

## Periodic Lateralized Epileptiform Discharges (PLEDs) as Early Indicator of Stroke in Full-Term Newborns

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■ We report on periodic lateralized epileptiform discharges (PLEDs) on EEG in two infants with neonatal convulsions. In both neonates, the EEG abnormalities were seen soon after the onset of seizures, at a time when cranial ultrasound scans were thought to be normal. Subsequent Magnetic Resonance Imaging scans demonstrated cerebral infarction in both patients. In one case, the localisation of the lesion on MRI was concordant with that of the EEG abnormalities, as usually observed in adults with focal lesions. The other infant showed similar EEG abnormalities, but her MRI showed a localised lesion in the basal ganglia, which has also been reported to be involved in the genesis of these abnormalities.

■ Key words: Stroke – Full-term newborn – Neonatal EEG

### Introduction

Until recently, neonatal infarctions were mainly detected in infants who suffered from birth asphyxia or other severe conditions. It is now well recognised that they more commonly occur in infants with no history of birth asphyxia who develop convulsions in the first 2–3 days of life [7]. The lesions cannot always be seen on cranial ultrasound scans at the time when the infants have convulsions. Because of this, the prevalence of strokes has been underestimated in the neonatal period and the diagnosis has been delayed to a later stage or only made if hemiplegia or other neurological abnormalities become evident.

We report on two cases of middle cerebral artery (MCA) infarction in whom the EEG performed soon after the onset of convulsions showed periodic lateralized epileptiform discharges (PLEDs), suggesting the presence of a lesion when it was not seen on cranial ultrasound scans.

### Case Reports

The infants, both female, were born at term by spontaneous vaginal delivery after uneventful pregnancies, with Apgar scores of 9 at one and five minutes; their weights were ad-

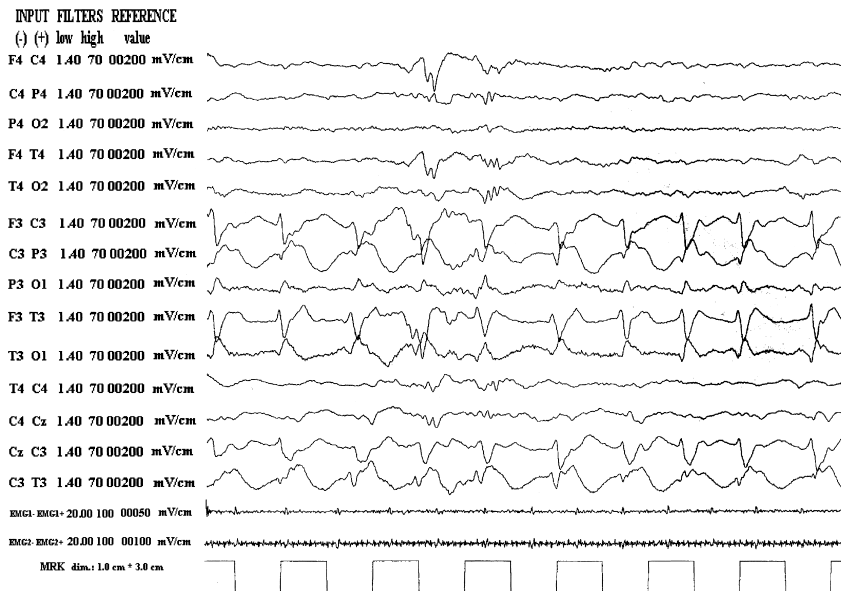
equated for gestational age. Both were thought to be doing well until they developed seizures. Patient 1 developed focal right-sided clonic seizures on day 2 and Patient 2 showed prolonged and recurrent periods of clonic jerking, especially of the left limbs, on day 4. Both infants were treated with phenobarbital and the seizures remitted shortly after therapy was started.

Routine metabolic and infective tests were normal. CSF was also normal.

