

Periventricular nodular heterotopia in adult with temporal epilepsy. *Forensic implications*

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Abstract: Neuronal heterotopias are malformations of neuronal migration, clinically associated with mental retardation, epilepsy and dyslexia. Nodular heterotopias are usually identified in childhood as part of syndromes associating multiple cerebral and systemic malformations. Milder forms may go unrecognized until adulthood when their initial symptoms are usually seizures. We present the case of a 54 years old woman, who is a medical nurse, with temporal lobe epilepsy, with late recognition of her disease. The clinical presentation suggested temporal lobe epilepsy with complex partial seizures, impaired consciousness and motor automatism. Video-EEG has simultaneously recorded the clinical seizure and the ictal paroxysmal discharges. The cause of the temporal epilepsy was proved to be periventricular nodular heterotopia (PVNH).

Key Words: neuronal migration, neuronal heterotopias, complex partial seizures, epilepsy.

Periventricular nodular heterotopia (PNH or PVNH) consist in a collection of cells normally found in the cerebral cortex (heterotopia), abnormally situated in the walls of the lateral ventricles, resembling a collection of lumps or „pearls on a string”, and is a type of cortical dysplasia determined by a migration disorder [1]. The disease has a X-chromosomal inheritance, caused by a deficit of the Filamin 1 gene, being more frequently clinically apparent in females[1].

Neuronal migration represents a process by which millions of neurons “migrate” from their original location (ventricular and subventricular areas) to their definitive positions in the central nervous system, where they shall remain for the entire life.

During first trimester of gestation, post mitotic neurons (that will ultimately reside in the cortex) arise in the periventricular area from which they migrate along the scaffold of radial glia to form the multi-layered cortex (1). Neurons moving up the scaffold must pass through neurons that are already in position in the cortex (“inside-out” lamination); the

most recently arrived neurons reside on the outermost surface forming the cortex [2]. The process continues during the next months of intrauterine life[3]. There are several types of neuronal migration [3]:

a) Radial neuronal migration – described by two models;

- glial-independent (somal translocation) – the neurons are moving continuously;

- glial-dependent (locomotion) – the neurons have a jumping movement pattern, the migrating neurons keep their extensions towards pial surface for guidance.

b) tangential neuronal migration represents a neurophilic process, in which neurons are moving parallel with the brain surface along neuronal axons.

Neuronal heterotopias are malformations of neuronal migration, and are represented by groups of neuronal cells that either:

- did not migrate, remaining in the subependymal region, corresponding to the primitive proliferating area (periventricular heterotopia) or
- have stopped from migration in their way

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towards the cortex surface (subcortical heterotopia) [3].

In neuronal heterotopias, clinical findings of possible functional significance are mental retardation, epilepsy and dyslexia. The degree of neuronal abnormality correlates with the severity of epilepsy and coexistent intellectual deficits [4,5].

Neuroimaging differential diagnosis could be made with tuberous sclerosis (Bourneville disease) – in case which cerebral IRM reveal hamartomatous subcortical lesions and CT identifies periventricular calcific lesions “brain stones” [6].

Periventricular nodular heterotopias are often associated with pharmaco-resistant epilepsy. They are considered part of a dysfunctional network, connected to the overlying cortex. Stereotactic neurosurgery – by radiofrequency lesioning for epileptogenic periventricular nodular heterotopia can reduce the surgical trauma and could be a useful therapeutic method [7].

Case Presentation

We present the case of a 54 years old, woman right-handed. There were no remarkable findings in her personal history from the childhood. She had a normal social and psychic development, and has a high-school

education (she is a nurse). Physical examination is unremarkable. Interictal neurological examination is normal. At 24 years old she experienced her first complex partial seizure.

Her seizures are described as follows:

- arrest(staring);
- keeps saying the same phrase several times with the content inadequate to the situation;
- motor automatisms (e.g. she is continuing to perform her professional activities, as injecting a patient; her patients reported sometimes that she was “distracted” during medical procedures);
- walking during seizure (only sometimes).

