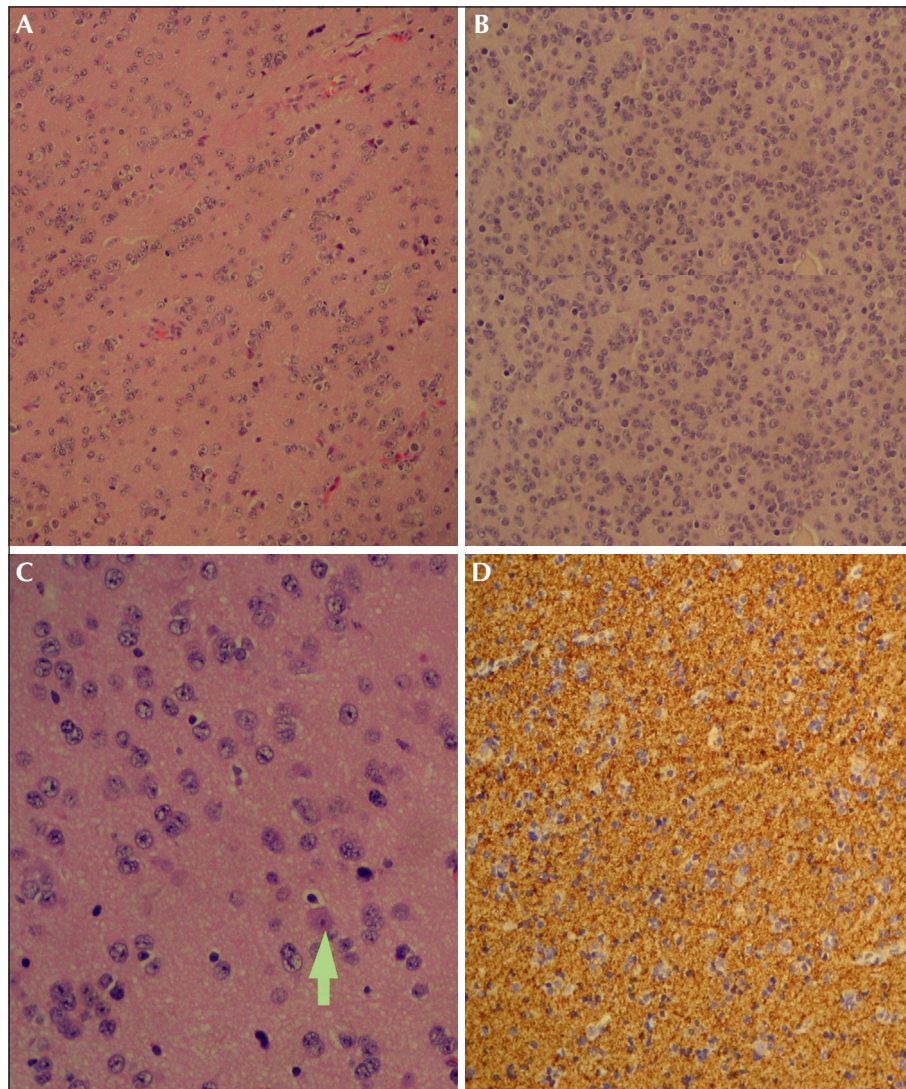


**Figure 2.** Scalp EEG findings. (A) Onset of ictal epileptic discharges of Patient 1 from the left temporal region. (B) Interictal epileptic discharges (IEDs) of Patient 2 were mainly found in the right temporal region.

right mesial temporal lobe, which appeared to be an enlarged hippocampus without obvious enhancement (*figure 1*). The preoperative diagnosis was low-grade glioma. Interictal EEG showed sporadic epileptic waves mainly in the right temporal region (*figure 2*). PET examination demonstrated broad hypometabolism of the right temporal lobe with the lesion itself being more hypometabolic (*figure 1*). The patient showed above-average intellectual ability and cognitive functions, despite slight depression and increased anxiety during neuropsychological tests. At surgery, EcoG captured multiple epileptic discharges from the anterior and mesial temporal lobe. We firstly removed 5 cm of anterior lobe to expose the mesial temporal struc-

tures. The tumour was grey-coloured with a poor blood supply and was poorly demarcated from the surrounding parenchyma. We finally achieved radical removal of the tumour as well as the mesial temporal structures. EcoG verified total removal of the epileptogenic focus. Histopathological studies confirmed diagnosis of mtEVN (*figure 2*). After surgery, the patient was totally seizure-free, achieving Engel class Ia with remission, and was free of tumour recurrence when examined during follow-up at 12 months (*figure 1*). There was no postoperative neurological deficit and neuropsychological follow-up at eight months postoperatively showed unchanged intellectual and cognitive abilities with no sign of depression or anxiety.





**Figure 3.** (A) and (B) Tumour cells of the neurocytoma, structured in sheets or linear arrays, have nondescript round regular nuclei, perinuclear halos, and fine neuropil matrix. (Hematoxylin & eosin staining x200; Patients 1 and 2). (C) Ganglion cell differentiation is identified (x400; Patient 1). (D) The tumour cells show intense staining with synaptophysin (SYN) in the fibrillary background (x200; Patient 1). The histopathological features in both cases were similar.

