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Case Report

Triple pathological findings in a surgically amenable patient with mesial temporal lobe epilepsy☆

Fumin Tong [a,*], Valerie Jewells [c], Dimitri G. Trembath [d], Eldad Hadar [b], Hae Won Shin [a]

[a] Department of Neurology, University of North Carolina, Chapel Hill, NC 27599, USA
[b] Department of Neurosurgery, University of North Carolina, Chapel Hill, NC 27599, USA
[c] Department of Radiology, University of North Carolina, Chapel Hill, NC 27599, USA
[d] Department of Pathology and Laboratory Medicine, University of North Carolina, Chapel Hill, NC 27599, USA

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ABSTRACT

Mesial temporal sclerosis (MTS) is a well-recognized cause of intractable epilepsy; however, coexistence with focal cortical dysplasia (FCD) is less common. Middle fossa epidermoid cysts are rare and may involve the temporal lobe. Most epidermoids are clinically silent, slow-growing, and seldom associated with overt symptomatology, including seizures. We describe a patient with multiple comorbidities including left MTS and a large epidermoid cyst involving the left quadrigeminal plate cistern compressing upon the cerebellar vermis and tail of the left hippocampus, resulting in refractory left temporal lobe epilepsy. The patient underwent left anterior temporal lobectomy. The surgical pathology demonstrated a third pathological finding of left temporal FCD type Ia. The patient has been seizure-free since the surgery. This case provides additional information with regard to the understanding of epileptogenicity and surgical planning in patients with MTS and epidermoid cysts.

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1. Introduction

Epidermoid cysts are benign, slow-growing ectodermal origin tumors that represent about 1% (0.3% to 1.8%) of all primary intracranial neoplasms [1–3]. Epidermoid cysts, also known as a cholesteatoma or pearly tumor, are filled with keratin debris as a result of progressive desquamation of epithelial cells [1,2,4–6]. They tend to extend into adjacent spaces as they enlarge and fill the subarachnoid space at their original intracranial location [4]. Epidermoid cysts remain clinically silent and are seldom associated with overt symptomatology including seizures [7–9]. Epidermoid cysts have been reported in various locations in the brain and spinal cord [10]. Common intracranial locations are the cerebellopontine angle (37.3%), parasellar region (30%), and middle cranial fossa regions [3,11,12]. Middle fossa epidermoid cysts arising directly from the parenchyma are rare. The origin of epidermoid tumors remains controversial. A plausible theory is that they originate from ectoderm derived cells that are displaced and trapped during neural tube closure within the primitive cerebral hemisphere between the third and fifth week of fetal development, which explains the potential sites including superficial, intraventricular, and intracerebral tumor locations [1,3,10,13].

In the literature, there are limited case reports of less than 50 patients with exclusive intracerebral epidermoid cysts. Less than 10% of the cases were associated with a clinical presentation of seizure disorder [8,9,14–16]. Most epidermoid cysts do not result in notable clinical symptoms, although hemiparesis, homonymous hemianopsia, headache, nausea, and vomiting may occur [9,14,17]. Differential diagnoses include dermoid cysts, arachnoid cysts, low-grade and cystic astrocytomas, dysembryoplastic neuroepithelial tumors (DNET), ganglioglioma, oligodendroglioma, and inflammatory cysts. Since epidermoids will show restricted diffusion on MRI, diffusion-weighted imaging may assist with the diagnosis preoperatively. Why epidermoid cysts are epileptogenic is unclear. It is thought that microruptures of the capsule can occur, causing an inflammatory reaction between the capsule and underlying structures resulting in dense adherence of the capsule to underlying structures [3,18,19].

Temporal lobe epilepsy (TLE) encompasses patients with similar seizure semiology and electrographic characterization consistent with an ictal onset zone in the temporal structures, either from the amygdalohippocampal area (limbic) or lateral temporal area (neocortical) [20]. The best available epidemiological data show that the prevalence of TLE in 1960 was 1.7 per 1000 people, with a corresponding rate of epilepsy in the entire population of 6.2 cases per 1000 people [21]. The diagnosis of TLE includes different etiologies, the most common being mesial temporal sclerosis (MTS), which is responsible for 60–

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* Corresponding author at: Department of Neurology, University of North Carolina, Chapel Hill, NC 27599, USA. Tel.: +1 919 966 8162.
E-mail address: tongfumin@yahoo.com (F. Tong).

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70% of cases. Other structural lesions, such as brain tumors, focal cortical dysplasias (FCDs), and vascular or ischemic lesions, account for 10–15% of TLE. However, 15–20% of patients with TLE have no detectable structural lesions even using modern neuroimaging protocols [22]. It is especially challenging to accurately delineate the ictogenic zone in FCD as subtle or nondetectable radiographic anomalies can produce devastating epilepsy.

