OBSERVATION

Identifying Subtle Cortical Gyral Abnormalities as a Predictor of Focal Cortical Dysplasia and a Cure for Epilepsy

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Objectives: To highlight a case series of 3 cases of focal cortical dysplasia that were unrecognized for many years though the patients were seen by various neurologists and received the appropriate neuroimaging studies, and to retrospectively characterize the clinical elements, neuroimaging, electroencephalography, and pathologic findings in these cases.

Design: Retrospective descriptive study.

Setting: Tertiary urban and suburban neurology and epilepsy outpatient and inpatient clinic settings and hospitals.

Patients: We analyze retrospectively 3 patients in whom magnetic resonance images were previously deemed as normal, who, in fact, exhibited subtle gyral abnormalities and who underwent focal surgical resections of these regions after invasive electroencephalography monitoring or electrocorticography and were cured of their epilepsy.

Main Outcome Measures: Clinical semiology and neuroimaging findings.

Results: Focal cortical dysplasias may present with subtle gyral abnormalities. These gyral abnormalities may guide invasive electroencephalography or electrocorticography and may delineate seizure onsets with precision. Resection of these areas in 3 such patients resulted in excellent surgical outcomes.

Conclusions: Subtle gyral abnormalities may be associated with intractable epilepsy and seizure onsets. Focal resection after appropriate evaluations in selected patients may be curative. The magnetic resonance imaging features of focal cortical dysplasia can be subtle and require a high index of suspicion based on ictal semiology and clinical presentation.

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IDENTIFYING NEUROIMAGING ABnormalities may lead to focal surgical resections and possible cures for medically intractable and disabling epilepsy. We present cases of focal cortical dysplasia (FCD) that were unrecognized for many years though the patients were seen by various neurologists and received the appropriate neuroimaging studies. Recognition of the FCD was possible only when the clinical semiology and neuroimaging findings were evaluated by experienced epileptologists.

REPORT OF CASES

CASE 1

A 16-year-old right-handed woman with 5 years' history of medically refractory epilepsy presented with focal epilepsy characterized by numbness and paresthesias of her left hand and left side of her face that would progress to tonic and then clonic contractions of the left hand and arm with the more prolonged spells. Her 1.5-T brain magnetic resonance imaging (MRI) scans were reported as "normal." We identified a small area of abnormality in the right postcentral gyrus consistent with the clinical suspicion of FCD (**Figure 1**). Video electroencephalography (EEG) monitoring revealed electrographic seizures over the right frontocentral region (**Figure 2**). Positron emission tomographic scan suggested an area of hypometabolism in the right frontocentral region (not shown). Intracranial grid monitoring demonstrated that her seizures were coming from the superior parietal region (Figure 2). She underwent a small right parietal topectomy. Results of histologic analysis revealed FCD (**Figure 3**). This patient has enjoyed seizure freedom for approximately 6 years following resection.

CASE 2

A 49-year-old right-handed woman with medically refractory epilepsy presented with 9 years' history of focal epilepsy characterized by numbness on the right side of the