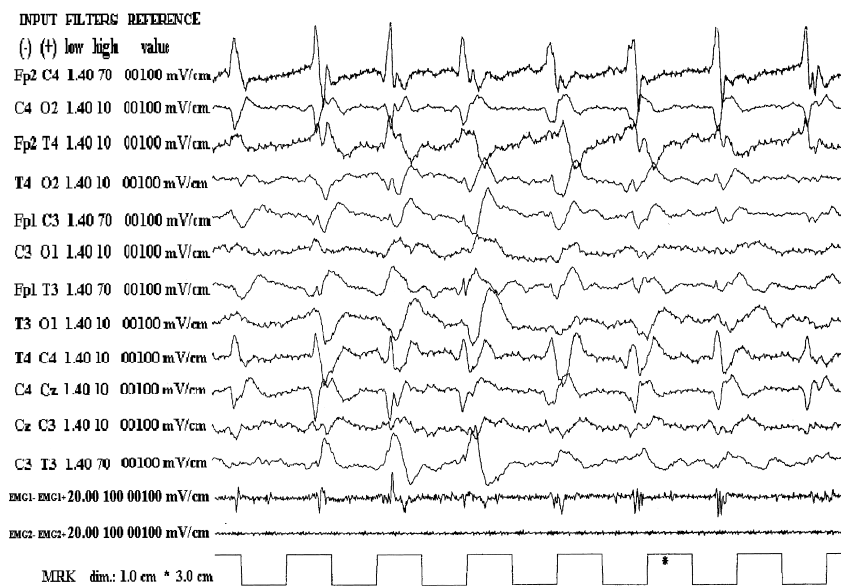
There was no evidence of coagulation disorders on the routine screening (PT, APTT, fibrinogen).

Cranial ultrasound scans, performed soon after the onset of the seizures and the day after that, were thought to be normal. Follow-up scans were performed on day 14 in Patient 1 and on day 7 in Patient 2 and showed localised changes consistent with a focal infarction.

EEG was performed in both cases soon after the onset of seizures using a digital Micromed system (Brain Quick), recording from 11 (Case 1) and 9 (Case 2) bipolar leads. The results showed normal background activity but several electroclinical or electrographic seizures were recorded, with focal onset in the left fronto-central areas in Patient 1 and right central areas in Patient 2, which tended to generalise. In both cases we also found repetitive focal discharges (every 1–2 seconds) consisting of initially negative 150–250 msec sharp biphasic transients, variable in amplitude (50–150 µV) (Fig. 1). The discharges lasted a few minutes and were intermixed with seizures. Clonic jerks were sometimes associated with the periodic spikes. In Patient 1, each periodic spike was followed by high voltage delta wave complexes lasting 1–2 seconds, with superimposed low-voltage alpha rhythm. The duration of periodic discharges was variable, but they were always observed in all the behavioural states recorded. These findings were consistent with periodic lateralized epileptiform discharges (PLEDs), according to the description of Lombroso and Holmes [5].



**Fig. 1 a** EEG and EMG of Case 1: over the left central area, periodic lateralized epileptiform discharges (PLEDs) of biphasic sharp waves, initially negative, of about 200 msec, occurring in 1-second epochs, with a voltage between 50 and 100  $\mu$ V; the spikes are generally followed by a very slow wave, sometimes with superimposed low-voltage alpha.



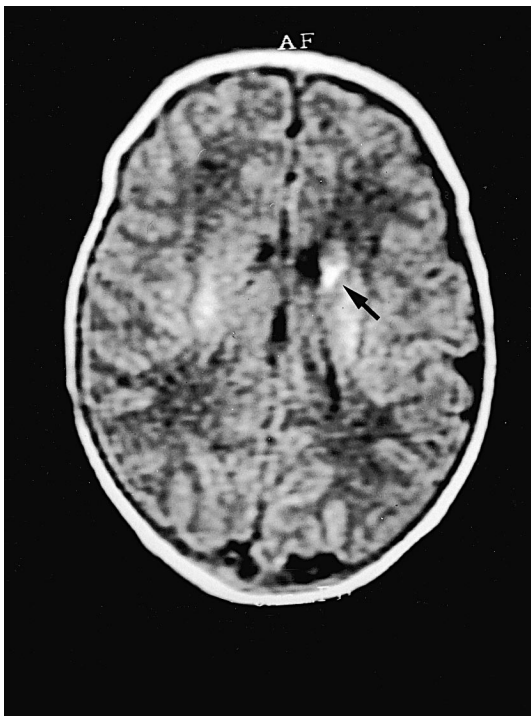
**Fig. 1 b** EEG and EMG of Case 2: repeating discharges of low frequency (1–2 Hz) biphasic sharp waves or alternating sharp and slow waves, lasting 200–300 msec, over the right central area; note the sporadic EMG signal of myoclonus of the left arm, corresponding with the discharges.

MRI was performed on day 14 in Patient 1 and on day 9 in Patient 2 using  $T_1$  and  $T_2$  sequences. Patient 1 showed abnormal signal intensity in the territory of the lenticulo-striate branch of the left middle cerebral artery involving the head of the caudate nucleus and the internal capsule. Patient 2 showed abnormal signal intensity in the parieto-occipital lobes, in the territory of one of the cortical branches of the middle cerebral artery (Fig. 2).

