

Cerebral Hemorrhage in CADASIL: First Report in Entre Ríos

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Abstract

Introduction: CADASIL is a hereditary disease of the cerebral small blood vessels. We describe the case of a patient with diagnosis of CADASIL and intracerebral hemorrhage.

Clinical case: A 47-year-old hypertensive male patient treated with antithrombotic agents, who was diagnosed with CADASIL by skin biopsy and admitted at the emergency department for sudden and intense headache. The MRI showed left occipital intracerebral hemorrhage.

Conclusion: In patients diagnosed with CADASIL, a positive echo-time for microbleeds could avoid the use of antithrombotic agents given the high risk of ICH. Thus avoid further damage to patients with a disease that currently has no specific treatment.

Keywords: Anatomopathology; CADASIL; Echo-time; Intracerebral hemorrhage; Microbleeds

Introduction

CADASIL or Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy is the most frequent hereditary small vessel cerebral arteriopathy. It is caused by mutations in the Notch 3 gene on chromosome 19. It causes an accumulation of the corresponding protein in the smooth muscle cells of the vascular wall, and progressive degeneration of the vessel. This deposit is called GOM in electron microscopy (Globular Osmiophilic Material). The main clinical features of the disease are: recurrent ischemic strokes, migraine and cognitive impairment that evolves into dementia. Other associated symptoms are seizures and psychiatric comorbidities such as: depression, behavioral changes and confusional state episodes. In this work, the case of a CADASIL diagnosed patient with cerebral hemorrhage is described.

Clinical Case

A 47-year-old hypertensive male, medicated with aspirin 100 mg and enalapril 10 mg, having good blood pressure controls since the diagnosis of CADASIL 1 year ago. The diagnosis was performed by skin biopsy showing GOM pathology (Figure 1). The patient was admitted at the emergency department with sudden and intense headache and blurry vision. On the neurological examination, right homonymous hemianopsia was found. Brain MRI in T2 gradient echo sequence shows left occipital intracerebral hemorrhage and multiple microbleeds in basal ganglia (Figure 2).

The patient has as family history associated to CADASIL. His deceased mother, passed away at the age of 65 with a presumptive diagnosis of CADASIL. Six of his eleven maternal uncles had dementia, four of whom died with a diagnosis of Alzheimer's disease. His mother was treated for progressive cognitive impairment, recurrent confusional state episodes and seizures. Prior to her death, a genetic study was performed at The Children's Hospital of Philadelphia, in USA, where exons 2 to 5, 8, 11, 14, 18, 19, 22 and 23 of the Notch 3 gene were amplified by PCR without detecting mutations. The brain MRI of his mother is shown (Figure 3).

The 47-year-old patient evolved favorably with an upper right homonymous quadrantsia, and migraine is well controlled with Valproate Magnesium at a dose of 800 mg daily.

Comments

In contrast to the vascular disease of small vessels of the hypertensive patient, where the association with ischemic and hemorrhagic strokes is clear, the possibility of intracerebral hemorrhage in CADASIL has not been thoroughly evaluated. However, multiple cerebral microbleeds have been reported in 31-69% of patients with this diagnosis [1]. Microbleeds are small focal cerebral hemorrhage on T2 gradient echo sequence representing old hemosiderin deposits and are associated with an increased risk of intracerebral hemorrhage [1,2].

25% of symptomatic patients with CADASIL have intracerebral hemorrhages as an initial manifestation or during the progression of the disease after its diagnosis. Most of these patients are medicated with antithrombotic agents for secondary prevention of stroke. In a recent work [3], it has been found that patients with CADASIL and hypertension have significantly higher prevalence of cerebral infarctions and hemorrhages, and more microbleeds than patients without hypertension [3]. Lian et al. reported a case with spontaneous intracerebral hemorrhage in CADASIL without hypertension but with microbleeds [4]. Hemorrhages are more frequent in patients using antithrombotic agents and in patients who show a high number of microbleeds in T2 gradient echo sequence. It has also been suggested that the neurological prognosis is worse in patients with hemorrhage than in those without hemorrhage [3-5].