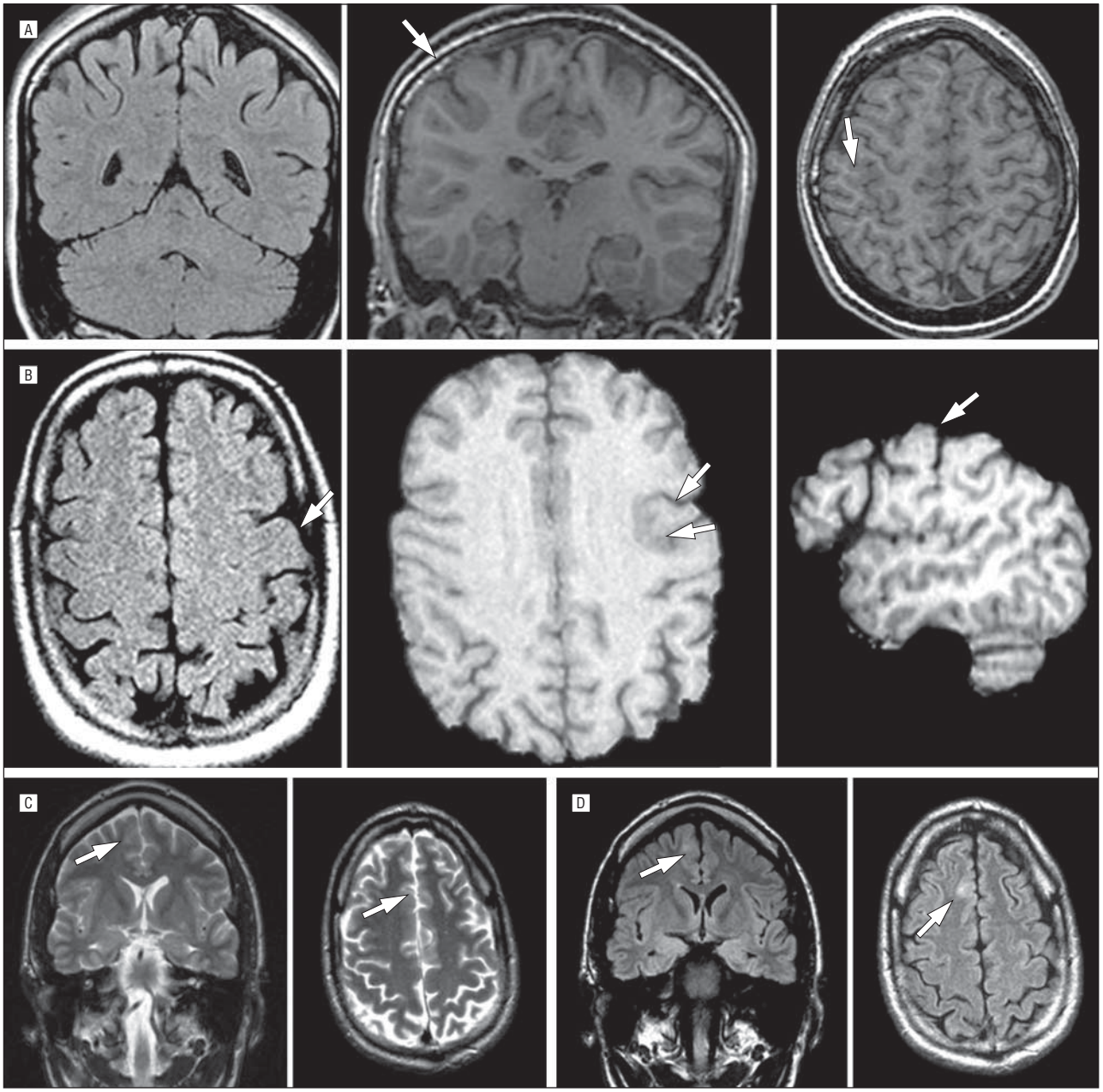

Figure 1. Selected magnetic resonance imaging (MRI) panels. A, The left panel is a coronal flair section and the middle panel is a coronal T1-weighted MRI. Note the subtle thickened cortical gyrus. This patient's MRI was deemed normal by outside evaluations. The right panel is an axial T1 MRI showing a subtle and thickened cortical gyral pattern (arrow). B, Axial flair, axial gradient echo, and sagittal gradient echo images identify cortical abnormalities ultimately consistent with focal cortical dysplasia and cure postresection. The left panel is an MRI that was deemed normal at an outside institution, and the middle and right panels were done as follow-up studies because of our clinical suspicions. C, The left panel is a T2 coronal section and the right panel is a T2 axial image. D, The left panel is a flair coronal section and the right panel is a fluid-attenuated inversion recovery axial image. Arrows in parts B-D denote the focal cortical dysplasia that was ultimately resected on neuroimaging and initially deemed normal at outside institutions.

tongue, tonic twitching on the right side of the tongue, and inability to get words out and sensation of choking and difficulty with swallowing. Her 1.5-T brain MRI done at another hospital was reported "normal." We identified subtle gyral abnormalities in the left inferior postcentral gyrus (Figure 1). Video EEG telemetry monitoring revealed a left frontal ictal-onset focus. Invasive grid electrode electrocorticography revealed seizure onset arising from the anterior portion of the left inferior rolandic cortex (Figure 2). Resection of the sensory and motor cortex of the tongue, lip, and face with sparing of the hand area resulted in cure of her epilepsy. This was guided by functional MRI preoperative data. Histologic examination of the resected area revealed FCD (Figure 3). This patient has experienced approximately 5 years of seizure freedom following resection.

