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

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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

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 approximately 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 classified 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.

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

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 electrocorticography (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, postoperatively, 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
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 structures. 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 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.
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, mtEVNs 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 neuronopil 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), 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.

References


