Generalized Epilepsy and Classic Spike-Wave Discharges With Unilateral Thalamic Lesions

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Background: Idiopathic generalized epilepsy (IGE) is a heterogeneous condition with a predominantly genetic origin. Clinical hallmarks of IGE syndromes include generalized spike and wave discharges and normal results on brain imaging.

Objective: To describe 2 patients with clinical presentations compatible with IGE but whose imaging studies revealed unilateral thalamic lesions.

Design: Case reports.

Setting: University-affiliated hospitals.

Patients: Two 21-year-old patients (1 man and 1 woman).

Main Outcome Measures: Magnetic resonance imaging findings.

Results: Magnetic resonance imaging unexpectedly revealed unilateral thalamic lesions.

Conclusions: We recommend doing magnetic resonance imaging studies in patients with IGE, especially in refractory or atypical cases. In rare cases, clinical features compatible with IGE may be associated with structural thalamic or other lesions.

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Diopathic Generalized Epilepsy (IGE) is a common and heterogeneous condition with a predominantly genetic origin and variable phenotypes. Clinically, IGE can be categorized as various syndromes, for example, juvenile myoclonic epilepsy, juvenile absence epilepsy, or epilepsy with grand mal seizures on awakening. These syndromes differ in their predominant seizure types (eg, typical absence attacks, tonic-clonic seizures, or myoclonic jerks), but they share some important clinical features, such as early age at onset of seizures, normal background activity with generalized spike and slow-wave discharges, and absence of pathologic findings on routine neuroradiological studies (ie, cerebral tomography or magnetic resonance imaging). We describe herein 2 patients with clinical histories compatible with IGE but whose imaging studies surprisingly revealed unilateral structural thalamic lesions.

Case 1

A 21-year-old man without obvious seizure risk factors or family history of seizures was initially seen at age 12 years because of occasional myoclonic seizures and nocturnal generalized tonic-clonic convulsions. He failed carbamazepine therapy and did not tolerate valproic acid treatment. He has been free of seizures for the last 2 years while receiving topiramate monotherapy, 100 mg/d. Findings from a neurological examination were normal. Pretreatment electroencephalograms revealed normal background activity with generalized polyspike and slow-wave discharges at 3 to 4 Hz, which worsened with hyperventilation and photic light stimulation. Magnetic resonance imaging revealed a 6-mm right thalamic lesion over the pulvinar, which has remained stable in size for the last 2 years (Figure, A and C).

Case 2

A 21-year-old woman had onset of seizures at age 6 years. Her condition was characterized by absence spells with eyelid myoclonia and rare myoclonic seizures, initially refractory to valproic acid and ethosuximide treatment but finally controlled by a combination of ethosuximide and acetazolamide therapy for many years before loss of control. Subsequent drug trials with nitrazepam, clobazam, and lamotrigine failed, with persistent absence and myoclonic spells. Family history was unavailable as she was adopted at birth. Findings from a neurological examination were unremarkable. Standard electroencephalographic and continuous video-electroencephalographic monitoring revealed a normal back-
Figure. Brain magnetic resonance images showing a unilateral nonenhancing thalamic lesion, most likely a low-grade glioma or a small infarct. A, Over the right pulvinar in patient 1. B, Over the left mediodorsal/laterodorsal nuclei in patient 2. C and D, Corresponding generalized spike and wave discharges (35-Hz high-frequency filter and 1-Hz low-frequency filter were used). EOG indicates electro-oculogram.
ground but with generalized spike and slow-wave discharges at 3 to 4 Hz. Magnetic resonance imaging showed a 6-mm left thalamic lesion (Figure B and D). Coherence and cross-phase spectral analysis of electroencephalograms showed high interhemispheric coherence values.

We describe herein 2 patients with unilateral circumscribed thalamic lesions with clinical features compatible with IGE. Epileptic seizures associated with thalamic lesions in humans have been previously reported, albeit without IGE-like phenotypes. Primary neonatal thalamic hemorrhage may manifest as inaugural focal or multifocal motor seizures, infantile spasms, or epilepsy with continuous spike-wave discharges during sleep.

Leiguarda et al described a 66-year-old woman with right-sided thalamic oligodendroglioma manifesting as gyratory epilepsy and sharp and slow waves over the right frontotemporal region. Inghilleri et al published a case report of a patient with a history of absence attacks in childhood in whom absence status with bilateral spike and wave discharges developed after left-sided thalamic ischemic insult. Bricolo et al reported features suggestive of generalized epilepsy following unilateral stereotaxic thalamotomy in 4 patients with Parkinsonism (among 1500 procedures). Although clinical symptoms were sometimes atypical (1 patient had 2 consecutive generalized tonic-clonic seizures, 1 patient showed progressive alteration of consciousness leading to akinetic mutism and subsequent alternating levels of vigilance and stupor, 1 patient demonstrated stupor in the setting of a severe pulmonary complication, and 1 patient had worsening Parkinsonism), all 4 patients had an electroencephalogram at some point demonstrating bilateral synchronous spike and wave discharges. In the 2 patients described herein, the age at onset, clinical seizures, and electroencephalographic findings were compatible with a diagnosis of IGE. Magnetic resonance imaging (performed because of comorbid headache in one patient and because of seizure intractability in the other patient) unexpectedly revealed unilateral thalamic lesions. These observations reinforce the importance of the thalamus in the genesis of generalized epileptic discharges. In these patients, the lesion might have altered the integrity of the thalamocorticothalamic circuits, generating abnormal rhythmic oscillations recruiting the contralateral cortex through the corpus callosum.

Idiopathic generalized epilepsy is a heterogeneous group of diseases, defined by distinct clinical and electroencephalographic features. By definition, there is no evidence of brain lesions in these syndromes. However, our cases add to the increasing number of reports describing various focal imaging abnormalities in individuals with clinical features otherwise compatible with primary generalized epilepsy. As an example, mesiofrontal lobe and hippocampal lesions have been reported in individuals with IGE. In addition, results of sophisticated image processing and quantitative magnetic resonance imaging studies have suggested that there may be a subtle structural abnormality in some cases. These abnormalities, as well as the thalamic lesions described herein, may be incidental findings. Nevertheless, we found striking similarities between both patients, including the irregular appearance of polyspike and wave discharges. We recommend doing magnetic resonance imaging studies in patients with IGE, at least in refractory or atypical cases. In conclusion, clinical features compatible with IGE may be associated with structural thalamic or other lesions in rare cases.

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