■ Electroclinical reasoning report

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Temporal lobe epilepsy with a contralateral parietal seizure-onset zone

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ABSTRACT

Achieving sustained seizure freedom following epilepsy surgery remains a challenge in some patients. Lesional temporal lobe epilepsy (TLE), for example, in patients with mesial temporal sclerosis or other MRI abnormalities, carries a good prognosis for seizure freedom compared to significantly lower chances of seizure freedom in patients with non-lesional epilepsy. However, even in some lesional TLE cases, persistent post-operative seizures suggest seizure onset from a brain region that is clinically and electrographically silent but manifests only after propagation to the temporal lobe. A notable example of such a brain region is the parietal lobe, which has extensive connectivity to various brain regions. While certain seizure semiologies, for example, sensory seizures, suggest parietal lobe onset, some medial parietal seizures may be semiologically indistinguishable from temporal lobe seizures. Here, we report a patient with focal impaired awareness seizures that manifested semiologically and electrographically as left TLE but proved to originate from the contralateral medial parietal lobe. We discuss putative seizure propagation pathways.

Key words: SEEG, TLE, MTS, parietal lobe, seizure propagation

Achieving sustained seizure freedom following surgery for intractable temporal lobe epilepsy (TLE) remains a challenge in some patients. Evidence suggests that the rate of seizure freedom, two years post-operation, is around 70% [1], which drops to 47% at five years and to 38% at 10 years [2]. Lesional TLE, such as in patients with mesial temporal sclerosis or other MRI abnormalities, carries a good prognosis for seizure freedom compared to significantly lower chances of seizure freedom in non-lesional epilepsy [3]. However, even in some lesional TLE cases, persistent post-operative seizures suggest seizure onset from a brain region that is clinically and electrographically silent but manifests only after propagation to the temporal lobe. A notable example of such a brain region is the parietal lobe, which has extensive connectivity with the temporal lobe [4]. The postoperative prognosis is favorable in lesional parietal lobe epilepsy (PLE) [5], but MRI-negative PLE can be difficult to diagnose. While certain seizure semiologies, for example sensory seizures, suggest parietal lobe onset, some medial parietal seizures may be indistinguishable from temporal lobe seizures [6, 7]. Here, we report a patient with focal impaired awareness seizures (FIAS) that manifested semiologically and electrographically as left TLE but proved to originate from the contralateral medial parietal lobe. We also discuss seizure propagation pathways.

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Case history

A 31-year-old, right-handed bilingual immigrant from Latin America presented for evaluation of medically intractable epilepsy. He denied a history of perinatal complications, febrile seizures, or head trauma, but reported a remote history of neurocysticercosis. His seizures started at age 12 years with an aura of piloerection on the left side of the body and occasionally on the right, followed by unresponsiveness and left-hand automatisms for 1-2 minutes. Several years after his seizure onset, he stopped having piloerection, and his auras became "difficult to describe". He described postictal weakness and exhaustion. At presentation, he was on polypharmacy with lacosamide, brivaracetam, and zonisamide with continued seizure frequency of 5-10 seizures per month. He had received and discontinued carbamazepine, eslicarbazepine, and levetiracetam due to side effects or ineffectiveness. His general and neurological examinations were normal.

Non-invasive investigations

Imaging

The CT scan and MRI of the brain showed a 0.7-cm cystic cortical lesion in the right precuneus with a rim of calcification, consistent with neurocysticercosis. Functional MRI with English language tasks lateralized to the left side for both expressive and receptive regions, and Spanish language tasks activated bilateral brain regions. An interictal fluoro-deoxyglucose PET scan showed left anterior temporal hypometabolism (laterally and medially), in addition to an expected lack of glucose uptake in the area of his cystic lesion. Diffusion tensor imaging (DTI) demonstrated abnormal peri-lesional tracts (*figure 1*).

Neuropsychological evaluation

Neuropsychological tests in Spanish and English revealed impaired naming, word list generation, mathematical computations, and memory for geometric designs. His impaired naming and category-guided word list generation suggested left hemispheric dysfunction, although his memory for words was within normal limits. His intellectual difficulties were attributed, at least in part, to his frequent seizures.

