

Hippocampal sclerosis and chronic epilepsy following posterior reversible encephalopathy syndrome

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Received April 12, 2013; Accepted October 4, 2013

ABSTRACT – Chronic epilepsy has rarely been reported after posterior reversible encephalopathy syndrome (PRES) and the association with hippocampal sclerosis has been suggested only once before. We report the case of a girl admitted at the age of 8 years with idiopathic nephrotic syndrome. On the second day of admission, she presented with focal complex seizures and cerebral MRI showed posterior encephalopathy and no hippocampal sclerosis. MRI after one month confirmed the diagnosis of PRES. The seizures recurred and the girl developed pharmacoresistant epilepsy and was admitted to our hospital for further investigation. Cerebral MRI three years after the diagnosis of PRES showed hippocampal sclerosis which was not present on the initial MRI. We conclude that there is a triggering role of PRES in the development of hippocampal sclerosis. Hippocampal sclerosis may have resulted from seizure-associated damage, alternatively, hypertensive encephalopathy may have led to hippocampal damage via a vascular mechanism.

Key words: epilepsy, complex partial seizures, hippocampal sclerosis, posterior reversible encephalopathy syndrome

Seizures are common in the acute phase of posterior reversible encephalopathy syndrome (PRES) (74%) (Fugate *et al.*, 2010) and often resolve spontaneously during the first 24 hours (Kastrup *et al.*, 2012). Consequently, chronic epilepsy has been rarely reported in patients with PRES. The possible association between PRES and hippocampal sclerosis (HS) has been suggested only once before (Solinas

et al., 2003). We report an MRI-documented case of a girl who presented with acquired HS and temporal lobe epilepsy after an episode of PRES related to arterial hypertension in childhood.

Case report

Our patient was initially admitted at the age of 8 years with idiopathic

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doi:10.1684/epd.2013.0617

nephrotic syndrome and generalised oedema. The patient was hospitalised for a renal biopsy, after steroid treatment for nephrotic syndrome for three weeks. Hypertension was noted but not treated. On the day of the biopsy, she developed confusion, vomiting and slurred speech, while blood pressure values of 160/120 were recorded. Later that day, she presented with her first seizure which initiated with staring. She then became motionless with subsequent orofacial clonic movements with right side predominance, nystagmus on the right side, and loss of consciousness. The duration of the first seizure was three minutes. The patient received lorazepam which prevented further seizures. She had no history of febrile or afebrile convulsions; pregnancy, birth, and early development were unremarkable. There was no family history of epilepsy or other neurological disorders. Antinuclear antibodies were found to be slightly elevated, but all other laboratory tests were normal and there was no evidence of an immunological disorder.

The cerebral MRI showed hyperintense cortico-subcortical lesions in the parietal lobes on FSET2 and FLAIR-weighted images, compatible with a diagnosis of PRES (*figure 1A*). The hippocampi were unremarkable (*figures 2A and B*). A routine EEG was performed 45 minutes after the first seizure and showed continuous slowing with lateralisation over the left hemisphere with predominance on the left temporal area. The background activity in the right occipital area was normal six days later, but not during the postictal EEG (slowed background). After control of the hypertension, no more seizures occurred. Follow-up MRI, one month later, showed the disappearance of the lesions, in line with the diagnosis of PRES, with intact hippocampi (*figure 1B*).

Sixteen months later, at the age of 9 years and 4 months, seizures recurred and could not be controlled, despite different antiepileptic drug regimens (oxcarbazepine, lamotrigine, valproate, and levetiracetam). The patient presented with two to three seizures per week for several weeks with long intervals of several months without any seizures at all. She never presented with secondary generalised seizures or status epilepticus.

There was no other associated medical condition. Pharmacoresistance was then diagnosed and the patient was referred to our centre for evaluation at the age of 16 years.

