

IDIOPATHIC GENERALIZED EPILEPSY IS NOT RESTRICTED TO YOUNG PATIENTS

Idiopathic Generalized Epilepsy of Adult Onset: Clinical Syndromes and Genetics

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OBJECTIVE: To study the clinical features and genetics of idiopathic generalised epilepsy (IGE) beginning in adult life.

METHODS: Consecutive patients with IGE, defined as generalised seizures with spike or polyspike and wave on EEG, were studied in the setting of a first seizure clinic where an early postictal EEG record is part of the protocol. Patients were divided into two groups: “classical IGE” with onset before 20 years and inclusive of all the IGE subsyndromes recognised by the international classification; and “adult onset IGE,” when seizure onset was at age 20 years or later. Seizure patterns, clinical features, and genetics of the adult onset group were examined.

RESULTS: Of 121 patients with an electro-clinical diagnosis of IGE, 34 (28%) were diagnosed as adult onset IGE. The seizure patterns in these 34 cases were tonic–clonic seizures + absences (3), tonic–clonic seizures + myoclonus (6), and tonic–clonic seizures alone (25). Tonic–clonic seizures were often precipitated by alcohol or sleep deprivation. The proportion of affected first and second degree relatives did not differ between the classical and adult onset IGE groups. Twenty adult onset cases were treated with sodium valproate, four with other antiepileptic drugs, and 10 were untreated. Follow up of 32 of the 34 cases (for 31 (22) months (mean (SD))) showed that tonic–clonic seizures recurred in eight patients: five with identified provocative factors and three without.

CONCLUSIONS: Adult onset IGE is a relatively frequent and benign disorder. Seizures are usually provoked and are easy to control. Patients in this age group may often be misdiagnosed as having non-lesional partial epilepsy. Early postictal EEG and sleep deprivation studies may

improve the detection of these patients. Pedigree analysis suggests that adult onset IGE, like classical IGE, has a genetic aetiology.

COMMENTARY

PPrimary idiopathic generalized epilepsy (IGE) affects children, adolescents, and young adults. The International classification of IGE includes four epileptic syndromes: childhood absence epilepsy (CAE), juvenile absence epilepsy (JAE), juvenile myoclonic epilepsy (JME), and IGE with tonic–clonic seizures alone (GTCA). In 1981, Gastaut et al., published data demonstrating that IGE may begin in adulthood in up to 35% of patients (1). In the present paper, Marini et al., remind us of this often-forgotten observation.

The researchers identified 121 patients with IGE, of whom 34 (28%) had seizures beginning at a mean age of 33 years (median 27), with a range spanning from 20 to 75 years. Five of the 34 patients had their seizures beginning after the age of 40. All patients had generalized tonic–clonic (GTC) seizures, but six patients also experienced myoclonic seizures and three individuals had absence seizures. Comparisons of precipitating factors, prior seizures, course of the disease, response to therapy, and family history of epilepsy failed to identify any differences between patients with IGE starting before or after the age of 20. Seizures, for both age groups, were often precipitated by sleep deprivation or alcohol abuse but generally responded well to pharmacotherapy. Ten patients with adult-onset IGE remained seizure free despite being off medication. A similar proportion of first- and second-degree relatives with epilepsy were identified in both age groups.

In an epidemiologic study carried out in France, Loiseau et al., failed to identify the disorder in any patient above the age of 60 (2). Most patient studies on JME place the high end of the age range for onset for this disorder at 30 years. Thus, it is surprising to find patients with myoclonic and GTC seizure disorders with an onset as late as age 75. However, recently, Gilliam and collaborators reported a series of 11 patients with adult-onset IGE (myoclonic and GTC), presenting with a mean age of onset of 39 years (range 28 to 53) (3). The 11 patients represented 10% of newly referred patients with IGE, who were

seen at an epilepsy center. The patients had an excellent response to pharmacotherapy, and 4 of the 11 patients had a family history of epilepsy. Similarly, Cutting and collaborators reported a series of 42 patients with adult-onset IGE (50% with myoclonic and GTC disorders), which was 13.2% of all patients presenting with IGE at their center (4). The oldest patient in this series was 55 years old. As with the other series, patients had an excellent response to therapy.

Interestingly, the authors found that one-third of the patients had experienced psychiatric disorders and 24% were on psychotropic medication. This is a very important observation, as IGE has been thought by many to have a low psychiatric comorbidity. The misconception has been clarified in recent years by several European studies that have revealed that patients with JME and CAE are likely to show problems with impulsivity, poor frustration tolerance, and poor attention span (5). In an analysis of the reported behavioral disturbances of patients with IGE, Janz concluded that patients with IGE show cognitive and psychiatric features suggestive of frontal lobe dysfunction. This impression was supported by Swartz et al. in a study that compared FDG-PET activation between patients with JME and normal controls during a memory test. Patients showed a decreased activation in dorsolateral prefrontal areas (6).

It is clear from the reported case series and a review of the literature that adult-onset IGE comprises between 10% and 35% of all patients with IGE. Yet, is it possible that we are inadequately detecting cases of adult-onset IGE and that many of

these cases are incorrectly given the diagnosis of partial epilepsy with secondarily GTC? The answer is: probably. A careful investigation of family history of epilepsy as well as a postictal electroencephalography (EEG) or a sleep deprived study, if the EEG is negative, may improve identification of cases with adult-onset IGE . . . but only if this entity is considered in differential diagnosis!

by *Andres M. Kanner, M.D.*

References

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