Case Report

Recurrent status epilepticus as the primary neurological manifestation of CADASIL: A case report

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Cerebral autosomal dominant arteriopathy with subcortical infarcts and leuкоencephalopathy (CADASIL) often presents with a history of migraine with aura and eventual manifestations of dementia with unrelenting, repeated cerebral vascular insults. Only 6–10% of patients with CADASIL have been reported to develop seizures, and status epilepticus (SE) is exceedingly rare. Here, we describe a patient who presented with recurrent SE, with eventual biopsy diagnosis of CADASIL.

An 80-year-old woman presented to our hospital three times in two years with decreased level of consciousness and subtle intermittent right-sided upper extremity and facial twitching. There was no known significant family history and no past medical history for seizures, stroke, migraine headache, or overt dementia. Electroencephalography revealed recurrent focal seizures with left hemispheric onset and evolution, fulfilling the criteria for focal SE each time. All three admissions required sedation with midazolam to control seizure activity, in addition to high doses of multiple antiepileptic drugs. Brain MRI repeatedly showed extensive abnormalities in the periventricular and deep white matter, subcortical white matter, and bilateral basal ganglia. Skin biopsy was obtained on the third admission, and electron microscopy showed numerous deposits of granular osmiophilic material, which are pathognomonic for CADASIL. Detailed investigations failed to reveal any other etiology for the patient’s condition. This case illustrates the potential for nonconvulsive SE to be the sole manifestation of CADASIL. With the appropriate brain MRI findings, CADASIL should be added to the list of rare causes of SE.

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1. Introduction

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leuкоencephalopathy (CADASIL) is a disease of the vascular smooth muscle typically caused by a mutation of the Notch3 gene [1]. Cerebral autosomal dominant arteriopathy with subcortical infarcts and leuкоencephalopathy often presents with a history of migraine with aura and eventual manifestations of dementia with unrelenting, repeated cerebral vascular insults [1,2]. Diagnoses have been made singularly or by a combination of genetic testing and skin biopsy [1]. Only 6–10% of patients with CADASIL have been reported to develop seizures, and status epilepticus (SE) is exceedingly rare [1–3]. Here, we describe a patient who presented three times in two years with SE of an unknown cause, with eventual biopsy diagnosis of CADASIL.

2. Case report

An 80-year-old woman presented to our hospital three times in two years with a decreased level of consciousness and subtle intermittent right-sided upper extremity and facial twitching. Her past medical history was only significant for well-controlled hypertension, with no history of seizures, migraine headaches, strokes, or overt dementia. There was no known significant family history.

Electroencephalography revealed recurrent focal seizures with left hemispheric onset and evolution, fulfilling the criteria for focal SE each time (Fig. 1). Brain MRI repeatedly showed extensive abnormalities in the periventricular and deep white matter, subcortical white matter, and bilateral basal ganglia (Fig. 2). No acute infarcts were seen. Cerebrospinal fluid studies consistently revealed culture-negative, predominantly neutrophilic pleocytosis (range: 27 to 92). Otherwise, detailed and

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repetitive investigations failed to reveal any clear etiology (metabolic, infectious, inflammatory, paraneoplastic, etc.) for the patient's condition.

All three admissions required sedation with midazolam to control seizure activity in addition to high doses of multiple antiepileptic drugs. The patient made a slow but full recovery after the first and second episodes, following five-week and four-week hospital stays, respectively. The third episode occurred despite the regular intake of antiepileptic drugs (valproate and levetiracetam), and the patient remained minimally responsive afterwards. The patient did eventually require tracheostomy and PEG tube placement and was discharged to a nursing home. Months after discharge, she is still in a nursing home with unimproved mental status.

On the third admission, the extensive MRI changes and recurrent episodes of stupor prompted consideration of CADASIL. Skin biopsy was

Fig. 1. A and B. EEG findings: A: EEG revealed recurrent focal seizures with left hemispheric onset and evolution, fulfilling the criteria for focal status epilepticus. B: Interictal left posterior quadrant sharp waves.
obtained and returned positive; electron microscopic images showed gaps and discontinuities in the perivascular smooth muscle layer with numerous deposits of granular osmiophilic material (Fig. 3). These findings are reported to be diagnostic of CADASIL [1]. Genetic testing was not pursued.

3. Discussion

To our knowledge, this is the first reported case of CADASIL presenting as nonconvulsive SE, without the other typical manifestations. Seizures are seen in a small percentage of patients with CADASIL, but they often follow a stroke and are not typically the first manifestation of the disease [1,2]. Status epilepticus is also very rare in this disease; we found only one published case report of EEG-proven nonconvulsive SE in a patient with established diagnosis of CADASIL [3]. Schon et al. described six patients with CADASIL with a reversible acute encephalopathy; four of them had seizures during their hospitalization. However, their EEG data did not show ictal seizure activity, although the recordings were apparently brief and not continuous [4]. Similar case reports can be found, again lacking adequate EEG data [5,6]. It is possible that the diagnosis of nonconvulsive SE was missed in at least some of these cases, suggesting that this complication of CADASIL is underdiagnosed.

Our case is also peculiar for its late onset. Manifestations of CADASIL usually start in early or mid-adulthood, with gradual accumulation of deficits. However, the phenotypic and prognostic variability has already been emphasized with 14% of biopsy-proven patients over 60 years of age having no disability at all [2]. Also, Mourad et al. reported on 4 patients diagnosed after age 60 [7]. The consistent CSF pleocytosis in this case is unusual for CADASIL [8], but the co-occurrence of SE may be a confounding factor.

This case illustrates the potential for nonconvulsive SE to be the sole manifestation of CADASIL. With the appropriate brain MRI findings, CADASIL should be added to the list of rare causes of SE, regardless of a subject’s advanced age.
Conflict of interest statement

The authors have no conflicts of interest to declare.

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