Scalp video-EEG study

Four focal impaired awareness seizures (FIAS) were captured on scalp video-EEG, all of which manifested with bilateral repetitive blinking at onset, left-hand automatisms, followed by a sigh, right facial clonic twitching and right arm tonic posturing for 3-5 seconds. The patient was not responsive during these seizures, and manifested with confusion and fatigue postictally. The ictal EEG showed delta activity over the left temporal region, evolving into sharply contoured rhythmic delta and subsequently theta activity with spread to the left parasagittal region. About 40 seconds into the seizure, the ictal discharge consisted of semi-periodic sharp waves over the left hemisphere, which appeared maximum over the left temporal derivations. Interictal EEG showed irregular left temporal slowing as well as left temporal intermittent rhythmic delta activity (TIRDA) and abundant left anterior temporal spikes.

Thus, the patient's ictal and interictal scalp EEG findings, ictal semiology, and FDG-PET suggested left hemispheric seizure onset. However, because of the discordant right parietal lobe lesion and his history of bilateral piloerections, we planned bilateral implantation with depth electrodes and strips with greater coverage over the left hemisphere.

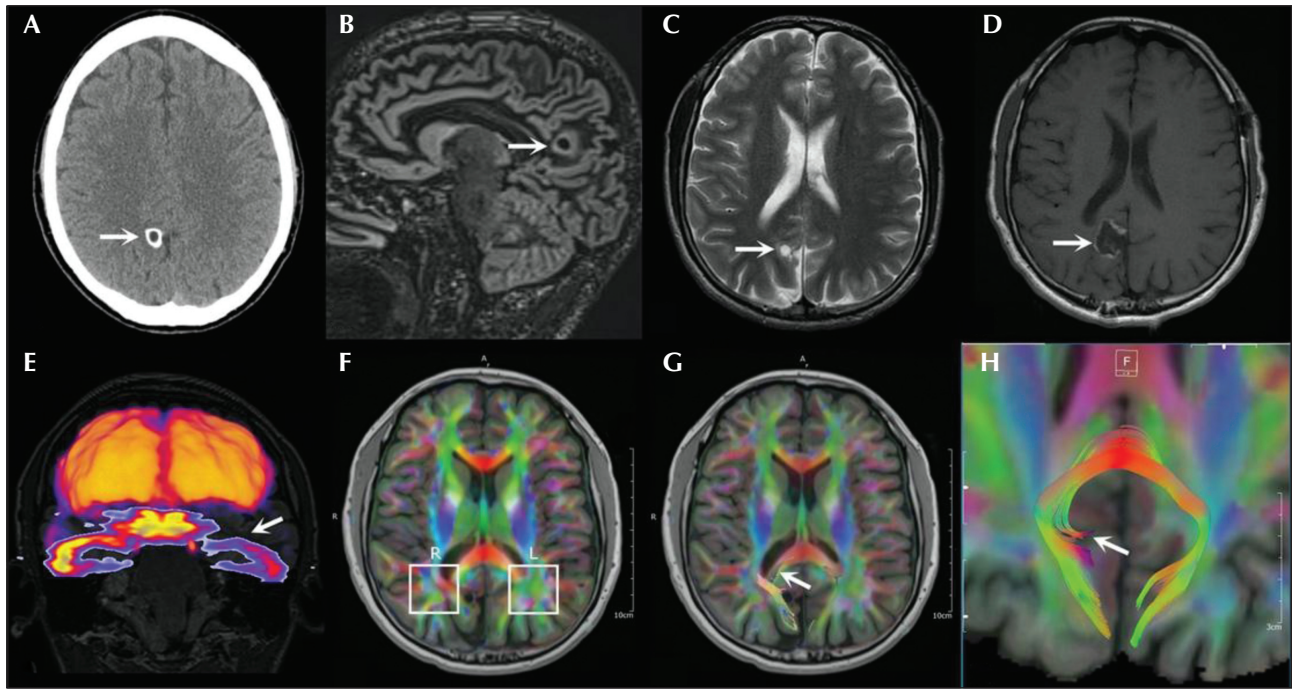
On the left hemisphere, stereotactic electroencephalography (SEEG) targeted the left entorhinal cortex, left insula, left posterior cingulate, and left hippocampus. Three subdural strip electrodes sampled activity from the left temporal lobe, including the temporal tip, anterolateral, and posterolateral regions. On the right, depth electrodes were inserted in the vicinity of the right parietal lesion and right hippocampus, in addition to subdural strips covering the right medial and lateral parietal lobe (*figure 2A*).