## Discussion

Temporal EVNs may be overlooked as a cause of intractable CPS and have a tendency to impinge on mesial structures (Rabinowicz *et al.*, 1995; Tortori-Donati *et al.*, 1999). However, EVNs derived from the mesial temporal lobe (mtEVNs) are extremely rare and there is only one such case associated with cortical dysplasia reported in the literature (Giulioni *et al.*, 2011). mtEVNs are distinct from ntEVNs, which are derived from the neocortex, with regards to demographics, aetiology, radiological features, and operative techniques. The clinical features of all temporal EVNs are summarised in *table 1*. It appears that patients with mtEVNs are younger than those with ntEVNs (with an

average age of 21.3 vs. 33.73 years, respectively;  $p < 0.05$  [student's test]), and there is a male predilection for mtEVNs (in the three cases, 100% were male).

Since PET is one of the techniques used in our routine examinations for epilepsy presurgical work-up, PET was used here, making this study the first to report 18-Fluorodeoxy glucose (18-FDG) PET of mtEVNs. Similar to central neurocytomas (Takao *et al.*, 2004), mtEVNs exhibit hypometabolism on 18-FDG PET. Normally, peritumoural parenchyma is also expected to be hypometabolic, however, the underlying reason remains unclear, although several distinct hypotheses have been proposed (Carne *et al.*, 2004). We agree that long-term epileptic discharges of the tumour-associated epileptogenic focus may be one reason for

this (Carne *et al.*, 2004); however, it is not possible to differentiate mtEVNs from other low-grade tumours using PET because both commonly demonstrate similar metabolic change.

The most important techniques which may aid presurgical diagnosis are MRI and CT, however, imaging of cerebral EVNs may not be as stereotypic as it is for central neurocytomas, which have characteristic features of multiple cystic components, attachment to the septum pellucidum, monro foramen location, calcification, and variable contrast enhancement (Kocaoglu *et al.*, 2009). As for extra-temporal EVNs, based on CT and MRI, ntEVNs tend to be well-defined and may contain calcification and haemorrhage, as well as cystic change and variform contrast enhancement (Brat *et al.*, 2001). However, radiologically, mtEVNs differ largely from them (Rabinowicz *et al.*, 1995; Tortori-Donati *et al.*, 1999). Uniquely, there is no enhancement after gadolinium administration and the lesions are not so circumscribed relative to ntEVNs; they usually bear no clear border with surrounding parenchyma and appear to blend in with the mesial structures. A typical MR image of mtEVN usually demonstrates enlargement and deformation of the mesial temporal lobe and narrowing of the temporal horn without obvious cystic change, in contrast to MTS. CT demonstrated no identifiable calcifications or haemorrhage of mtEVNs in our two cases (CT was not reported in the only case in the literature). ntEVNs usually present with negligible peritumoural oedema, as well as no obvious mass effect (Nishio *et al.*, 1992; Tortori-Donati *et al.*, 1999). However, according to the three reported cases of mtEVNs, there is also no visible peritumoural oedema, yet the mass effect may be striking.

In contrast to ntEVNs (Rabinowicz *et al.*, 1995), at surgery, mtEVNs were not clearly demarcated from the surrounding parenchyma. They are usually incorporated into the mesial structures, such as the uncus-amygdala and hippocampus, and cannot generally be distinguished from each other. Radical removal of the tumour, as well as involved mesial structures, is the treatment of choice and the most critical factor in determining favourable outcome (Tortori-Donati *et al.*, 1999; Morioka *et al.*, 2000). Neuronal tumours such as gangliogliomas, which are reported to coexist with cortical dysplasia and cerebral microdysgenesis, which is intrinsically epileptogenic, have been shown to sometimes surround EVNs (Morioka *et al.*, 2000; Giulioni *et al.*, 2011). Although no such structural anomaly was found based on histopathological examination in our cases, we recommend enlarged resection of the peritumoural parenchyma, based on the fact it is generally expected to be epileptogenic.

After successful tailored resection, including resection of the entire tumour under EcoG monitoring, the prognosis of mtEVNs is excellent and seizures can be

controlled. According to the literature, usually, if EVNs are totally resected, radiotherapy is not necessary. However, for subtotal resection, most patients suffer from tumour recurrence and uncontrollable seizure attacks even with early adjuvant radiotherapy.

Microscopically, EVNs are solid lesions composed of nondescript round neurocytic tumour cells, arranged in sheets, clusters, or rosettes. Usually, there is neuropil dispersed either in broad zones (neuropil islands can be a cue to accurate diagnosis) between these cell arrangements or localised within the rosettes (Brat *et al.*, 2001). Mitotic activity is usually low, and neuronal maturation can be frequent. Synaptophysin (Syn) immunoreactivity is almost always strong and diffuse (Brat *et al.*, 2001), but unlike central neurocytomas, many cases of EVNs express focal GFAP reactivity in tumour cells. Ganglion cell differentiation can be seen in most EVNs. Oligodendrogliomas should be considered for differential diagnosis due to the similarity of histological features, however, Syn negative reactivity and their increased nature of infiltration may help to distinguish them from EVNs.

There are distinguishing features between mtEVNs and ntEVNs, and the former, which are usually confused with other low-grade gliomas, should be considered in the differential diagnosis of tumour-related CPS. After successful removal of the entire tumour and involved mesial temporal structures under EcoG monitoring, the prognosis of this clinical entity is excellent. □

#### Disclosures.

None of the authors have any conflict of interest to disclose.

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