During the seizure she is unresponsive, unable to carry out simple commands and she has no recollection of the crisis. The duration of the seizure is two to three minutes. The frequency of seizures has increased in time: from one seizure to several years, up to two a month. She did not report the seizures until they became frequent and the patients reported that she was “distracted” when making the injections.

Interictal EEG was repeated several times and showed discharges of sharp waves and slow electrical activity on bilateral temporal regions. Video EEG monitoring was performed after antiepileptic drug deprivation and 3 complex partial seizures were recorded.

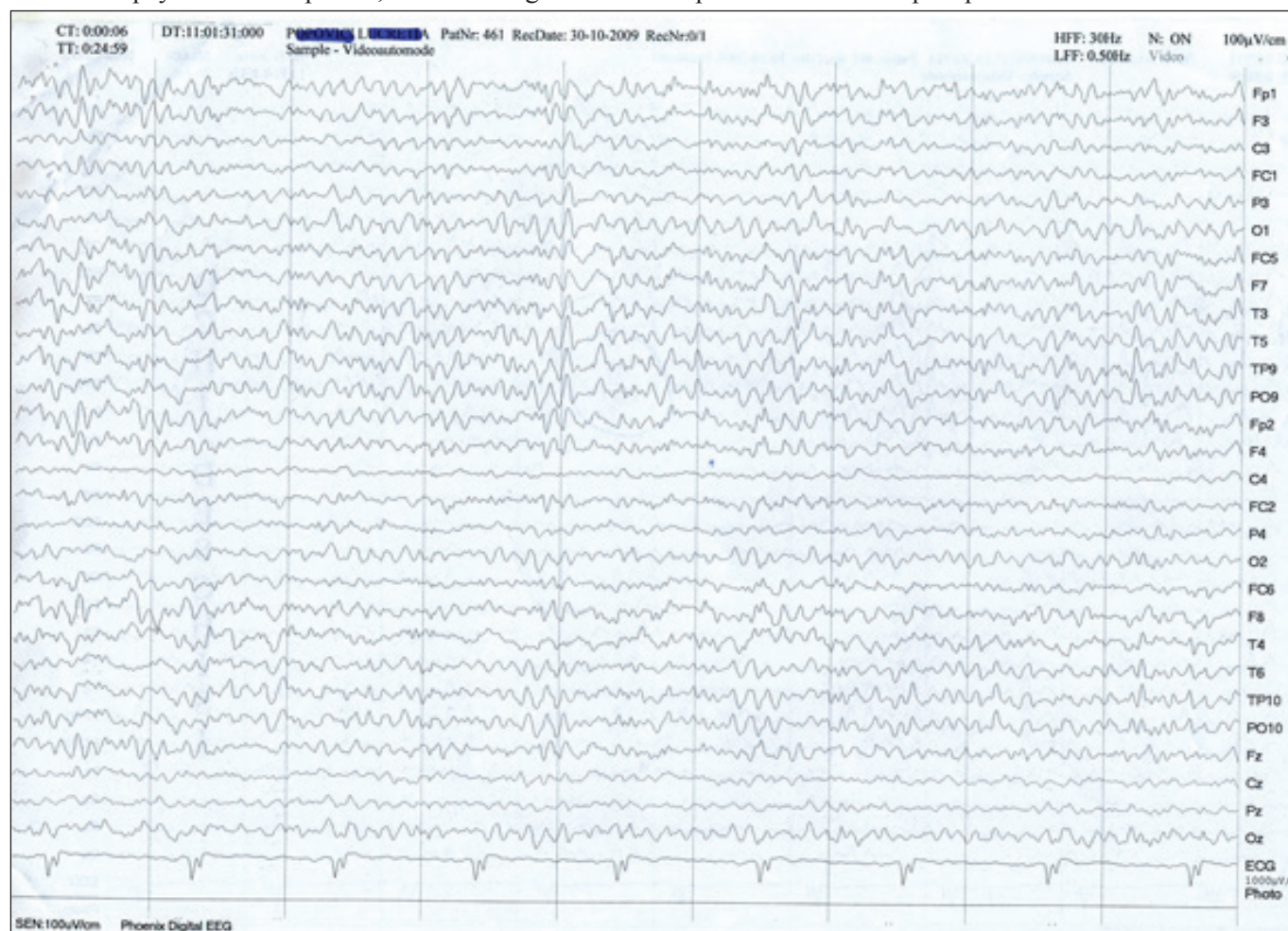


Figure 1. Interictal EEG

Discharges of sharp waves discharges and slowing on bilateral temporal regions.