A positive T2 gradient echo sequence for multiple cerebral microbleeds could alert the physician not to prescribe antithrombotic agents in a patient with high risk of cerebral hemorrhage. Thus avoid additional damage to patients with an illness which currently has no specific treatment.

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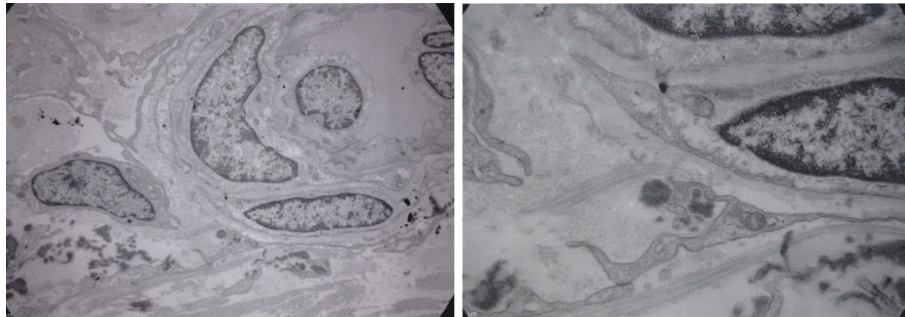


Figure 1: Rounded eosinophilic mass in contact with cells of vessel wall.

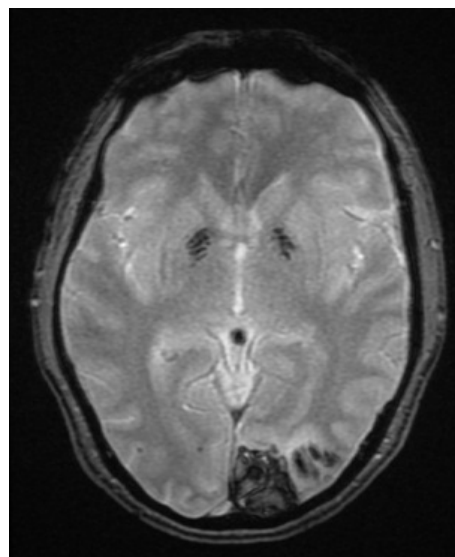


Figure 2: T2 gradient echo sequence shows left occipital intracerebral hemorrhage and multiple brain microbleeds in basal ganglia.

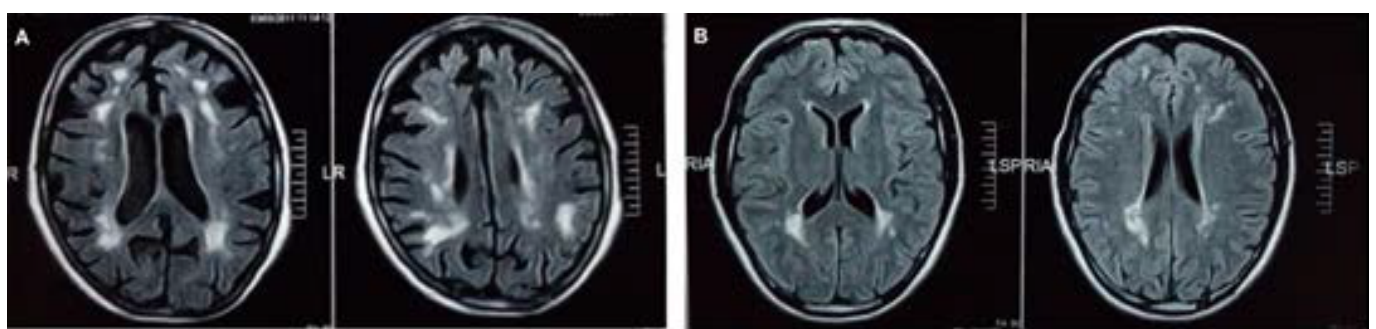


Figure 3: A) Magnetic resonance imaging of the deceased mother. B) Magnetic resonance imaging before bleeding.

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