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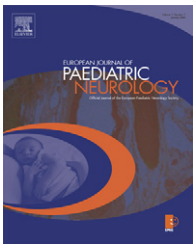

Original article

Typical absence epilepsy presenting prior to age of 3 years: An uncommon form of idiopathic generalized epilepsy

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ABSTRACT

Purpose: An attempt to allocate patients with the clinical features and electroencephalography (EEG) abnormalities of typical absence epilepsy presenting before the age of 3 years, similar to childhood and juvenile absence epilepsy (JAE) and delineate the clinical manifestations, EEG abnormalities, therapy and outcome of such an epileptic disorder by conducting a nationwide survey.

Results: Overall, eight infants, six males and two females, abided by the inclusion criteria of typical absence epilepsy: They were born after an unremarkable pregnancy and labor presenting at the age of 12–34 months (mean: 19.6 months) with frequent absences time-linked with an EEG demonstrating generalized occasionally irregular epileptiform discharges of 3–4 Hz spike/wave and normal background activity along with an electrographic photosensitive response in one patient. Neurological examination was intact in all infants. All eight infants were initially treated with valproic acid, of whom seven immediately responded and one had increase in frequency and duration of absences completely aborted with treatment of lamotrigine. Three relapsed after termination of therapy of whom two again presented with recurrent absences and another one with generalized tonic–clonic seizures and as such these children had virtually transformed into a later form of idiopathic generalized epilepsy (IGE) during childhood. All eight patients are seizure-free, seven still on therapy; seven children within a follow-up period of 2–7 years and the most recently diagnosed infant for 6 months. Cognitive skills were found normal in all children within the low normal range in three children with short attention and concentration spans.

Conclusion: The data presented here delineate a very rare form of idiopathic benign generalized epilepsy presenting with typical absences before age of 3 years and a favorable outcome, similar to childhood and JAE, recognized as distinct IGE syndromes by the International League Against Epilepsy (ILAE) classification.

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Abbreviations: ADHD, attention deficit hyperactivity disorder; CAE, childhood absence epilepsy; EEG, electroencephalography; JAE, juvenile absence epilepsy; ILAE, International League against Epilepsy; TAEI, typical absence epilepsy during infancy; IGE, idiopathic generalized epilepsy; GTCS, generalized tonic-clonic seizures; AEDs, anti-epileptic drugs; LTG, lamotrigine; VPA, valproic acid

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1. Introduction

According to the International League Against Epilepsy (ILAE) commission on classification and terminology of epilepsies and epileptic syndromes in 1989[1] and the following update proposal in 2001,[2] childhood absence epilepsy (CAE) constitutes a unique epileptic disorder within the group of idiopathic generalized epilepsies (IGEs). Absence epilepsy commonly presents with recurrent freezing episodes corroborating with typical electroencephalography (EEG) abnormalities consisting of 3 Hz spike/wave discharges and normal background activity.[3] An extensive review on CAE reveals onset at 4–7 years with the first peak around 6–7 years and that of JAE presenting at the age of 11–12 years.[4] Four IGE syndromes also including typical absences were included in the 1989 ILAE classification[1]: CAE, juvenile absence epilepsy (JAE), juvenile myoclonic epilepsy, epilepsy with specific modes of seizure precipitation and myoclonic absence epilepsy.

The final classification of IGE syndromes still remains controversial between authorities suggesting the existence of a single broad epileptic syndrome with different presentations on one hand versus the suggestion of isolated unique presentations comprising distinct syndromes on the other hand. In as much, additional epileptic disorders including absences were described but as yet not included in the 1989 ILAE classification[1] or even in the 2001 revision attempt.[2] These epileptic disorders include absences with eyelid myoclonia (Jeavons syndrome), perioral myoclonia with absences and IGE with phantom absences, extensively reviewed recently by Panayiotopoulos in 2005.[5] In his review he also refers to the possible very rare occurrence of absence epilepsy with early onset prior to age of 4 years. In fact, a presentation of typical absences with onset prior to age of 3 years, even early as 6 months of age, was previously recorded presenting with clinical manifestations and EEG abnormalities as well as response to therapy similar to the distinct syndromes of CAE or JAE.[6–13] However, other authorities argued that absences during infancy are merely a denominator of various other less benign IGE syndromes during infancy rather than a distinct epileptic disorder.[14,15]

The purpose of the present study is an attempt to allocate infants presenting prior to age of 3 years with the clinical epileptic manifestations and EEG abnormalities similar or even identical to the presentation of typical absence epilepsy during childhood or adolescence,[1,2] hypothesizing that such an epileptic syndrome may exist during infancy.

2. Methods and patients

2.1. *Selection of participants*

The following diagnostic criteria of a possible diagnosis of typical absence epilepsy during infancy (TAEI) were required for inclusion into the study simulating the clinical presentations and EEG perturbations of CAE or JAE included as distinct syndromes in the 1989 ILAE classification[1] and the 2001 proposed update[2]: (1) age of onset: up to 3 years; (2) clinical presentation: recurrent absences in clusters manifested by freezing for seconds; (3) EEG abnormalities: 3 Hz spike/wave generalized epileptiform discharges and intact background activity corroborating with clinically suspected absences; (4) unremarkable pregnancy, delivery and labor as well as a postnatal course; (5) rapid and sustained control of seizures using relatively small doses of anti-epileptic drugs (AEDs), preferably monotherapy; (6) cognitive and verbal skills within the normal range prior and following control of seizures; (7) absence of a detectable cortical abnormality, especially focal abnormalities diagnosed with imaging studies. Infants excluded from the study: (1) seizures: myoclonic jerks including eyelid and oral myoclonias, focal seizures and drop attacks; (2) perinatal and postnatal disorders; (3) abnormal neurological examination as well as overt cognitive impairment below the normal range at presentation; (4) evidence of a cortical disorder, either structural or metabolic.

2.2. Demographics

A national survey of six pediatric neurology centers was performed by distributing a uniform data collection form in an attempt to trace patients with possible typical absence observed prior to age of 3 years implementing the diagnostic criteria of either CAE and/or JAE[1–4] during a period of the last 10 years screening approximately 900 infants younger than 3 years of age with a suspected seizure disorder. In all suspected patients, the clinical presentations of seizures were documented along with the documentation of the perinatal and postnatal course, the neuro-developmental status at onset of seizures and family history of seizures.

2.3. *Diagnostic assessment*

All infants underwent repeat thorough neurological examinations as well as developmental assessments including cognitive, language and motor skills upon presentation and on repeat periodic follow-up assessments performed by the responsible attending neurologist as well as neuro-developmental specialists including psychology, occupational therapy and speech therapy applying the appropriate for age testing accompanied by school reports of teachers, school counselors and educational psychologists.

2.4. *Electroencephalography*

Repeat surface EEG recordings were performed in infants with suspected absence epilepsy according to the accepted International 10–20 System using bipolar and referential montages during wakefulness, drowsiness and if feasible during natural sleep. No sedatives or hypnotics were used prior to the performance of all EEGs. Recording of 3 per second generalized epileptic discharges and normal background activity, time-linked with clinical absences validated the diagnosis of typical absence epilepsy.