



## Case report

## Focal epilepsy as first symptom in CADASIL

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## ABSTRACT

Recurrent transient ischemic attacks, migraine and dementia represent the principal symptoms of cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy (CADASIL). During the course of the disease, about 10% of patients may experience epileptic seizures, mainly related to the presence of an ischemic stroke. We present a 30-year-old woman with new-onset focal epilepsy leading to the diagnosis of CADASIL. The neuropsychological testing revealed no cognitive impairment. Interictal EEG demonstrated spikes and polyspikes with low amplitude over the right occipital region during NREM sleep. MRI showed white-matter hyperintensities on both hemispheres with confluent lesions at the right parieto-occipital junction, with juxtacortical components. Like in multiple sclerosis, we can suppose that this type of white matter lesions, close to the cortex, may be causative of seizures.

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## 1. Introduction

The phenotypic characteristics of cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy (CADASIL) were precisely described and genetically mapped in the last decade of the XX century.<sup>1</sup> Recurrent transient ischemic attacks migraine and dementia represent the principal symptoms in this systemic vascular disease, caused by mutations in the NOTCH3 gene on chromosome 19p13. During the course of the disease, about 10% of patients may experience epileptic seizures, mainly related to the presence of an ischemic stroke.<sup>2</sup> Rarely, seizures may precede the ischemic events and the cognitive impairment.<sup>3,4</sup> We present the case of new-onset focal epilepsy leading to the diagnosis of CADASIL.

## 2. Case report

A 30-year-old, right-handed woman was referred in our centre in April 2009 for the assessment of new-onset epilepsy. She complained of repetitive stereotyped seizures which had begun 5–6 months earlier. She experienced rising anxiety with unpleasant smell and dizziness without loss of consciousness. The seizures lasted 30–40 s, sometimes were grouped up to 3–4 and were followed by headache and asthenia. Her medical history revealed

frequent headaches lasting some minutes. They did not fit the diagnostic criteria of migraine and they did not require any radiological examination. Her mother had migraine and her maternal grand-father had a stroke at the age of 45 and died 5 years later. Her maternal grand-mother had repetitive deep vein thrombosis of the lower extremities. Nobody in the family suffered from epilepsy. The general and neurological examinations of the patient were normal. The routine biological tests display a slight hypercholesterolemia without any other abnormalities. Levetiracetam was started, 500 mg/d then increased to 750 mg/d and the patient has been seizure-free for 12 months.

Brain MRI showed diffuse white matter hyper intensity (T2-weighted images and FLAIR) in particular at both temporal poles (Fig. 1). A 48 h long term video-EEG demonstrated during NREM sleep the presence of spikes and polyspikes with low amplitude over the occipital regions with a right predominance (Fig. 1). Additional analyses included cardiac echography, thyroid function tests, HIV, TPHA, homocysteine, anti-cardiolipid, anti-nuclear and anti-beta2GPI antibodies and they all resulted normal. The NOTCH3 gene analysis was performed and the typical CADASIL mutation in exon 2 was found. The neuropsychological testing revealed no cognitive impairment. The first cognitive test was normal. Four months later, once the diagnosis was made, slight executive abnormalities were noted (sensibility in the interference and planning failure) but the patient was anxious and depressive.

## 3. Discussion

Epileptic seizures are rarely early symptoms in CADASIL patients. The initial seizures are usually generalized tonic-clonic.<sup>4,5</sup>

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**Fig. 1.** Top: MRI (axial FLAIR and sagittal T2). Typical lesions of CADASIL, especially at both temporal poles. Note the confluent lesions at the right parieto-occipital junction with juxtacortical components. Bottom: EEG (International 10–20 electrode placement system with supplementary anterior/inferior temporal electrodes (TA1, T1, TA2, T2) and EMG (right and left deltoide, chin). Left segment at 15 mm/s and 100 µV/cm. Spike and polyspikes (\*) during NREM sleep over the temporal posterior and occipital regions with predominance on the right side. Right segment, another example at 30 mm/s and 70 µV/cm.

Dichgans et al. found 10 cases with seizures in 102 cases of CADASIL, the age at onset ranging from 23 to 63.<sup>2</sup> In 9 of the 10 patients, seizures had occurred after the onset of stroke. All but one were demented. Nine had generalized tonic-clonic seizures and one focal seizures. In none of the cases, epilepsy took a progressive course. Pooled analysis of 105 CADASIL patients revealed 6 with epileptic seizures: in three of them the seizures were the first symptom.<sup>3</sup>

Our case shows that simple focal seizures can also be an early symptom in patients with CADASIL. Interictal EEG was in favor of a posterior onset of the seizures. The semiology with dizziness and post-ictal headache is concordant with this origin. The seizures quickly propagate toward the medial temporal lobe structures (rising anxiety with unpleasant smell without loss of consciousness). MRI showed white-matter hyperintensities on both hemispheres with confluent lesions at the right parieto-occipital junction, with juxtacortical components. Such white matter

lesions, close to the cortex, may be causative of seizures, like in multiple sclerosis.

#### Conflict of interest

The authors declare no conflicts of interest.

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