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Original article

Pediatric epilepsy following neonatal seizures symptomatic of stroke

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Abstract

Background: Neonatal seizures are a risk factor for later epilepsy and their etiology is known to be implicated in the outcome but, little is known about this issue in the subgroup of seizures symptomatic of perinatal arterial ischemic stroke. The aim of this study was to describe the long term risk of epilepsy after electroencephalographic confirmed neonatal seizures symptomatic of perinatal arterial ischemic stroke.

Design/subject: Fifty-five patients with electroclinical ictal data, vascular territory confirmed by neuroimaging and a minimum follow up of 3.5 years were identified from a multi-centre prospective neonatal seizures registry. Primary outcome was occurrence of post-neonatal epilepsy. The association of outcome with family history of epilepsy, gender, location of the infarct, neonatal clinical and electroencephalogram data were also studied.

Results: During a mean follow up of 8 years and 5 months, 16.4% of the patients developed post neonatal epilepsy. The mean age at first post neonatal seizure was 4 years and 2 months (range 1–10 years and 6 months). Location of the infarct was the only statistically significant risk factor ($p = 0.001$); epilepsy was more represented in males but the difference was not statistically significant.

Conclusions: Neonatal seizures symptomatic of perinatal arterial ischemic stroke had lower risk and later onset of post-neonatal epilepsy, compared to seizures described in the setting of other perinatal brain insults. Our data have implications for counseling to the family at discharge from neonatal intensive care unit.

Keywords: Arterial ischemic stroke; Outcome; Thrombosis; EEG monitoring; Seizures etiology

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1. Introduction

Seizures are more common in the neonatal period than in any other period of life, affecting 2.6 per 1000 live births in population based studies [1] and 8.6% of infants admitted to Neonatal Intensive Care Units [2].

Occurrence of seizures in a neonate often reflects a severe underlying neurological dysfunction and is a risk factor for adverse neurological outcome. Post-neonatal epilepsy has been reported in up to 56% of children with history of neonatal seizures, but estimates vary widely [3–6]. The major determinant of post-neonatal epilepsy in neonates with seizures, among multiple predictors reported in the literature, was etiology [7] but, when evaluating the outcome of neonates with seizures, a variety of etiologies of perinatal brain damage are grouped together. The International League Against Epilepsy recently suggested the categorization of epileptic conditions on the basis of etiology, the syndrome definition in the case of acute symptomatic seizures [8] will includes the perinatal brain insult leading to seizures (defined as a constellation) [9,10].

Perinatal arterial ischemic stroke is the second most common etiology of neonatal seizures, following perinatal asphyxia [7], but, in the literature, there has been little emphasis on the occurrence of later epilepsy in the well defined epileptic condition of acute symptomatic seizures due to perinatal arterial stroke. Indeed, acute presentation with neonatal seizures is seen in up to 72% of the patients affected by perinatal arterial ischemic stroke [11]; the remaining patients may present acutely with altered level of consciousness and muscle tone, respiratory and feeding difficulties [11] or with hemiparesis in the first months of life (so called presumed perinatal stroke or delayed presentation of perinatal stroke) [12] which are considered a different population in terms of pathogenesis of brain damage and outcome [13]. Differential diagnosis with other conditions mimicking stroke in a neonate with seizures involves neuroimaging documenting an ischemic lesion in a known vascular territory [8].

The diagnosis of neonatal seizures cannot be based on clinical observation alone but requires video-EEG documentation. In fact the clinical correlate of ictal EEG pattern may be minimal, or, by contrast, abnormal non epileptic movements may mimic seizures [14].

In order to recruit adequate number of patients homogeneous for etiology, multi-center studies are needed.

The present study aimed to describe the long term risk of developing epilepsy and to identify possible risk factors in the well characterized and homogeneous population of patients with EEG confirmed neonatal seizures symptomatic of arterial ischemic stroke recruited from a multi-center prospective registry.

2. Patients and methods

From the registry of the Study Group on Neonatal Seizures of the Italian League Against Epilepsy and the Neonatal Neurology Section of the Italian Society of Neonatology we identified patients presenting with neonatal seizures symptomatic of arterial ischemic stroke in the period from 1st January 1990 to 30th June 2010. Inclusion criteria were: seizures confirmed by ictal EEG recording, arterial ischemic stroke confirmed by neuroimaging documenting abnormal signal intensity in a vascular territory and follow up $\geqslant$3.5 years.

In order to avoid factors possibly confounding prognosis, we did not select patients having dysmorphic features suggestive of a genetic syndrome, congenital cyanotic heart disease, sepsis, metabolic disorders and those in whom arterial ischemic stroke occurred associated to clinical or neuroimaging evidence of global perinatal asphyxia.

The retrospective study was performed with data, previously agreed by the study group. In the registry, data are collected prospectively and included in a report file after clinical and video-EEG discussion which takes place monthly. The format for prospective data collection agreed by the study group include: family history, demographic and perinatal data, neonatal neurological examination [15] and neurological examination at follow up [16], EEG background activity and ictal EEG pattern [17], classification of neonatal seizures [9,18,19], status epilepticus [14]. A neonatal seizure was defined as a sudden rhythmic, repetitive, and stereotyped EEG discharge lasting for at least 10 s on two or more EEG channels [9,18,19]; clinical only seizures were not classified as seizures. Status epilepticus was defined as a continuous seizure lasting at least 30 minutes or repeated seizures whose total duration exceeds 50% of one hour EEG tracing [14].

The EEG of each neonate was discussed by the multidisciplinary team of the Study Group including at least two electroencephalographers experts of neonatal EEG. Consensus regarding the definitions of status epilepticus, electrographic seizure and background activity was reached before inclusion in the Registry.

From the report file of each patient, we collected family history of epilepsy, perinatal data, neonatal neurological status, electro-clinical characteristics of neonatal seizures and neuroimaging data. We also inspected follow up data and, in case of diagnosis of post-neonatal epilepsy, we evaluated age at onset of epilepsy, epileptic diagnosis, antiepileptic treatment and response to treatment. Post neonatal epilepsy was defined and classified based on the International Classification of seizures and of Epileptic Syndromes [10,20].