TWO NEW GENETIC MUTATIONS OF CADASIL DISEASE

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BACKGROUND AND AIMS

CADASIL disease is a genetic disease that causes microvascular dysfunction. More than 200 mutations have been described, especially involving cysteine residues.

We present two cases of patients with CADASIL disease due to two new different mutations in NOTCH 3 gene.

METHOD

Case 1: 73-year-old female admitted for an acute lacunar stroke in 2016. The personal history included lacunar infarcts in 1997, 2013 and 2015. Her mother had stroke and dementia and her daughter had migraine. Later on, she developed subcortical cognitive impairment.

Cranial MRI showed multiple chronic ischemic lesions in deep white matter, chronic lacunar infarcts (A), an acute lacunar infarction (B) and thalamic-mesencephalic microbleeds (C):

Cranial MRI. FLAIR sequence. Axial view

Cranial MRI. DWI sequence. Axial view

Cranial MRI. T2 gradient echo. Axial view

Case 2: 61-year-old female consulted for a prolonged episode of migraine. She has a family history of migraine. She had no cardiovascular risk factors nor history of stroke. Cranial MRI showed extensive leukoencephalopathy due to small vessel disease:

Cranial MRI. T2 sequence. Axial view

Cranial MRI. T2 FLAIR sequence. Coronal view

Cranial MRI. T2 FLAIR sequence. Coronal view

RESULTS

Case 1: The molecular NOTCH 3 study showed an heterozygosity mutation 19th exon [c.3748T> C (p.Cys1250Arg)].

Case 2: The molecular NOTCH 3 study showed an heterozygosity mutation 19th exon [c.3875> G (p.Ser1292Cys)].

CONCLUSIONS

These mutations have not been described in molecular databases but the analysis with prediction programs indicates that they are probably pathogenic. Since the clinical and radiological data are highly suggestive of CADASIL disease, we have requested a cutaneous biopsy to confirm the diagnosis and to give genetic counseling. These new pathogenic mutations would enrich the mutation spectrum of NOTCH3 gene.