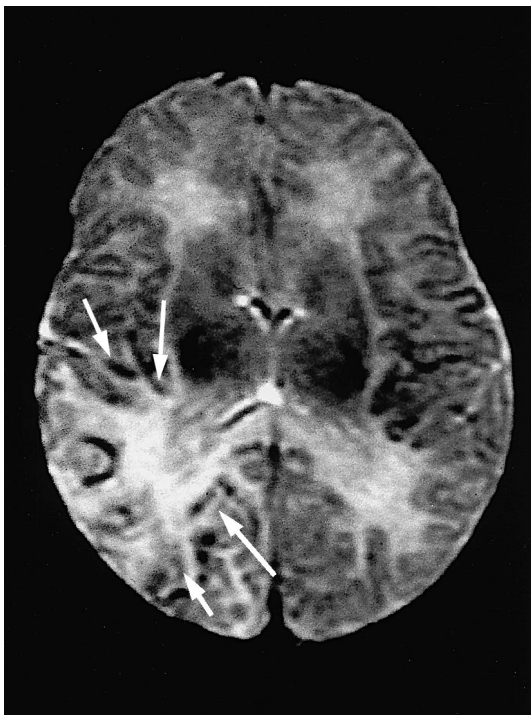
## Discussion

Several studies reported on EEG changes in infants with neonatal cerebral infarction, ranging from focal slowing of background activities to focal spikes and sharp waves, with or without abnormal background activity [2,7]. Newborns with cerebral infarction but normal EEG activity have also been described [7].

Since the description given by Chatrian et al [1] about periodic paroxysms in EEG, PLEDs have been largely studied in adults with acute cerebral diseases or with metabolic disorders. In children and infants, PLEDs are less commonly reported but they have been described in neonates with birth asphyxia [6] or with other brain lesions. Unlike adults, however, neonatal PLEDs are generally not associated with a depressed level of consciousness. The EEG changes observed in our patients were consistent with the patterns described by Chatrian et al [1], Kuroiwa and Celesia [4] and in newborns by Lombroso and Holmes [5]. These consist of repetitive stereotyped discharges of 200 msec occurring every 1–2 seconds, initially negative, biphasic, and with an amplitude of 100–150  $\mu$ V. The periodic patterns were observed during all the behavioural states in agreement with the criteria used by Kuroiwa and Celesia [4]. In agreement with previous studies [6], we also observed clinical or electrographic seizures, independent or superimposed upon simultaneous PLEDs, which did not significantly change



**Fig. 2a** Case 1: axial proton density MRI showing a small left ischaemic lesion as high-intensity lesion (arrow) involving the head of caudate nucleus and the anterior arm of internal capsule.



**Fig. 2b** Case 2: axial scan with spin echos of 3000/100 msec, demonstrating a large right posterior ischaemic area involving the parietal cortex.

the morphology and/or the repetition rate of the periodic pattern.

In Patient 2, the EEG showed periodic sharp waves or sharp-wave and slow-wave complexes, in the central right area, lasting for 200–300 msec. The localisation of the EEG abnormalities in this case was concordant with that of the lesion on MRI, as usually observed in adults. To our knowledge, this is the first description of a focal concordance between PLEDs and lesion in the neonatal period when, probably because of the immaturity of intracortical circuits, focal periodic patterns have been generally found in infants with diffuse or multifocal lesions such as birth asphyxia or herpes simplex encephalitis or cysticercosis [6].

In the other case, the MRI did not show a hemispheric infarction but a localised lesion in the basal ganglia, in the territory of the lenticulo-striate branch of the middle cerebral artery. The presence of PLEDs on the EEG in this case raised the question of their pathogenesis. Previous studies have reported different theories. Although a major role for the cortex has been stressed [1,4], the theory of cortical isolation is contrasted to other hypotheses suggesting that the cause of periodic patterns might lie in the prolonged neuronal recovery cycle of both cortical and subcortical structures. The association of PLEDs and subcortical lesion in one of our patients supports the hypothesis that subcortical structures might play a role in the genesis of PLEDs [10].

In both patients, the EEG abnormalities suggested the presence of the infarction soon after the onset of seizures and several days before cranial ultrasound could detect them. Several studies have already reported that perinatal infarction can be missed on the scan performed on the first days after birth, at the time when the infants develop seizures. Conventional MRI and new sophisticated MRI techniques, such as diffusion-weighted imaging technique, can more frequently detect lesions soon after the onset of seizures, but these techniques are not always easily available. Although EEG is a safe, inexpensive tool and it is easy to perform in full-term infants who do not require intensive care, its routine use in infants with convulsions is still limited. Our results suggest that EEG monitoring should be used in these infants as this would provide information on the electroclinical pattern of the seizures and might help to identify early infants who need further investigations, such as MRI, which are not always part of the routine examination in infants with seizures. Further studies are needed to establish whether PLEDs are a consistent finding in infants with cerebral infarction and to confirm their diagnostic value.

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