The neurological status was normal in this otherwise healthy, right-handed girl. Cerebral MRI, three years after the diagnosis of PRES, confirmed left hippocampal sclerosis (*figures 2C and D*). During long-term video-EEG monitoring, one partial complex seizure with left temporal onset was recorded. The interictal EEG was characterised by frequent left temporal spikes, concordant with hypometabolism of the left temporal lobe, based on FDG-PET. The neuropsychological examination showed a discrete weakness in executive functions, as well as mild difficulties during denomination and verbal memory tests. Left temporal lobe epilepsy, symptomatic of hippocampal sclerosis, was diagnosed and surgical treatment proposed, but, to date, has not yet been performed.

Discussion

To the best of our knowledge, this is the first documented case of secondary hippocampal sclerosis and chronic temporal lobe epilepsy (TLE) related to PRES.

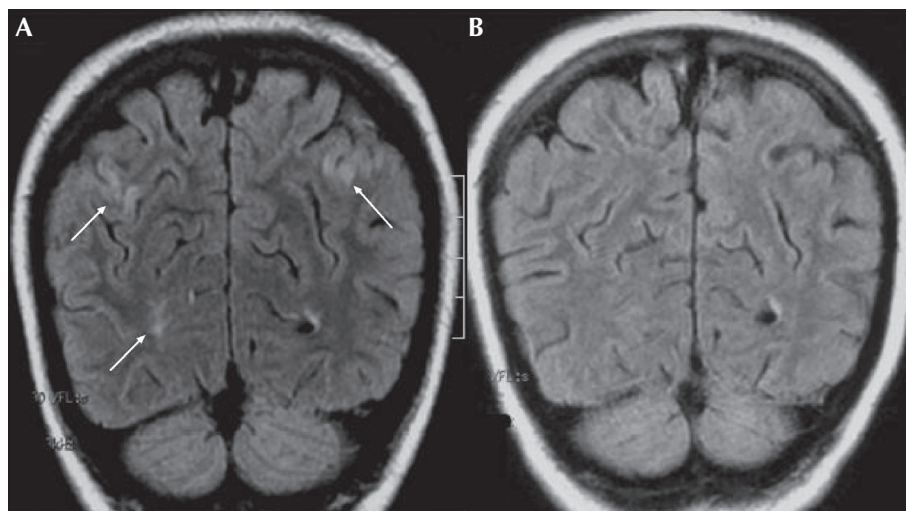


Figure 1. (A) MRI at the time of the PRES episode (at 8 years of age); (FLAIR) hyperintense lesions in the parietal lobes (arrows) are observed, typical of PRES. (B) One month after the PRES episode (FLAIR), there is a disappearance of the posterior lesions. Note: right side of the brain corresponds to the left side of the image.

