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Reflex myoclonic epilepsy in infancy: A multicenter clinical study

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KEYWORDS
Reflex myoclonic epilepsy in infancy;
Long-term cognitive outcome;
Acoustic and/or tactile stimuli;
Valproate treatment;
Idiopathic generalized epilepsy

Summary:
Purpose: To describe the clinical and electroencephalographic (EEG) features of reflex myoclonic epilepsy in infancy (RMEI) and long-term cognitive outcome.
Methods: We enrolled 31 children from 16 neuropediatric centres in Italy, who underwent clinical and video-EEG evaluation. Cognitive assessment was performed in all patients using standardized psychometric tests.
Results: The age at onset ranged from 3 to 24 months of age. Seizures were characterised in all patients by symmetric myoclonic seizures (MS), triggered by sudden unexpected acoustic (38.7%) or tactile stimuli (29%) or both (29%). Spontaneous attacks were reported in 32.2% of the cases. Ictal EEG showed generalized high-amplitude 3 Hz polyspike and wave discharges, synchronous with brief rhythmic bursts of electromyographic activity. Patients were re-evaluated after a period of 7.2 ± 5.6 years. The prognosis for seizure control was excellent in all cases and reflex MS disappeared spontaneously or after valproate treatment. The cognitive outcome was excellent in 90.3% of children.
Conclusions: RMEI appears to be a variety of idiopathic generalized epilepsy with specific features that occurs in developmentally normal children.

Introduction

Benign myoclonic epilepsy in infancy (BMEI) is characterized by the occurrence of myoclonic seizures (MS) in the first 3 years of life in normal infants (Dravet et al., 1985, 1992). It has been classified among the idiopathic generalized epilepsies (IGE) in the 1989 International Classification (Commission on Classification and Terminology of the International League Against Epilepsy, 1989); and now included as Myoclonic epilepsy in infancy (MEI) among the electroclinical syndromes arranged by age at onset in infancy, in the recent report of the ILAE Commission on Classification and Terminology (Berg et al., 2010).

Recently, some authors have described cases with ''reflex MS'', triggered by unexpected noise or touch and have proposed to name this clinical entity: ''reflex myoclonic epilepsy in infancy-RMEI'' (Ricci et al., 1995). RMEI is extremely rare and, to the best of our knowledge, there are 25 cases published in the literature (Ricci et al., 1995; Cuvellier et al., 1997; Giovanardi Rossi et al., 1997; Deonna, 1998; Fernandez-Lorente et al., 1999; Zafeiriou et al., 2003; Kurian and King, 2003; Caraballo et al., 2003), all showed generalized reflex myoclonic jerks starting in the first 2 years of life. RMEI merits greater interest because it shows clinical and electroencephalographic (EEG) features similar to MEI, but differentiated by the presence of reflex MS. Other seizures (e.g. atonic and/or tonic seizures) are not part of RMEI.

RMEI may be underdescribed and underevaluated because the short duration of the event, possibly misinterpreted as ''excessive startle reaction'' in otherwise healthy children.

Data on long-term follow-up are still limited.

To gain further insights into the clinical and EEG characteristics of this syndrome and to evaluate the long-term neurodevelopmental outcome, a multicenter study is carried out by collecting data of children with RMEI.

Methods

Patients were recruited from 16 Pediatric Neurology Department in Italy.

All children had diagnosis based upon the following criteria: (1) symmetric myoclonic jerks, triggered by sudden unexpected tactile or acoustic stimuli; (2) onset of MS in the first 2 years of life; (3) normal pregnancies and perinatal history; (4) normal neuroradiological and metabolic investigations; (5) MS associated with an EEG discharge of generalized high-amplitude spike-wave (SW) or polyspike-wave (PSW) at 3 Hz on normal background activity.

The exclusion criteria were: (1) other seizures types (partial, tonic, tonic-clonic, atonic, asymmetric myoclonias, atypical absences); (2) abnormal pre-, peri- and post-natal history; (3) pathological neurological examination; (4) abnormal psychomotor development (delay or regression); (5) pathological findings on neuroradiological and metabolic investigations.

For each patient, personal and family histories of epilepsy or febrile seizures were documented.

The children were evaluated periodically and the final evaluation was performed after 7.2 ± 5.6 years (mean $\pm$ standard deviation) from the onset.

Developmental and cognitive assessment was performed in all patients using standardized psychometric tests according to their age. In particular, Griffith's mental development scales (GMDS) were performed to measure development trends which are significant for intelligence, or indicative of functional mental growth from birth to a developmental age of eight years. There are two sets of scales, one for each age group, 0—2 years and 2—8 years. Within the 0—2 year scales, a profile is obtained from five subscales examining locomotor, personal-social, language, eye-and-hand coordination and performance. In the 2—8 year scales, this profile is expanded to add a practical reasoning subscale. These scales provide a general developmental quotient (GDQ) and separate subquotients (DQs) for each area of development.

In 6 years old children and older, cognitive functions were analysed by means of the Wechsler Intelligence Scale for Children — Third edition (WISC III): standardized intelligence test for children aged 6.0—16.11 years (Wechsler, 1991).

Wechsler Adult Intelligence Scale — Third edition (WAIS III) is designed to assess cognitive functions in adolescents and young adults older than 17 years (Wechsler, 1997).

All children underwent periodical clinical evaluation and repeated video-EEG and polygraphic recording during