Invasive video-EEG study

Eight FIAS were captured during the invasive recordings, five of which had similar semiology to those previously recorded. The remaining three seizures consisted of brief left-hand automatism, forward leaning and sighing for 20 seconds, with post-ictal fatigue. On intracranial EEG, the seizure started with spiking and low-voltage fast activity in the medial and lateral parietal contacts, which was around the time of rapid blinking, evident on concurrent scalp EEG. The ictal discharge then propagated to the left mesial temporal structures and soon evolved over the lateral temporal strip (and left temporal scalp) electrodes as rhythmic slowing then repetitive spikes. As the seizure evolved, the right posterior quadrant activity appeared to be temporally linked to the activity in the left amygdala (*figure 2B*).

Surgery and outcome

After discussion of the findings and appropriate consent, the patient underwent a right parietal-occipital craniotomy (interhemispheric parafalcine approach) for resection of the cystic lesion and perilesional brain

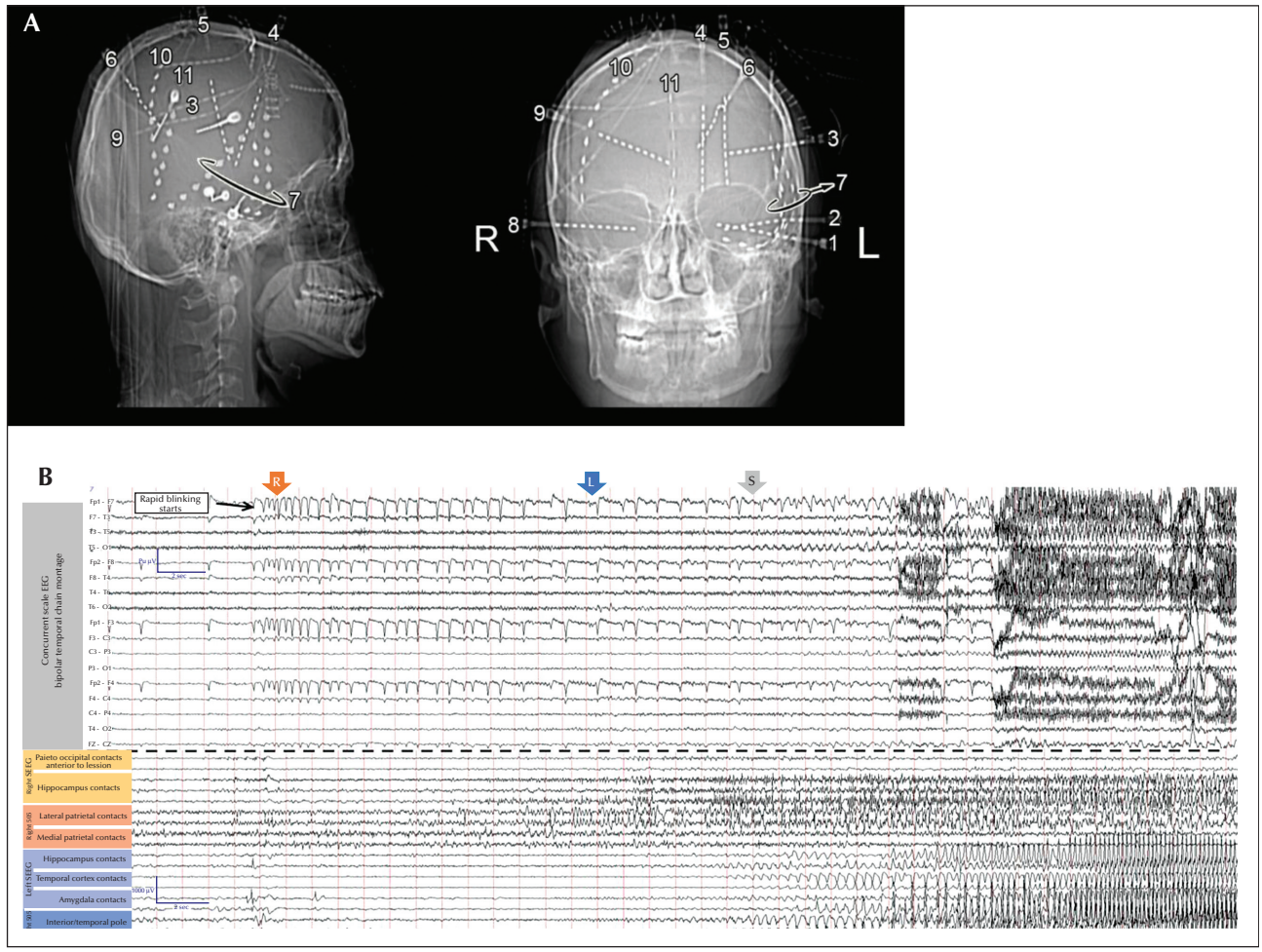


■ **Figure 1.** (A) Axial CT image demonstrating peripherally calcified lesion in the paramedian right parietal lobe without surrounding edema. (B) Sagittal MRI double-inversion recovery (DIR) sequence showing lesion in the cuneus gyrus with mild surrounding gliosis. (C) Axial MRI T2 sequence showing lesion as T2 hyperintense suggesting a cystic nature. (D) Postoperative axial MRI T1 sequence demonstrating the resection cavity from a posterior midline approach and a thin rim of blood products. (E) Coronal co-registered PET/MRI showing decreased activity in the left temporal lobe. (F) Axial MRI diffusion tensor imaging (DTI) through the level of the lesion demonstrating asymmetric appearance and color pattern of the parietal lobar white matter (squares) lateral to the lesion with the contralateral (left) side, showing the more expected appearance and predominantly green color of the