In this paper, we present a patient with refractory left temporal lobe epilepsy who was found to have a large 6.5 × 3.6 cm epidermoid cyst involving the left quadrigeminal plate cistern, extending into the cerebellar vermis and tail of the left hippocampus. The patient underwent left anterior temporal lobectomy and has been seizure-free for over 10 months postoperation. The surgical pathology findings are interesting due to the triple comorbidity including MTS, an epidermoid cyst, and an incidental finding of FCD. This case provides additional information with regard to the understanding of clinical manifestations, epileptogenicity, and surgical strategies in patients with multiple comorbidities such as MTS and epidermoid cysts.

2. Case presentation

A 55-year-old right-handed female presented with late onset medication refractory epilepsy at age 47 years. Her seizure semiology included staring, lip smacking, unresponsiveness and asymmetric body posturing without head turning or eye deviation, followed by a generalized convulsion. Most of her seizures occurred during sleep, lasting 3–5min followed by postictal confusion for 20 min or longer. The seizures were commonly clustered with a frequency of once every 2–3 months. She was on multiple antiepileptic medications including maximal doses of levetiracetam, lacosamide, and lamotrigine. The patient demonstrated no neurological deficits.

Brain MRI revealed a large 6.5 × 3.6 cm nonenhancing lobulated mass lesion involving the left quadrigeminal plate cistern, cerebellar vermis and tail of the left hippocampus. The mass was hypointense on T1 and apparent diffusion coefficient images (ADC) (Fig. 1A and D), and hyperintense on T2 (Fig. 1B), diffusion-weighted (DWI) (Fig. 1C), and fluid-attenuated inversion recovery images (FLAIR) (not shown). Of note, CSF will not be bright on FLAIR, but proteinacous fluid/structures with debris will. A hyperintense signal on the DWI and hypointense signal on the ADC indicate restricted diffusion, a typical finding with an epidermoid cyst. There was secondary involvement of the tail of the left hippocampus (Fig. 1E). In addition, the left hippocampus was small with hyperintense T2 signal, compatible with MTS (Fig. 1F). The MRI reading was left parahippocampal sulcus and quadrigeminal plate cistern epidermoid cyst with left MTS based on typical brain MRI characteristics of atrophy and increased signal.

A neuropsychological evaluation indicated average cognitive functioning and mildly impaired memory with some lateralization to the left. An intracarotid sodium amobarbital procedure (Wada) demonstrated left hemisphere dominance for language function and strong bilateral memory functions.

Long-term video-electroencephalography (EEG) monitoring captured multiple seizures with stereotypical oral automatism, arising from the left anterior-midtemporal region with rhythmic theta activity at the onset (Fig. 2A). Interictal EEG showed frequent left anterior-midtemporal theta/delta slowing (Fig. 2B) and occasional sharp wave

