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Refractory spasms of focal onset—A potentially curable disease that should lead to rapid surgical evaluation

Mathilde Chipaux[a,*], Georg Dorfmüller[a,b], Martine Fohlen[a], Nathalie Dorison[a], Marie-Astrid Metten[c], Olivier Delalande[a], Sarah Ferrand-Sorbets[a], Delphine Taussig[a]

[a] Pediatric Neurosurgery Unit, Rothschild Foundation Hospital, Paris, France
[b] Inserm, U663, Paris, F-75015 France, University Paris Descartes, 75005 Paris, France
[c] Clinical Research Unit, Rothschild Foundation Hospital, Paris, France

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ABSTRACT

Purpose: Infantile spasms (IS) can occur as the only seizure type in children with surgically amenable epilepsies. Although early surgery has shown positive effects, little is known regarding outcomes.
Methods: We retrospectively reviewed all children with IS referred to our tertiary center between 2002 and 2014 and try to define factors of outcome.
Results: Sixty-eight children with focal onset seizures were referred: twenty children with a hemispheric implication and 48 with one or more lobes involved. The age of onset was significantly earlier in the hemispheric population (8.0 versus 16.7 months in the focal population). There was no difference in the age of onset between anterior and posterior onset zones, as we could expect regarding the maturation gradient. The epilepsy began earlier in life in tuberous sclerosis than in DNET. Only three children of the 48 non-hemispheric patients had a normal MRI at the time of the surgery. Temporal lobe was involved only in a third of the population. More than 86% of the patients were operated on. Patients with hemispheric lesions were operated on younger (2.6 years +/− 2.1 years) compared to 4.6 +/− 3.5 years in the whole population. The most frequent etiologies were in descending order: dysplasia, ganglioglioma or dysembryoplastic tumours and tuberous sclerosis. The global seizure outcome was favorable (Engel 1a) in 74.6% of the patients, and 87.9% if the delay between the first seizure and the surgery was less than 36 months. It fell to 64.7% if the delay exceeded 50 months.
Conclusion: Spasms of focal onset have a similar postsurgical outcome as other seizure types so surgery may be an excellent option for treating selected patients with focal infantile spasms. Volume and type but not topography of the lesion influence the age of onset. MRI is very helpful to locate the pathology in the pediatric population, since only a small portion had a normal MRI.

1. Introduction

Infantile spasms (IS) are defined as brief axial contraction, lasting less than two seconds, recurring in short clusters [1]; they can be considered as focal or generalized seizures [2]. The onset is often in infancy but sometimes later in life. They are often associated with severe encephalopathy and hypsarrythmia (West syndrome) but do not necessarily indicate generalized epilepsy since they can occur as the only seizure type in surgically curable focal and hemispheric epilepsies [3,4,5] or be associated with other types of partial seizures [6,7]. These patients must be considered as potential candidates for epilepsy surgery, particularly when MRI exhibits unilateral focal abnormalities. A presurgical evaluation is required with clinical and neurological data, imaging, EEG, and discussion with a multidisciplinary pediatric team to decide upon the appropriate surgical strategy among a variety of options [8,9,10]. Surgical treatment may lead to seizure remission and neurocognitive improvement [10,11]. IS are often considered as a factor of bad development and poor post-operative outcome, even if little is known about their physiopathology and about the factors influencing the outcome. We tried to define factors of outcome in a population of focal IS referred for pre-operative evaluation. As defined by EEG, spasms with focal onset, hereinafter referred to as “focal spasms”, are opposed to multifocal and generalized onset spasms.

* Corresponding author.
E-mail address: mchipaux@for.paris (M. Chipaux).

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2. Methods

The aim of this study was to describe the population of children with refractory focal spasms referred to our epilepsy surgery unit and to define factors of outcome regarding the age of onset, the age of surgery, the topography of the lesion, and the type of pathology.

Children with IS referred to the Department of Pediatric Neurosurgery, Rothschild Foundation Hospital, were recruited between 2002 and 2014. We included every children with IS as described above, with an interictal focus on the EEG, hypsarrythmia was not mandatory. Pre-operative evaluations included interictal and ictal videoelectroencephalography (EEG), magnetic resonance imaging (MRI), 18F-fluorodeoxyglucose positron emission tomography (FDG-PET). When data obtained at this stage was insufficient to define a surgical scheme, Stereo-electroencephalography (SEEG) was decided by a trained multidisciplinary team (pediatric neurosurgeons, child epileptologists, neuroradiologists and neurophysiologists). The electrode implantation scheme was validated during our weekly case conference, and the results of the SEEG recordings were discussed, during our multidisciplinary staff conference, in order to decide on a tailored resection. SEEG was performed with DIXI® or ALCIS® electrodes as described by Taussig et al. [12,13], and analyzed by a trained neurophysiologist. Post-operative seizure control was assessed using Engel classification [Engel, 1993]. Pre- and post-operative developmental quotients were evaluated using a scale adapted to age and mental retardation (Vineland scale, Achenbach scale, Connors scale, Brunet-Lezine, WIPPSI and WISC). Medical records were retrospectively reviewed for age at onset of seizures, age at surgery, seizure types, and pre and post-surgical outcomes for both seizures and development. Video-EEG and SEEG recordings were independently reviewed by two different neurophysiologists.