anteroposterior direction of the fiber tracts. (G) A region of interest (ROI) drawn sagittally, immediately lateral to the lesion, showing fiber tracts that trace into the splenium of the corpus callosum and eventually to the contralateral side. (H) Drawing of a sagittal ROI in the midline splenium of the corpus callosum showing the asymmetric white matter tracts on each side near the lesion, highlighting additional and abnormal peri-lesional tracts of the right tracing from the corpus callosum.

tissue in conjunction with right hemispheric intraoperative EEG monitoring. Grossly, the cystic lesion was consistent with neurocysticercosis. There was no evidence of viable parasite in the cyst or tissue on pathological examination. The cystic lesion was suctioned, and the surrounding brain tissue (approximately 1.5 cm beyond cyst borders) was resected using stereotactic neuronavigation. The patient continues to be seizure-free 20 months postoperatively on two of his previous three seizure medications.

Discussion

Based on scalp EEG recordings, seizure semiology, and PET scan, our initial hypothesis was that the patient's seizures originated from the left temporal lobe, assuming that the right parietal lesion was simply an incidental finding. However, the patient's past auras of piloerection and his blinking at seizure onsets necessitated sampling the right precuneus. Importantly, his ictal blinking preceded the electrographic ictal onset on scalp EEG by a few seconds. Investigating the competing hypotheses of left temporal vs. right parietal seizure focus warranted an invasive monitoring study using a combination of bilateral SEEG and strips in multiple lobes [8]. Invasive ictal recording demonstrated unequivocal seizure onset from the right posterior quadrant. Rapid dissipation of discharges from the right parietal epileptogenic zone suggested a rapid spread to manifest semiologically and electrographically as left temporal lobe seizures, as opposed to having an independent left temporal focus.