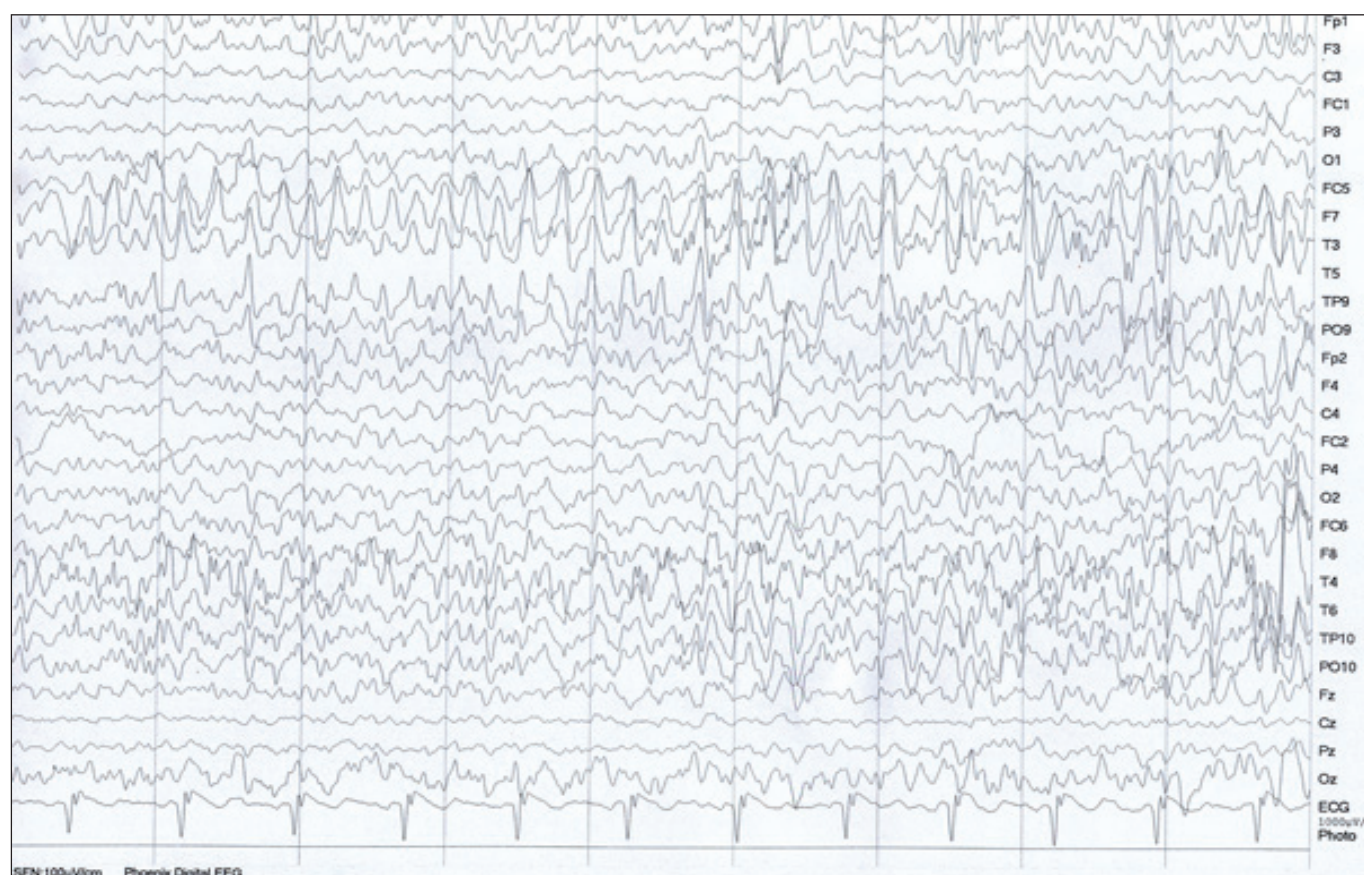


Figure 2. Ictal EEG

Seizure onset at right temporal region with spike-wave discharges.

