

Malignant migrating partial seizures in a 4-month-old boy

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ABSTRACT – Malignant migrating partial seizures in infancy is an epilepsy syndrome characterised by an onset before the age of six months, multifocal seizures and an EEG pattern consisting of seizures which occur independently and sequentially from both hemispheres. The clinical course of a four-month-old boy with this syndrome, illustrated by video material of the seizures and EEG recordings, is described. The possible neurophysiological mechanism of epileptogenic activity alternating or ‘migrating’ from one hemisphere to the other is discussed.

Key words: migrating partial seizures, children

We examined a four-month-old boy with progressive multifocal seizures and an EEG pattern consisting of seizures which occurred independently and sequentially from both hemispheres.

Case study

A four-month-old boy of non-consanguineous parents was referred to our clinic because of frequent epileptic seizures. Except for maternal diabetes gravidarum, the pregnancy was uneventful. At the age of 10 weeks he started to have jerks in the left side of his mouth and left arm and leg whilst turning his eyes to the left. In the beginning, the attacks lasted a few seconds and occurred four times a day. Soon

after, the frequency increased to four times per hour while having similar attacks in the right arm and leg. Valproic acid was prescribed, together with phenobarbital, with no effect on the symptoms. At examination, the baby was healthy with no morphological abnormalities. Neurological examination revealed an absent blink reflex and generalised hypotonia. During examination, complex partial seizures were observed with clonic attacks of the left, right, or both arms and legs. Brain MRI, cerebral spinal fluid, metabolic screening and routine haematological and chemical examination were normal. Genome screening by array and analysis of *SCN1A*, *CDLK5*, *STXBP1*, and *ARX* genes showed no abnormalities. Electroencephalography

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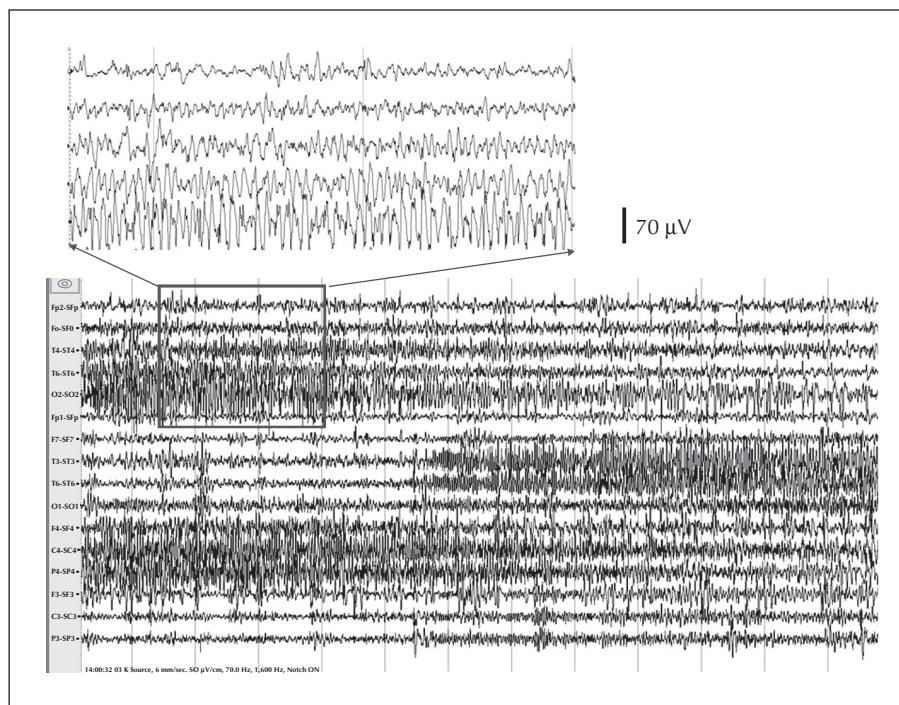


Figure 1. EEG recording at the age of four months shows epileptiform discharges over the right hemisphere, lasting one to two minutes, which terminate and migrate to the left hemisphere. The inset shows the continuous spike discharges in a larger scale. Time scale of the lower panel is five seconds per division.

(EEG) showed initially a symmetric background pattern with diffuse slowing in the posterior areas. Almost continuously, discharges lasting up to a maximum of two minutes were seen over one hemisphere, “jumping” from one side to the other (*figure 1*). The diagnosis “malignant migrating partial seizures in infancy” was established. On examination, one and a half years later, he made noises and demonstrated occasional eye contact. The hypotonia remained unchanged and he was fed using a PEG tube. He still suffered from complex partial seizures despite treatment with phenobarbital, valproic acid, phenytoin, and vagus nerve stimulation. EEG showed multifocal epileptic activity without the typical “jumping”, as seen in earlier recordings.

Discussion

First reported in 1995, the syndrome of malignant migrating partial seizures in infancy is characterised by an onset before the age of six months, multifocal seizures and an EEG pattern consisting of seizures which occur independently and sequentially from both hemispheres (Coppola *et al.*, 1995). Early seizures are mainly focal with rapid secondary generalisation and autonomic manifestations such as apnoea, flushing or cyanosis. After a few months, focal

polymorphous seizures occur 5-30 times a day, or almost continuously for days. Symptoms include lateral deviation of the head, clonic or tonic jerks of one or both limbs on one side, chewing movements, and secondary tonic-clonic generalisation (Coppola, 2009). At the start, EEG shows diffuse slowing with slow waves shifting from one side to the other. Later, the EEG is characterised by focal discharges, typically migrating from a cortical area and expanding to contiguous regions. Seizures develop in different areas of the same or opposite hemisphere with a clear correlation between the topography of the discharges and the clinical features (Coppola, 2009). The seizures are pharmacoresistant in the majority of cases, and most patients either die within a few years or show severe psychomotor retardation (Caraballo *et al.*, 2008). Whether neuropsychological impairment is due to an underlying progressive encephalopathy or to the refractory seizures, is unknown. Neuropathological examination has so far been limited to three cases, of which severe hippocampal neural loss and gliosis was found in two (Coppola *et al.*, 1995; Wilmschurst *et al.*, 2000). No cause has been identified so far.

Given the electroclinical features, migrating focal seizures in infancy is regarded as a specific epileptic syndrome within the category of epileptic encephalopathies (Caraballo *et al.*, 2008). The multifocal propagation of the seizures suggests that the

entire brain is abnormally excitable (Caraballo *et al.*, 2008). The prominent aspect of epileptogenic activity alternating or “migrating” from one hemisphere to the other could be related to the phenomenon of interhemispheric inhibition, the neurophysiological mechanism by which one hemisphere inhibits the other. This inhibition is mediated via a transcallosal pathway. Ni *et al.* found a widely distributed system of interhemispheric inhibition from the motor cortex to the contralateral side through the corpus callosum which was mediated by different neuronal populations in healthy volunteers (Ni *et al.*, 2009). Interhemispheric inhibition is thought to be mediated by postsynaptic gamma aminobutyric acid type (GABA_B) receptors (Irbacher *et al.*, 2007).

In conclusion, the shifting clinical and EEG pattern of convulsions should alert the clinician to the possible diagnosis of this grave and pharmacoresistant syndrome. □

Disclosure.

None of the authors has any conflict of interest or financial support to disclose.

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