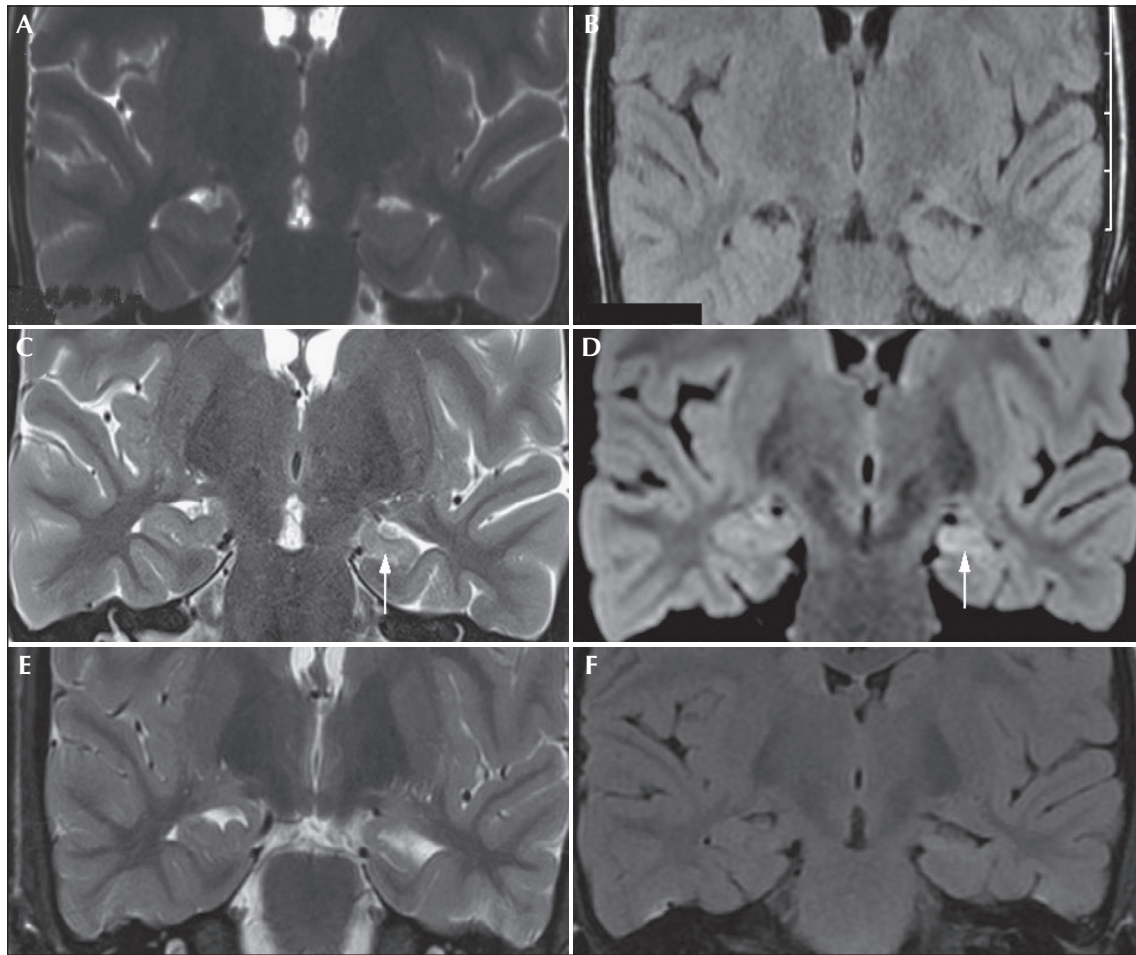


Figure 2. MRI at the time of the PRES episode (at 8 years of age); (A) coronal fast spin echo (FSE) T2-weighted images and (B) coronal fluid-attenuated inversion recovery (FLAIR) weighted images: both hippocampi were intact (no asymmetry, no hyperintensity). (C) and (D) At the age of 11 years, the MRI showed the typical features of hippocampal sclerosis, *i.e.* unilateral (left) volume loss and increased signal intensity on FSE T2-weighted (C) and FLAIR images (D); see arrows. (E) and (F) At the age of 16 years, at admission for epilepsy evaluation, the MRI confirmed the typical features of hippocampal sclerosis, *i.e.* unilateral (left) volume loss and increased signal intensity on FSE T2-weighted (E) and FLAIR images (F). Note: right side of the brain corresponds to the left side of the image.

An association between HS and PRES has been suspected by Solinas *et al.* (2003) who described three patients with TLE following an episode of hypertensive encephalopathy as the only significant antecedent event, as was the case in our patient. However, MRI was not performed during the acute phase in their patients, thus it is not possible to definitively exclude that HS was not already present before. In our case, HS was not observed on MRI during the acute phase, supporting the hypothesis of secondary HS related to PRES, as formulated by Solinas *et al.* (2003).