CASE 3

A 44-year-old ambidextrous carpenter presented with 22 years' history of medically refractory epilepsy. His ictus occurred mostly at night and consisted of episodes

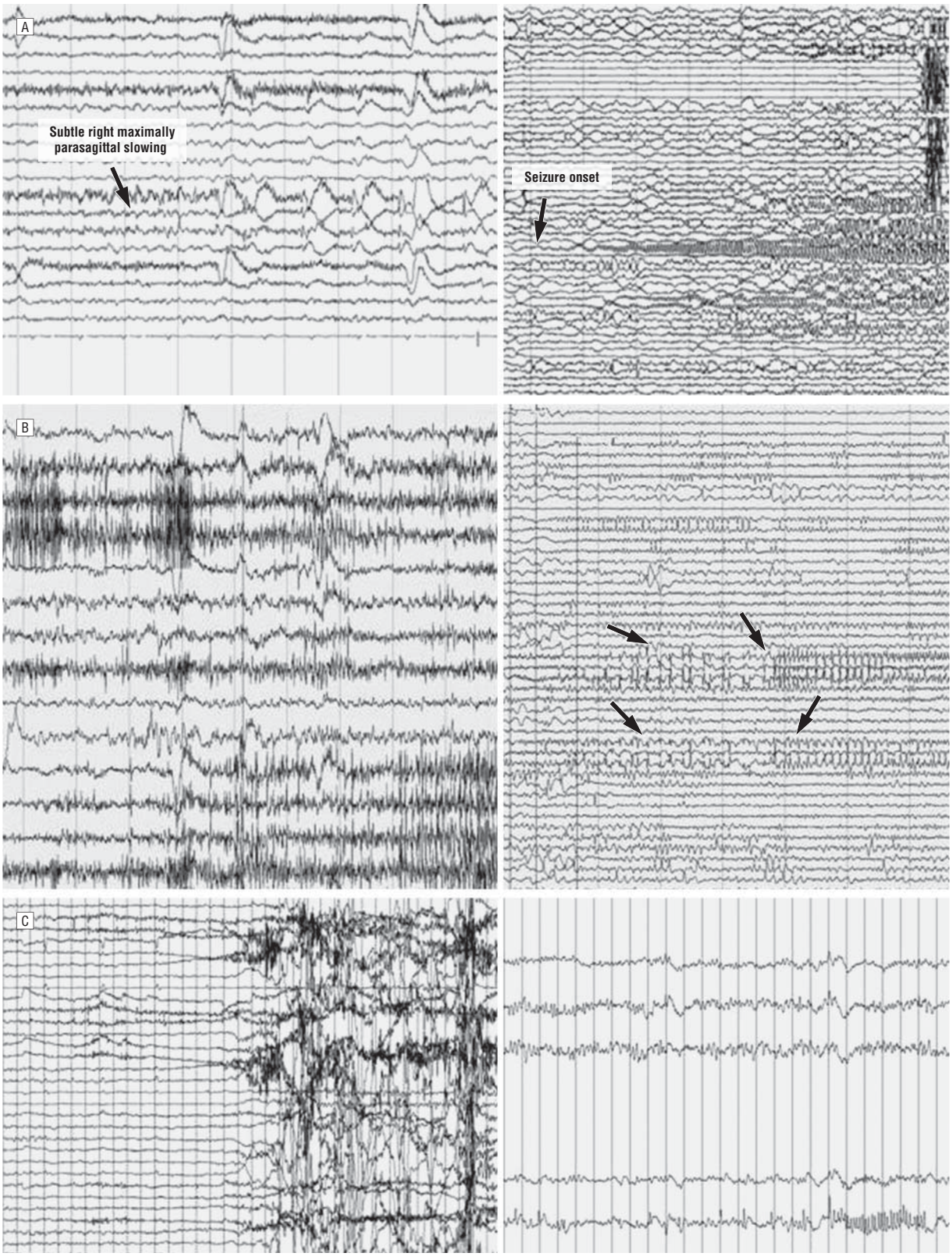

Figure 2. Selected electroencephalography (EEG) panels. A, The left panel is a surface EEG monitoring of seizure onsets showing relatively mild subtle slowing in the right hemisphere. The right panel is an invasive EEG via a 64-contact grid. Note the focal onset of seizure activity, which corresponded to the lesion noted on magnetic resonance imaging (arrows). B, Surface (left panel) and invasive (right panel) EEG monitoring. Note the lack of ictal signature on surface monitoring and the recurrent volleys of spikes seen with invasive surface monitoring (arrows) using a grid array that corresponded to a regional area ultimately parallel to the noted lesion on neuroimaging. C, Surface monitoring (left panel) identifies only muscle artifact but since the region of seizure onset is so small, no abnormalities are noted at seizure onset on the scalp. The right panel denotes recurrent trains and volleys of spikes in the region of the ultimately resected focal cortical dysplasia.