Ictal EEG showed seizure onset in the right temporal region with spike-wave discharges and slow electrical activity on bilateral temporal regions – mainly to the right at seizure onset with rapid generalization of the slow rhythms.

Neuroradiologic examinations were performed

in order to look for structural lesions. Brain MRI had shown nodular signals of grey matter on T1-weighted images adjacent to lateral ventricle, in the posterior regions, bilaterally – mainly to the right. These MRI findings are suggestive for a periventricular nodular heterotopia (PVNH) [2-3,7]. Also a right parietal schizencephaly is present.

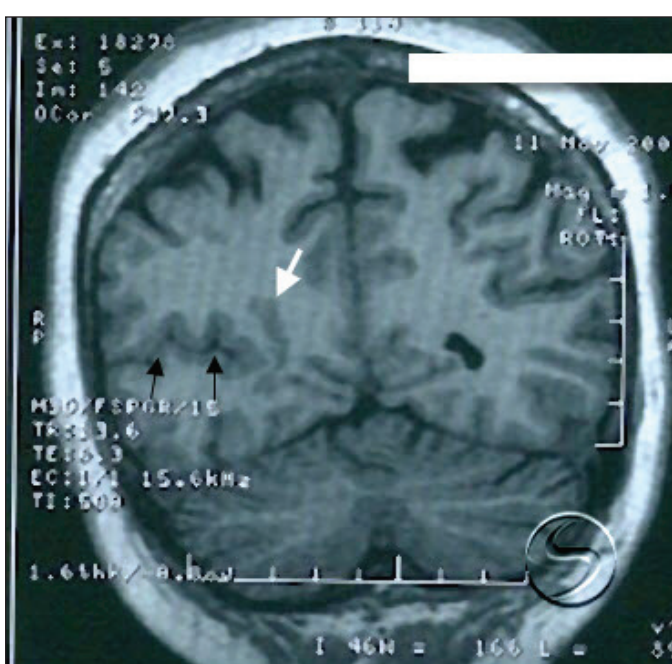


Figure 3 – Cerebral MRI

Nodular signals of grey matter on T1 on cerebral IRM adjacent to lateral ventricle (white arrow), suggestive for a periventricular nodular heterotopia. Also a right parietal schizencephaly is present (black arrows).

Discussions

The patient is a 54 years old nurse, experiencing her first epileptic seizures 30 years ago. She patient did not remember the initial seizures because of their low frequency and mild clinical picture (she did not experienced generalised tonic-clonic seizures), being only recognised later on by the others. During the seizures with motor automatisms she sometimes performed her medical duties (she is continuing to inject the patient). As patients sometimes reportes that she was “distracted” during medical procedures, she consulted to a neurologist. Our patient was “lucky” as long as she had not any malpraxis complaints during these years, but there was the possibility to cause unconscious damage to the patient during the seizures.

The clinical picture suggested temporal lobe epilepsy with complex partial seizures, with impaired consciousness. The semiology of the seizures with speech preservation allowed us to detect the localization of the epileptic focus in the non-dominant hemisphere - right hemisphere, in a right-handed person. Ictal EEG was concordant with this lateralization - showing the seizure onset in the right temporal lobe. It is unclear whether the epileptogenic focus is the nodule, overlying cortex, or both. New techniques as EEG-fMRI and functional connectivity can help identify which of the multiple abnormal regions are epileptogenic in PVNH[6].

As the disease is genetic, even if the diagnosis was made at 54 years old, genetic testing of her offspring could be of importance as it may detect a deficiency of Filamin 1 with potential clinical consequences.

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