The pathophysiology of PRES remains unclear but several mechanisms have been proposed. Imaging demonstrates subcortical vasogenic oedema, usually reversible, and it has been proposed that PRES is the result of a breakdown of cerebral autoregulation, hyperperfusion, protein, and fluid extravasation,

leading to vasogenic oedema (Fugate *et al.*, 2010). Hypertensive encephalopathy in our patient may have led to hippocampal damage *via* a vascular mechanism, as suggested by Solinas *et al.* (2003). However, there is growing evidence that the oedema is actually due to a change in vessel autoregulation associated with an endothelial dysfunction, secondary to vasoconstriction, as suggested by reduced blood flow in the affected areas (Bartynski, 2008). Moreover, most patients have a mean arterial blood pressure below the limit of autoregulation (<150–160 mm HG) or no hypertension at all. Since most PRES patients do not develop HS or chronic TLE, our patient and those of Solinas *et al.* (2003) might have also been predisposed to hippocampal damage.

The hippocampus is usually not involved in PRES but the frequency of temporal lobe involvement in

patients with PRES has been reported to be 64% (Fugate *et al.*, 2010). Since cerebral MRI is not performed at later time intervals in patients with PRES, we do not know the incidence of clinically-silent HS.

Unilateral appearance of hippocampal sclerosis following a "bilateral" medical disease has been described in other pathologies, e.g. febrile convulsions (Perez *et al.*, 2000) or limbic encephalitis (Bien *et al.*, 2007), pointing to a susceptibility to asymmetric hippocampal damage, at least in some subjects. Prospective studies in patients with nephrotic syndrome are required to determine if this is a frequent consequence of high blood pressure values in children, similar to the cases of Solinas *et al.* (2003). HS may also be acquired after recurrent seizures or status epilepticus (Briellmann *et al.*, 2001, Wieshmann *et al.*, 1997), however, our patient had only complex partial seizures without secondary generalisation and no status epilepticus.

The occurrence of both PRES and HS in this patient may simply be due to chance, however, the temporal sequence of events suggests a causal relationship. Although we cannot exclude that HS may have resulted from another, yet unknown, mechanism, our case supports a triggering role of PRES in the development of HS, resulting in a typical clinical picture of chronic TLE within three years.

Acknowledgements and disclosures.

This work was supported by the Swiss National Science Foundation (grants n° 3CM30-140338 and n° 33CM30-140332 and n° 141165).

None of the authors has any conflict of interests to disclose.

References

- Bartynski WS. Posterior reversible encephalopathy syndrome, Part 1: Fundamental imaging and clinical features. *AJNR* 2008; 29: 1036-42.
- Bien CG, Urbach H, Schramm J. Limbic encephalitis as a precipitating event in adult onset temporal lobe epilepsy. *Neurology* 2007; 69: 1236.
- Briellmann RS, Newton MR, Wellard M, Jackson G. Hippocampal sclerosis following brief generalized seizures in adulthood. *Neurology* 2001; 57: 315.
- Fugate J-F, Claassen DO, Cloft HJ, Kallmes DF, Kozak OS, Rabinstein AA. Posterior reversible encephalopathy syndrome: associated clinical and radiologic findings. *Mayo Clin Proc* 2010; 85: 427-32.
- Kastrup O, Gerwig M, Frings M, Diener H-C. Posterior reversible encephalopathy syndrome (PRES): electroencephalographic findings and seizure patterns. *J Neurol* 2012; 259: 1383-9.
- Perez ER, Maeder P, Villemure KM, Vischer VC, Villemure JG, Deonna T. Acquired hippocampal damage after temporal lobe seizures in 2 infants. *Ann Neurol* 2000; 48: 384-7.
- Solinas C, Briellmann RS, Harvey AS, Mitchell LA, Berkovic SF. Hypertensive encephalopathy: antecedent to hippocampal sclerosis and temporal lobe epilepsy? *Neurology* 2003; 60: 1534-6.
- Wieshmann UC, Woermann FG, Lemieux L, *et al.* Development of hippocampal atrophy: a serial magnetic resonance imaging study in a patient who developed epilepsy after generalized status epilepticus. *Epilepsia* 1997; 38: 1238-41.