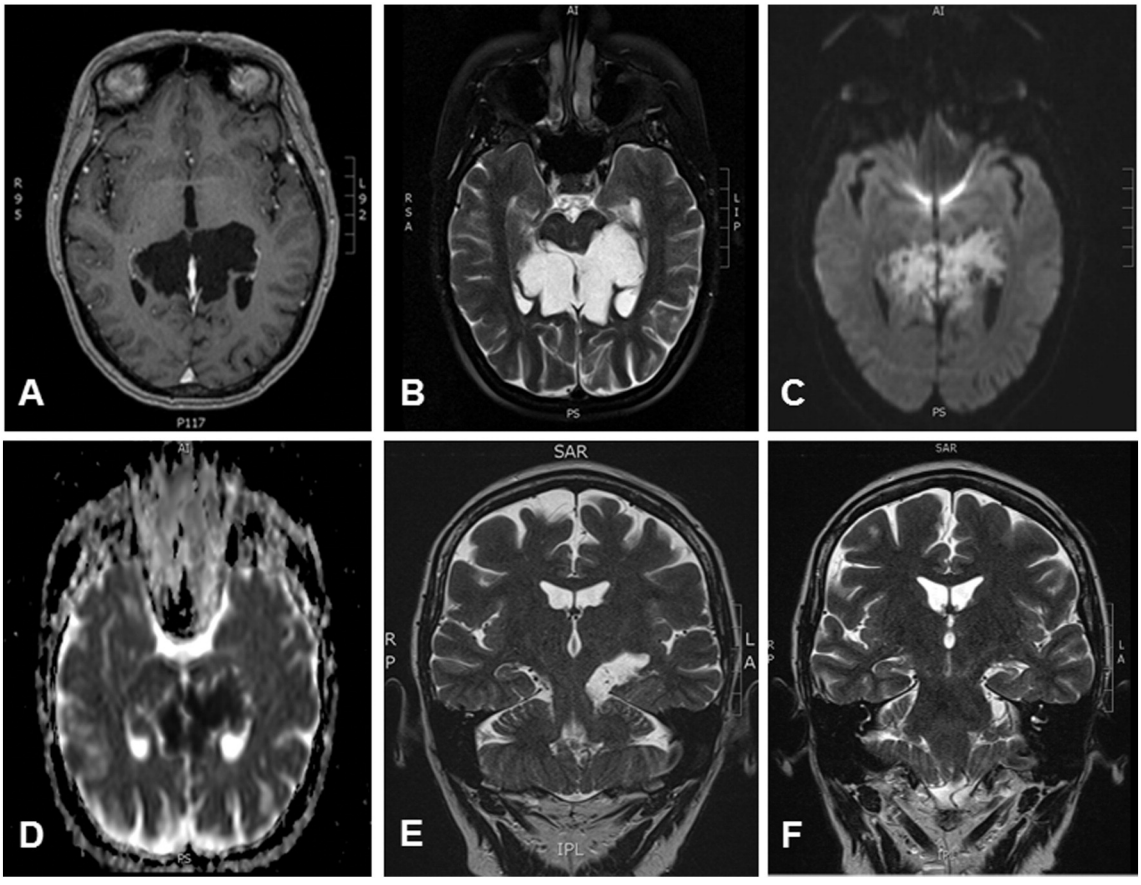

Fig. 1. Preoperative brain MRI demonstrates a mass lesion located in the left quadrigeminal plate cistern compressing the cerebellar vermis and tail of the left hippocampus. The epidermoid exhibits typical imaging findings on axial (A) T1 (low signal), (B) T2 (high signal), (C) bright signal on the diffusion-weighted image B1000, (D) dark signal/restricted diffusion on the ADC, (E) coronal T2-weighted images demonstrate involvement of the tail of the left hippocampus, and (F) the left mesial temporal sclerosis demonstrated by an atrophic hippocampus with hyperintense T2 signal. There is no edematous reaction or fluid collection in the surrounding tissues; no evidence of intracranial hemorrhage or acute infarct.

