OBSERVATION

Acute Unilateral Visual Loss as the First Symptom of Cerebral Autosomal Dominant Arteriopathy With Subcortical Infarcts and Leukoencephalopathy

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Background: Although cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is considered a cerebrovascular disorder with almost exclusively neurological symptoms, the arteriopathy is generalized and involves choroidal and retinal vasculature as demonstrated by fluorescein angiographic and ocular electrophysiological abnormalities. The occurrence of acute visual loss due to nonarteritic anterior ischemic optic neuropathy (NAION) has not previously been reported in CADASIL.

Objective: To describe acute visual loss due to NAION as a possible manifestation of CADASIL.

Patients and Methods: The patient was a 60-year-old man with subcortical diffuse leukoencephalopathy, multi-infarct dementia, tetraparesis, visual loss, and a family history of stroke. We performed clinical and neuro-ophthalmological evaluation, electrophysiological assessment, brain magnetic resonance imaging, and genetic screening for mutations or small deletions of the *Notch3* gene, (causing CADASIL).

Results: The patient's first symptom was acute visual loss in the right eye due to NAION at age 27 years, in absence of the common cardiovascular risk factors and before any neurological impairment. The patient was re-evaluated at age 60 years, and neuro-ophthalmological examination showed optic disc atrophy in the right eye with arteriolar narrowing and a reduction in visual acuity in the left eye. Fluorescein angiography of the right eye showed evidence of persistent peripapillary hypofluorescence with a retinal pigment epithelial windows defect in the inferior temporal area. Pattern reversal visual evoked potentials were abolished in the right eye. The P100 latency of the left eye was delayed and reduced in amplitude. The diagnosis of CADASIL was confirmed by molecular analysis (heterozygotes for the C406T mutation on exon 3 of the *Notch3* gene). There was a family history of cerebrovascular disorders and ocular impairment.

Conclusions: Visual loss due to transient or stable ischemic events involving the optic nerve head should be considered in the CADASIL phenotype. The possibility of CADASIL should also be evaluated in patients with NAION who do not have cardiovascular risk factors but do have a family history of stroke.

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CEREBRAL AUTOSOMAL dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is an inherited small artery disease[1] due to mutations of the *Notch3* gene at chromosome locus 19p13.[2,3] The *Notch3* gene encodes for a large transmembrane receptor protein, which in adults is expressed only in vascular smooth muscle cells. Gradual accumulation of the extracellular domain of the receptor protein leads to progressive loss of function of these cells with subsequent wall thickening and lumen narrowing in small and medium-sized penetrating arteries.[4] Although the symptoms of CADASIL are almost exclusively neurological, vascular abnormalities are not limited to the cerebral arterioles but are observed in the small arteries of almost all organs.[5] Symptoms appear at ages 30 to 50 years, beginning with transitory ischemic attacks or strokes, migraine, mood disturbances, and seizures and progressing to severe motor disability, dementia, and premature death.[6] Although the clinical picture can vary greatly and differences in the onset and progression of symptoms have been reported in affected members of the same family,[7] acute visual loss is not usually included in the classical phenotype.