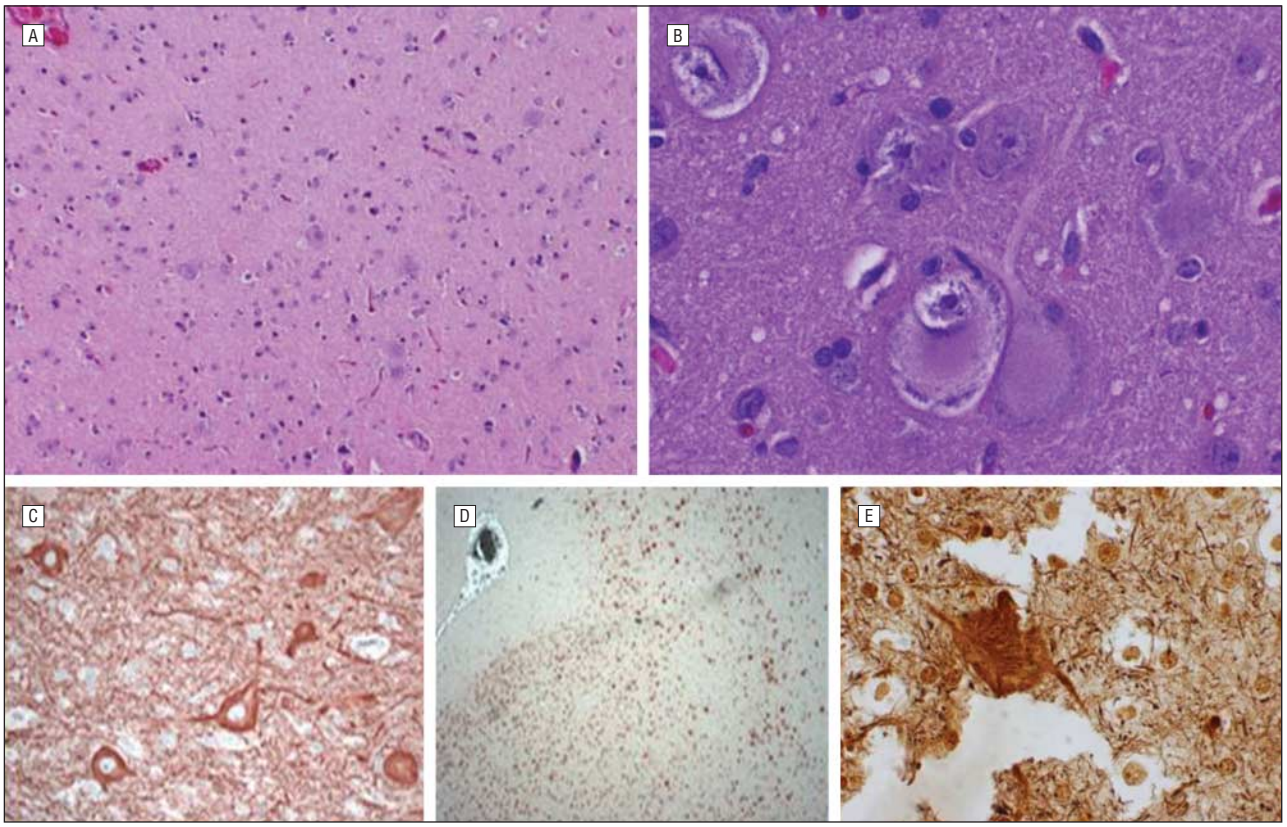

Figure 3. Selected composite pathology. A, Case 2. Low-power hematoxylin-eosin–stained section showing large atypical neurons. B, Case 1. Higher-power hematoxylin-eosin–stained section. C and E, Bielschowsky-stained section at low (C) and high (E) power, in cases 3 and 2, respectively, identifying an abnormal filamentous process within the cytoplasm and 2 large processes leaving the cell at opposite poles. D, Case 3. NeuN-stained section showing loss of normal lamination.

of sudden panic with speech arrest and bilateral thrusting movements of the upper and lower extremities with retention of consciousness. Multiple antiepileptic treatments failed, including phenytoin, carbamazepine, lamotrigine, oxcarbazepine, topiramate, and levetiracetam. His 1.5-T MRI of the brain revealed a subtle focal area of cortical thickening in the medial aspect of the right superior frontal gyrus (Figure 1). Video EEG monitoring revealed 5 events but no electrographic localization before, during, or after seizures (Figure 2). Invasive depth electrode monitoring into the noted region demonstrated frequent epileptiform discharges. He underwent excision of the lesion in the right superior frontal gyrus, resulting in seizure control while taking 1 antiepileptic medication (carbamazepine) 6 years after surgery. Pathologic analysis revealed a cortical dysplasia (Figure 3).