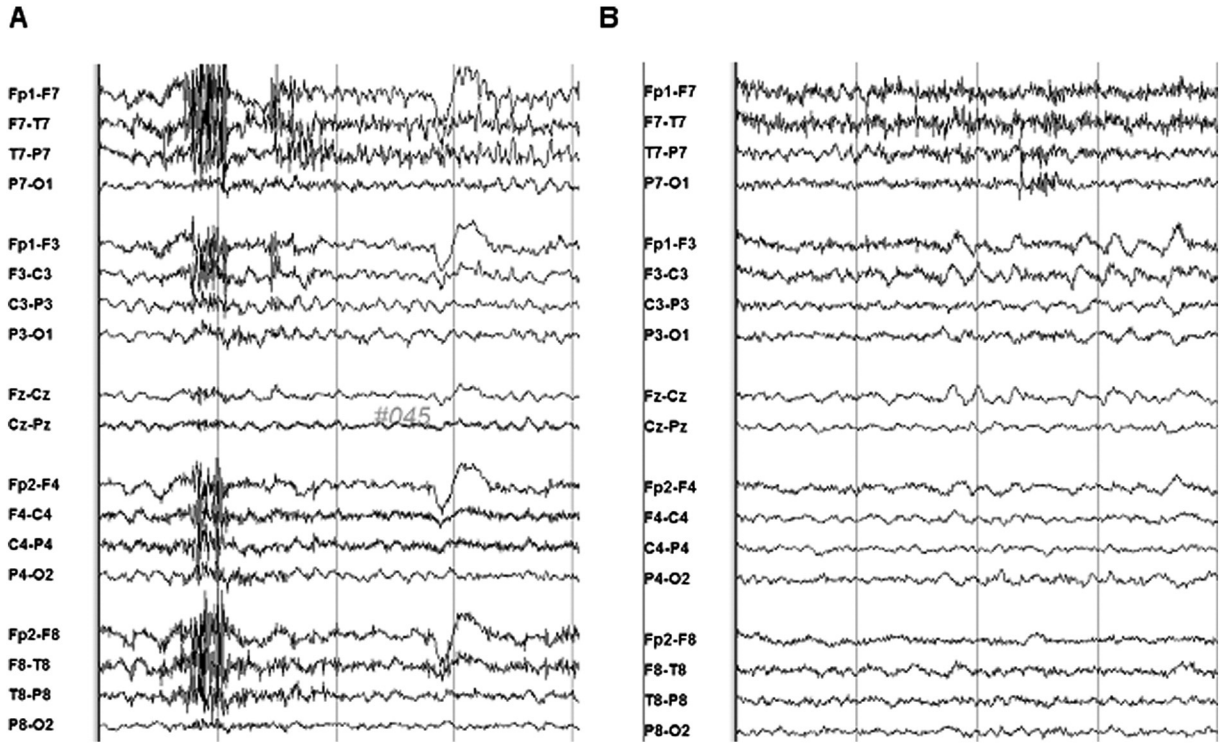

Fig. 2. The long-term video-electroencephalography (EEG) monitoring. (A) Ictal activities arose from the left anterior-midtemporal region with rhythmic theta activity at the onset; (B) interictal EEG showed frequent left anterior-midtemporal theta/delta slowing and rare sharp wave discharges (not shown on this EEG).

discharges. The EEG suggested hippocampal seizure pattern rather than a neocortical pattern. Her seizures were likely caused by the left MTS, not the epidermoid cyst.

After multidisciplinary evaluation, the patient underwent a left anterior temporal lobectomy without resection of the epidermoid cyst. Microscopic examination of the temporal lobe resection demonstrated abnormal cortical architecture, with neurons present within the molecular layer and microcolumnar arrangements of neurons within layers 2–5 of the cortex (Fig. 3A and B), consistent with focal cortical dysplasia type 1a. Immunohistochemical stain for Neu-N outlined the

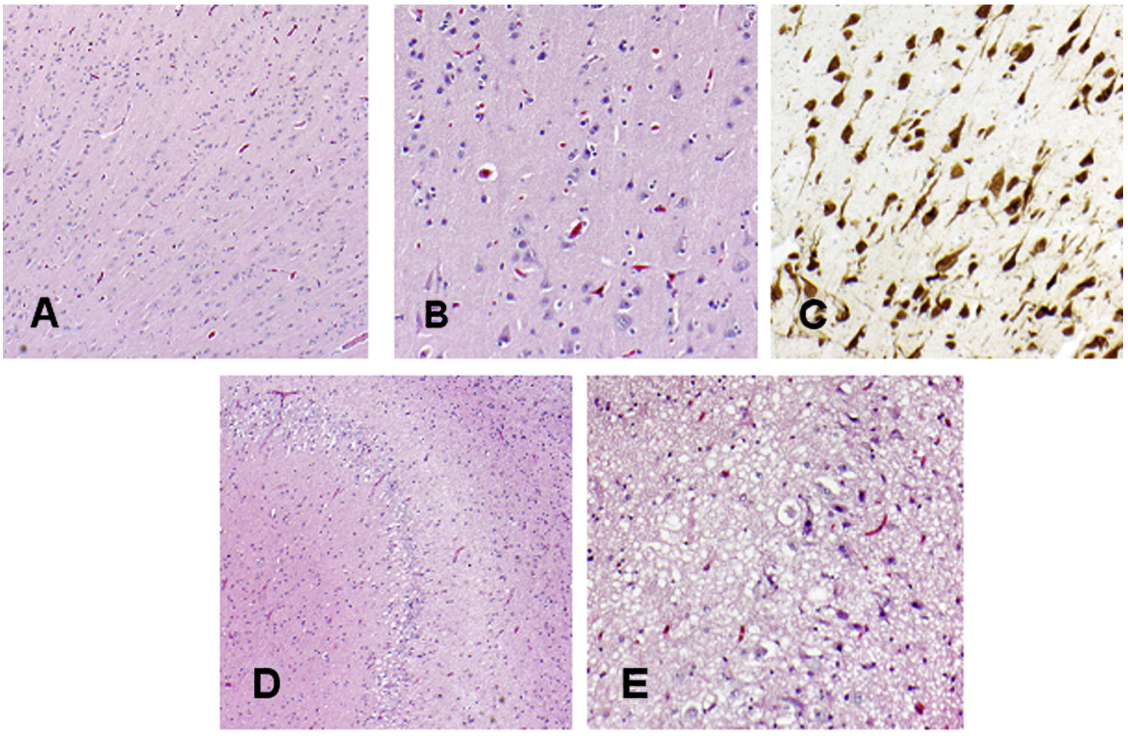

Fig. 3. (A) An H&E stained section shows abnormal cortical architecture in the temporal lobe (40×). Note: neurons present within layer 1 (L1). (B) Columnar architecture is noted in layers 2–5 (L2–L5, 100×). (C) Neu-N immunohistochemical stain demonstrates distinct microcolumnar arrangements of neurons (100×). (D) The hippocampus demonstrates neuronal loss and disordered architecture characteristic of mesial temporal sclerosis (40×). (E) Neuronal loss and reactive gliosis of mesial temporal sclerosis is also identified (100×).

microcolumnar architecture (Fig. 3C). No definitive dysplastic neurons or balloon cells were seen. The hippocampus showed marked neuronal loss, gliosis, and edema, consistent with MTS (Fig. 3D and E).