■ **Figure 2.** (A) Lateral and anterior-posterior x-rays depicting locations of the depth and subdural strip electrodes. Left panel: depth electrodes are inserted in the amygdala (1), hippocampus (2), secondary somatosensory area (3), entorhinal cortex (4), insula (5), and posterior cingulate gyrus (6). Additionally, three strips (7) sampled the left lateral and inferior temporal lobe, extending medially to the parahippocampal gyrus. Right panel: depth electrodes targeting the hippocampus (8) and precuneus with medial contacts near the neurocysticercosis lesion (9). Two subdural strips sampled the lateral parietal lobe (10) and medial parietal lobe (11) adjacent to the lesion. (B) Scalp (upper panel) and concurrent intracranial (lower panel) recording of an electroclinical seizure. The scalp EEG shows a clinical onset of rapid blinking, annotated on the top left corner. The red arrow marks the transition of the right-sided parieto-occipital polyspikes to low-voltage fast activity, representing the ictal onset. The blue arrow represents the onset of ictal patterns over the left hippocampus and amygdala depth electrodes. Note the delay between clinical onset and left intracranial onset, as well as scalp onset (gray arrow). Relevant electrode locations are represented as right and left SEEG contacts, as well as subdural strips (SDS).

Seizure propagation from medial parietal areas to ipsilateral or even contralateral mesial temporal structures has been described [7]. In our patient, seizure onset occurred from perilesional cortex in the right precuneus, which likely propagated to the homologous region on left via callosal pathways, followed by propagation to the left mesial temporal lobe given the high functional connectivity of mesial and lateral anterior temporal regions with medial parietal cortex. The early blinking pattern can represent posterior spread to the visual cortex as the earliest symptomatic zone.

In rodents, connectivity between retrosplenial cortex and the hippocampal and parahippocampal region

[10], as well as postrhinal and entorhinal cortex and the hippocampus [11] has been demonstrated. Moreover, the retrosplenial cortex receives visuo-spatial inputs from the occipital cortex; therefore, all this information gets passed to the hippocampus to be processed [11, 12].

Ictal blinking is not unusual and can be unilateral, but mostly bilateral [13]. It is often seen in association with seizures originating from the posterior quadrant as well as in temporal and insular seizures [13, 14]. In our case, blinking started prior to temporal lobe involvement which may indicate propagation to the retrosplenial and visual cortices as a first ictal manifestation. A study of 38 patients explored the characteristics and surgical outcomes of patients with parietal lobe epilepsy (PLE). Remarkably, 60% of patients were thought not to have PLE and 70% of patients presented with FIAS mimicking TLE [15].

Another structure adjacent to the epileptogenic lesion in our case was the posterior cingulate gyrus, which has known connections to frontal and temporal structures, including the limbic network, and posterior cingulate seizures can manifest with semiologies suggestive of frontal or temporal seizures [6]. Posterior cingulate seizure spread favors ipsilateral temporal propagation rather than contralateral spread [9]. Potentially, electrical stimulation studies, in particular cortico-cortical evoked potentials, could have helped highlight effective connectivity in this seizure network, but unfortunately, we did not perform electrical stimulation.

Various interhemispheric pathways have been studied using diffusion tensor imaging in patients with epilepsy. These tracts include the anterior commissure, posterior commissure, fornix, and tapetum of the corpus callosum. One study investigated patients with left or right temporal lobe epilepsy who had bilateral spikes on EEG. The study concluded that the CC tapetum is significantly associated with contralateral epileptiform discharges [16]. The two connections between hippocampi include the ventral hippocampal commissure and the dorsal hippocampal commissure that connects entorhinal cortices. Gloor *et al*. suggested that the dorsal hippocampal commissure is an essential pathway in contralateral seizure spread based on depth electrode analysis in patients with temporal lobe seizures [17].

In summary, we present a case of right parietal epilepsy masquerading as a bona fide contralateral TLE, and clarification provided by seizure network analysis using intracranial studies. This is an example of why bilateral implantation of SEEG should be considered in patients with non-lesional TLE, as scalp EEG may not reveal any indication of ictal onset or even interictal discharges in the hemisphere of origin. ■

Supplementary material.
Summary slides accompanying the manuscript are available at www.epilepticdisorders.com.

Disclosures.
The authors report no disclosures.

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TEST YOURSELF

(1) What does ictal blinking imply?

(2) In this case, why was it important to recognize that the clinical onset started before the delta activity over the left temporal area on surface EEG?

(3) Name a few interhemispheric connections that may be involved in seizure propagation.

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com.