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Focal seizures versus epileptic spasms in children with focal cortical dysplasia and epilepsy onset in the first year

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Summary
Purpose: Focal cortical dysplasia (FCD) has been recognized as one of the most frequent causes of drug resistant epilepsy, especially in children. In infancy, onset of FCD-related epilepsy is substantially characterized by epileptic spasms (ES) or focal seizures. Which elements pertaining to the FCD are responsible for the onset of one type of seizure over the other is still unclear. Purpose of our study was to compare the characteristics of FCDs in terms of lateralization and site in patients with epileptic spasms versus patients with focal seizures.
Methods: We retrospectively reviewed data from 41 patients with FCD related epilepsy with onset during the first 14 months of life. Seizure semeiology and drug resistance were analyzed, as were age at onset and FCD site and lateralization.
Results: Twenty-one children had focal seizures, 11 had ES and nine had focal seizures followed by ES. Mean age at onset was respectively 8.2, 5.1 and 1.8 months. Drug resistance was present in respectively 38.5%, 34.6% and 26.9% of children. Among patients with only ES, 90.9% had an exclusively frontal FCD localization, versus 42.9% of patients with focal seizures and 11.1% of patients with focal seizures followed by ES. FCD lateralization was right sided respectively in 47.6%, 81.8% and 66.7% of patients.
Conclusions: Frontal lobe localization of FCDs was closely associated with ES ($p = 0.001$). Moreover we also found that patients with focal seizures followed by ES had a significantly earlier

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age at onset compared to patients with focal seizures only ($p < 0.001$). The association between ES and right-sided FCD lateralization, even if numerically suggestive, did not reach statistical significance ($p = 0.16$). There was no significant association between seizure type and drug resistance ($p = 0.08$).

Introduction

Since the first description by Taylor et al. (1971), focal cortical dysplasia (FCD) has been recognized as one of the most frequent causes of drug resistant epilepsy, especially in children (Gaitanis and Donahue, 2013). The clinical and electrophysiological characteristics of patients with FCD-related epilepsy have been widely reported (Chassoux et al., 2012; Dhamija et al., 2011; Krsek et al., 2009; Leventer et al., 1999; Mazurkiewicz-Bełdzińska et al., 2006; Montenegro et al., 2007). Recent researches strive toward finding specific correlations between FCD characteristics and epileptic phenotypes since they might shed light on epileptogenesis in FCD patients. It has been suggested that epileptic spasms in focal or diffuse cortical malformations result from age-dependent abnormal functional interactions between the lesion and the brainstem raphe nuclei which in turn project widely throughout the brain, thus explaining both the bilateral clinical involvement and the diffuse hypsarrhythmic pattern (Juhász et al., 2001). Many series of patients with cortical malformation-related ES have been published (Asano et al., 2001; Cusmai et al., 1988; Hamano et al., 2000; Jellinger, 1987; Kobayashi et al., 2001; Koo and Hwang, 1996; Meencke and Gerhard, 1985; Yum et al., 2011), however these studies either reported a very limited number of cases or took into account a wide variety of lesions, including migrational defects, tumors and hemimegalencephaly. The aim of our study was to compare the clinical and electrophysiological characteristics of FCD-related epilepsy in pediatric patients with focal seizures versus ES.

Patients and methods

Patient selection

The series includes 41 patients with FCD and onset of seizures during the first 14 months of life, collected at the Bambino Gesù Children Hospital in Rome, and at the Carlo Besta Neurological Institute in Milan between January 1988 and December 2012. The diagnosis of FCD was based on the following MRI characteristics: increased cortical thickness, blurring of the cortical—white matter junction, increased signal on T2-weighted images, a radially oriented linear or conical transmantle stripe of T2 hyperintensity, cortical thinning, and localized brain atrophy (Figs. 1 and 2A and B).

Medical records were reviewed for age at onset, seizure type, ictal video-EEG recordings at clinical onset, localization of FCD and drug resistance. Patients were divided into three groups according to seizure type: ES, focal seizures and focal seizures followed by ES. ES were defined as sudden and brief contractions of axial and proximal limb muscles associated with diffuse high amplitude slow waves at the EEG (Fig. 1C—D). Focal seizures were defined as seizures with a focal clinical onset associated with a focal paroxysmal discharge on EEG. Focal seizures followed by ES were defined as seizures characterized by ES appearing no later than 60 s from the end of a focal seizure (Fig. 2C—D).

In the 13 surgically treated patients, histopathological classification of FCD was also reviewed.

Patient drug history was reviewed for efficacy. Drugs were considered ''effective'' when complete seizure control was obtained, ''effective in combination'' when part of an effective polytherapy, ''partially effective'' when partial seizure control was obtained either in monotherapy or in polytherapy, ''temporarily effective'' when seizure control was obtained for a limited amount of time and ''non-effective'' when the drug had no effect on seizure frequency.

Statistical analysis

Descriptive statistics were performed for quantitative variables mean (±standard deviation — SD). Probabilities for comparisons among means were tested with Student's *t*-test or ANOVA (with post hoc Bonferroni's test) and for comparisons among proportions with chi-square test. A p value <0.05 was considered as statistically significant.

Analysis was performed with the Statistical Package for Social Sciences (SPSS).

Results

Patient characteristics

A total of 41 patients was enlisted in the study. Mean age at onset of seizures was 6.0 ± 4.3 months (focal seizures 8.2 months, ES 5.1 months and focal seizures followed by ES 1.8 months). Seizure semeiology was characterized by focal seizures in 21 patients, ES in 11 patients and focal seizures followed by ES in nine patients. As expected, interictal EEG was either multifocal or hypsarrhythmic in patients with ES and focal seizures followed by ES, and exclusively focal in patients presenting with focal seizures. FCD were right-sided in 25 patients and left-sided in the remaining 16. FCDs were lobar in 33 cases and multi-lobar in eight. Lobar FCDs were frontal in 20 patients, temporal in 10 patients and occipital in one patient. Multilobar FCDs were frontal parietal in three patients, frontal temporal in one patient, parietal temporal in three patients, temporal occipital in one patient and temporal parietal occipital in one patient (Table 1). Twenty-six patients were drug resistant, six patients obtained seizure control with surgery and four with medication, five patients were lost at follow-up. For 13 patients histopathological