Postoperatively, the patient suffered mild right-sided weakness and aphasia, but no stroke was shown on the brain MRI study. She had a full recovery of strength and significant recovery of aphasia. She has been seizure-free for the past 10 months since the surgery. A repeat routine EEG at the recent follow-up visit showed left temporal mild slowing and breach rhythm, but no interictal epileptiform discharges, which might indicate a favorable prognosis of seizure control.

3. Discussion

This case report documents a patient with a large epidermoid cyst presenting with seizures. This unusual case of refractory left TLE has dual pathology of mesial temporal sclerosis and epidermoid cyst which were identified prior to the surgery, and a third incidental finding of extrahippocampal focal cortical dysplasia on postsurgical histopathological examination, which was not clearly shown on the initial brain MRI. A previous study reported that among patients with dual pathology, only 20% became seizure-free post temporal lobectomy, even when the atrophic hippocampus appeared to be the epileptogenic focus [23]. Therefore, it is critically important to analyze all the possible epileptogenicity causes and decide which one/ones need to be addressed by epilepsy surgery.

In our case, all three pathological findings are highly epileptogenic which could potentially have contributed to her refractory temporal epilepsy. During the phase I evaluation, multiple seizures were captured, and the EEG showed no evidence of neocortical/lateral temporal epilepsy pattern. In addition, the postresection electrocorticography (ECoG) and scalp EEG showed no epileptiform discharges. In our opinion, there appears to be a lack of direct connection between the common hippocampal epileptogenic mechanism and the relatively rare extrahippocampal cortical dysplasia. However, long-term follow-up will answer this question.

Additonally, we suspect the epidermoid cyst indirectly contributed to epileptogenicity by local irritation from keratin chemical substances in the cyst, resulting in an inflammatory hippocampal response creating edema and gliosis. Brain MRI illustrated epidermoid cyst compression of the left hippocampus, and the hippocampus exhibited hippocampal atrophy/signal abnormality consistent with mesial temporal sclerosis. This anatomical location and the nature of the epidermoid cyst contents appear to have been critical for the development of the hippocampal sclerosis. The subsequent neuron loss and damage might have developed after repeated abnormal discharges from the hippocampus.

Different surgical strategies have been attempted in isolated cases to treat patients suffering from epidermoid cysts and refractory epilepsy, including anterior temporal lobectomy with or without tumor resection; resection of amygdala, hippocampus and surrounding gliotic tissue have also been reported in the literature as part of the surgical approach [9,14,15]. The optimal surgical strategy in patients with an epidermoid cyst and epilepsy needs to be individualized depending upon the tumor location and size, further characterization of the epilepsy, and a comprehensive presurgical epilepsy workup. We considered resection of the cyst but decided against it for four reasons. First, the phase I presurgical EEG showed a pattern consistent with MTS, and there was no sign of neocortical or lateral temporal lobe involvement both on the EEG and neuroimaging studies. Second, the operative exposure needed for resection of the cyst is completely different than the approach used for temporal lobe resection. Third, resection of the cyst would be a high risk due to its interface with the vein of Galen. Finally, we were concerned that incomplete resection of the cyst would result in spillage of cyst contents into the cerebrospinal fluid, potentially causing chemical meningitis. Due to all of the above considerations, we decided not to pursue cyst resection. In our experience, additional neurophysiological evaluation may help provide better localization and epileptigenic focus characterization. Other tests such as high quality structural and functional neuroimaging, and neuropsychological testing may also contribute to a better understanding of the epilepsy surgical planning.

4. Conclusions

We present an unusual case with triple pathological findings that include epidermoid cyst, mesial temporal sclerosis, and focal cortical dysplasia. The pathological features of this case suggested that the chronic irritation by the epidermoid cyst and subsequent local inflammatory response within the hippocampus/parenchyma were the likely epileptogenic mechanism and cause of MTS. This case provides additional information in the understanding of epileptogenicity and surgical strategy in patients with MTS and FCD, and additional pathologies such as epidermoid cysts.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

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