COMMENT

About 30% of patients with epilepsy are refractory to medical therapy.[1] For such patients, surgery offers their best option to either cure their epilepsy or significantly reduce the frequency of their seizures, as these cases collectively indicate. Magnetic resonance imaging is the diagnostic technique of choice in the presurgical evaluation of patients with refractory epilepsy.[2] With respect to FCD, the main neuroimaging and pathologic findings include focal cortical thickening, blurring of the gray-white matter junction, and often on T2-weighted images, there may be hyperintensity in the corresponding region along with elements of aberrant subcortical white matter tapering toward the ventricle.[3,4] There may also be dual pathology in these cases, which includes hippocampal sclerosis.[3,4] Focal cortical dysplasia was originally described in 1971 by Taylor et al[5] as a neuronal and glial proliferation disorder that includes cortical laminar disorganization, giant neurons, and dysmorphic and ectopic neuronal elements, and it was initially postulated that this entity might only be found in anecdotal reports in some articles.[6]

Focal cortical dysplasia was found in up to 24% of surgically resected specimens from patients with medically refractory epilepsy.[3] In 33% to 50% of histologically confirmed FCD, the MRI retrospectively was unrevealing.[4] It has been suggested that the diagnostic yield of MRI in FCD depends on the specific histopathologic findings and the location of the lesion. Simple partial motor, partial complex, or secondarily generalized seizures are associated with FCD and the location of the FCD dictates the clinical semiology.[7-10] Most patients have extratemporal localization, and in these cases, the frontal lobes and the precentral and postcentral gyri are involved most often.[8] It has been previously suggested that FCD usually presents with seizures at an early age, whereas adult onset of epilepsy may be uncommon.[8] Seizures are often quite refractory. The MRI findings include gyral thickening or subtle diffusion tensor abnormalities.[1-9]

Interictal EEG and ictal EEG might show focal discharges or identify specific focal onsets with invasive EEG monitoring.[10] In the literature, the extent of resection and having clear margins correlate with seizure freedom, and recurrence might correlate with the extent of the remaining nonresected regions of the remaining epileptogenic pathology.[11,12] Outcome seems to depend on the histopathologic findings in some series.[11,12]

While an extensive literature exists on FCD, we present cases of FCD that were unrecognized for many years, although the patients were seen by various neurologists and received the appropriate neuroimaging studies. Therefore, it is our opinion that the MRI features of FCD can be quite subtle and require a high index of suspicion based on ictal semiology and clinical presentation. To reduce the possibility of failure in diagnosis of FCD, we believe that the epilepsy team should examine the MRI very closely themselves, preferably with an experienced neuroradiologist in attendance, to corroborate or confirm impressions.

In particular, the team should examine carefully the white matter on fluid-attenuated inversion recovery and T2 sequences for subcortical abnormalities along with carefully inspecting the gray matter thickness and gray-white matter interface. Overall, an experienced and detailed knowledge of sulcal anatomy and cortical topography is helpful. In our opinion, T1-weighted spoiled gradient recalled echo is a useful MRI sequence to evaluate cortical thickness and sulcal anatomy. Seizure semiology that clearly lateralizes and localizes to a specific brain region will then focus the team's attention to look especially carefully in that specific region. What was striking in this series was that these MRIs were deemed "normal" by neuroradiologic report and at other centers where the patients were also evaluated for intractable seizures. Almost all patients with FCD might be able to undergo resection and the goal needs to be the complete removal of the FCD. The identification of the cases in this series collectively spanned several years at 2 institutions. The literature does identify that approximately 47% of patients with nonlesional epilepsy in 1 series were subsequently found to have a lesion.[13] Recognition of FCD in each case of our case series was possible only when the clinical semiology and neuroimaging findings were evaluated by epileptologists.

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