

Clinical commentary

Cerebellar arteriovenous malformation and vertebral artery aneurysm in a CADASIL patient

Pescini F, Sarti C, Pantoni L, Mangiafico S, Bianchi S, Dotti MT, Federico A, Inzitari D. Cerebellar arteriovenous malformation and vertebral artery aneurysm in a CADASIL patient. *Acta Neurol Scand* 2006; 113: 62–63. © Blackwell Munksgaard 2006.

The presence of large vessels malformations has not been reported in cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL). We describe a CADASIL patient in whom a brain cerebellar arteriovenous malformation was revealed by magnetic resonance (MR) imaging. An MR angiogram documented also an aneurysm along the right intracranial vertebral artery at the junction with the posterior–inferior cerebellar artery. The aneurysm was successfully treated by means of endovascular coil embolization. No neurological complication occurred in our patient during the angiographic procedure. In this case, in addition to an incidental coexistence of CADASIL and large vessels abnormalities, a causal role of the Notch pathway alteration could be hypothesized. Dysregulation of the Notch pathway is linked to several human diseases besides CADASIL. In one of these (the Alagille syndrome) intracranial aneurysms are reported. This hypothesis contrasts however with the absence of similar reports in other CADASIL cases and needs corroboration in large series.

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Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is an inherited non-arteriosclerotic, non-amyloid angiopathy caused by a mutation of the Notch3 gene located on chromosome 19p13.1 (1). Clinically it is characterized by recurrent cerebral ischemic episodes, migraine, psychiatric disturbances, and cognitive deficits (2, 3). On neuroimaging the hallmarks of the disease are subcortical, bilateral hyperintense areas (on T2-MRI sequences), most frequently associated with multiple lacunar infarcts (4). The presence of vascular malformations has not been reported in CADASIL.

Case report

A 26-year-old woman presented for genetic analysis after her mother had been diagnosed with

CADASIL. The patient had suffered from migraine with aura (sensory symptoms) since the age of 10. No other neurological symptoms or signs were present. The genetic analysis revealed a heterozygous mutation C1897T/R607C in exon 11. A cerebral magnetic resonance imaging (MRI) did not reveal white matter changes or subcortical infarcts but showed a large arteriovenous malformation involving the right cerebellar hemisphere (Fig. 1). An MR angiogram documented also an aneurysm along the medial profile of the right intracranial vertebral artery at the junction with the posterior–inferior cerebellar artery. A cerebral angiogram successively performed for therapeutic purpose confirmed the presence of the aneurysm that was successfully treated by means of endovascular coil embolization (Fig. 2). The arteriovenous malformation was not treated because of a high estimated risk/benefit ratio.

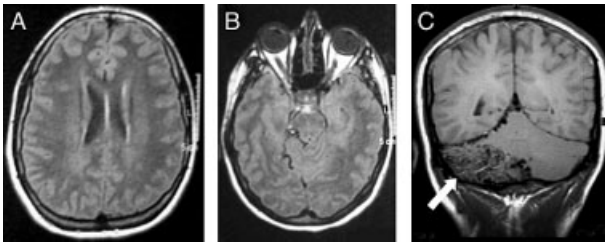


Figure 1. Cerebral MRI: absence of alterations in both periventricular and tempolar pole white matter (A, B); large arteriovenous malformation (arrowed) involving the right cerebellar hemisphere (C).

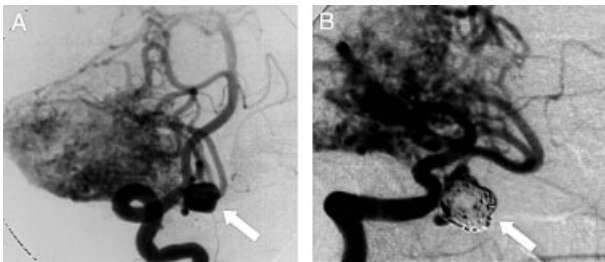


Figure 2. Cerebral digital subtraction angiogram: 10 mm diameter aneurysm (arrowed) along the medial profile of the right intracranial vertebral artery at the junction with the posterior-inferior cerebellar artery (A); exclusion of the aneurysm (arrowed) treated by means of endovascular coil embolization from blood circulation (B).

Discussion

To the best of our knowledge, this is the first report of an arteriovenous malformation associated with an intracranial aneurysm in CADASIL. Considering the large series of CADASIL patients have been reported without similar descriptions, our finding is probably due to chance. Alternatively, Notch3 mutation could have a causal effect on the development of such brain vessel anomalies. Notch3 gene encoded for a transmembrane receptor that is expressed in adults on vascular smooth muscle cells (5). It has been hypothesized that Notch3 mutations induce a conformational change of the receptor interfering with signal transduction and, possibly, with the prevention of apoptosis of vessel smooth muscle cells (6). Moreover, the Notch3 receptor belongs to the Notch signaling pathway, that, according to recent evidence, is involved in multiple aspects of vascular development (7). Dysregulation of the Notch pathway is linked to several human diseases besides CADASIL including the Alagille syndrome, an autosomal dominant developmental disease with systemic disorders and multiple vessel anomalies among

which intracranial aneurysms have been described (8). We could then speculate that Notch3 mutation predisposed our CADASIL patient to vascular abnormalities.

Another interesting point of this report is that no neurological complication occurred in our patient during the angiographic procedure. A few studies have reported a high incidence of focal neurological deficits related to cerebral angiography in CADASIL (9, 10). It has been hypothesized that the structural and functional small vessel alterations predispose to the toxic effects of contrast agents used for angiography (10). It is worthy to note that all the previously reported CADASIL cases with angiographic complications had a moderate-to-severe disease degree on MRI in terms of white matter changes extensions and lacunar infarcts or a history of recurrent cerebral ischemic episodes (9, 10). Conversely, our patient may be considered in the early phase of the disease from both the radiological and the clinical viewpoints. Cerebral angiography in CADASIL patients should only be performed if no other diagnostic or therapeutic means are available.

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