Qualitative variables and quantitative variables were presented as number of patients (%) and mean ± standard deviation (minimum-maximum), respectively. Univariate analysis was conducted to explore predictors of surgery success defined using Engel classification. Pearson's chi-square tests or Fisher non-parametric tests were used to compare categorical variables. Mann-Whitney tests or Kruskal-Wallis tests were used to analyze quantitative variables between groups. P-values of less than 0.05 on tow-tailed tests were considered as statistically significant. Statistical analysis was performed using R software version 3.3.2.

3. Results

Between 2002 and 2014, 99 children with refractory IS were referred to our center (Fig. 1).

Among them, 31 were considered bilateral multifocal with an EEG compatible with Lennox-Gastaut syndrome or epileptic encephalopathies. For the purpose of this study, we analyzed the remaining 68 children, considered as monofocal regarding the EEG and MRI: 20 were hemispheric and 48 children were more focal, concerning one or more lobes (Table 1). The hemispheric onset group was defined as page8

DNET: dysembryoplastic neuroepithelial tumor; ANET: angiocentric neuroepithelial tumor; Mild mental retardation defined as IQ = 55-75, Moderate mental retardation defined as IQ = 35-55; Severe mental retardation defined as IQ < 35, HH: hypothalamic hamartoma, TSC: tuberous sclerosis complex

3.1. Clinical data

The mean age of epilepsy onset was 14.1 +/− 17.7 months (from the first week of life to 72 months) (Fig. 2). The onset was during neonatal period for 14.9% of the children, between 1 months and 1 year for 44.7% and after 12 months for 40.3%. The age of onset was statistically earlier in the hemispheric group compared to the posterior temporo-occipital or frontal patients (respectively

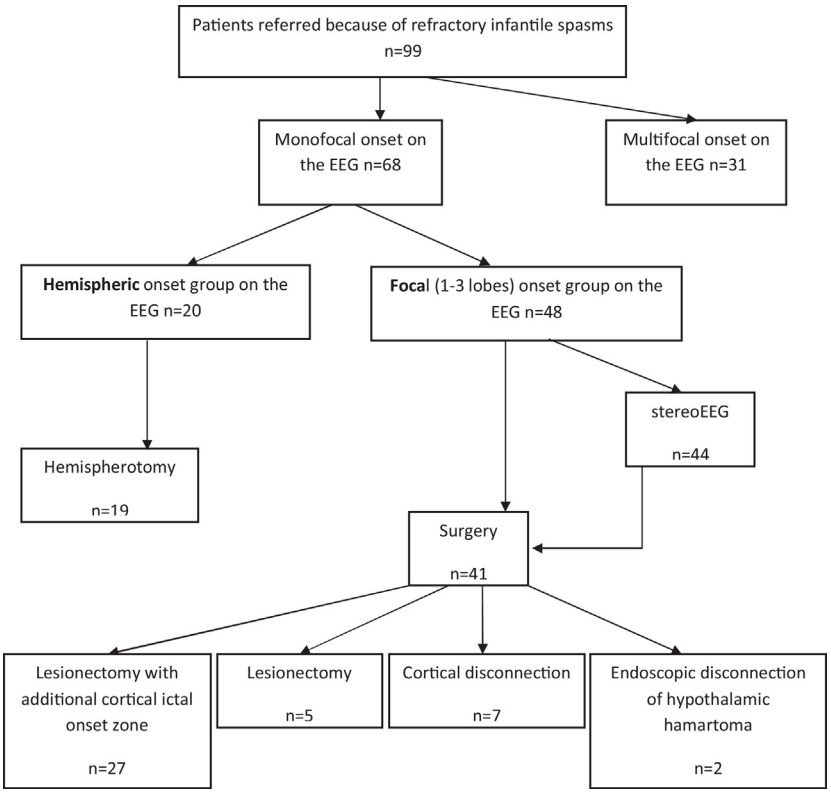

Fig. 1. Scheme of the described population.