ORIGINAL CONTRIBUTION

Hemodynamic Evaluation of the Optic Nerve Head in Cerebral Autosomal Dominant Arteriopathy With Subcortical Infarcts and Leukoencephalopathy

Alessandra Rufa, MD; Maria Teresa Dotti, MD; Paolo Frezzotti, MD; Nicola De Stefano, MD; Aldo Caporossi, MD; Antonio Federico, MD

Background: Although cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is considered a cerebrovascular disorder with almost exclusively neurological symptoms, arteriopathy is generalized and also involves the choroid and retina.

Objective: To study optic nerve head microvascular function in CADASIL by assessing blood flow, volume, and velocity with a retina flowmeter.

Patients and Methods: Scanning laser Doppler flowmetry permits the noninvasive assessment of relative blood velocity, volume, and flow in a sample volume of either retina or anterior optic nerve head. Measurements were performed in a first group of 9 eyes of 5 patients with CADASIL and a second group of 8 eyes of 4 healthy subjects. Hemodynamic parameters were computed in 4 quadrants of the optic disc (superior nasal, superior temporal, inferior nasal, and inferior temporal). The Wilcoxon rank sum test was used to assess differences in relative flow, volume, and velocity in each quadrant and between the 2 groups and differences in overall optic nerve head blood flow, volume, and velocity.

Results: Patients with CADASIL had a significant decrease in overall blood flow and volume compared with healthy subjects ($P < .05$). The reduction in blood flow and volume was particularly significant in the superior and inferior temporal quadrants. No significant differences were found nasally between the patients and the control groups.

Conclusion: Our results suggest that hemodynamic parameters are abnormal in the superficial nerve fiber layer of the optic nerve head of patients with CADASIL, especially in the temporal quadrants of the neuroretinal rim.

Arch Neurol. 2004;61:1230-1233

CEREBRAL AUTOSOMAL dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is an inherited late-onset brain arteriopathy.[1] Symptoms usually appear at 30 to 50 years of age and are characterized by recurrent transient ischemic attacks, stroke, migraine, psychiatric disorders, and seizures, progressing to severe motor disability, subcortical dementia, and premature death.[2] The disease is caused by mutations or small deletions in the Notch 3 gene.[3] In adults, Notch 3 is only expressed in vascular medial smooth muscle cells. Progressive accumulation of the extracellular domain of Notch 3 at the surface of medial smooth muscle cells of arterioles, capillaries, and venules leads to degeneration of smooth muscle cells and progressive adventitial fibrosis of brain vessels.[4]

Vascular abnormalities in CADASIL are not limited to the cerebral arterioles but are also observed in systemic arterioles,[5] including those in the retina[6] and optic nerve head.[7] Optic nerve and retinal vascular hemodynamic changes have not yet been investigated. The Heidelberg Retina Flowmeter (HRF) (Heidelberg Engineering, Dossenheim, Germany) is a noninvasive and standardized method for retinal or optic nerve head blood flow measurement. Reproducibility and reliability of the HRF measurements have been documented extensively.[8] The aim of this study was to assess optic nerve head blood flow, volume, and velocity using an HRF in 9 eyes of 5 patients with genetically confirmed CADASIL and in 8 eyes of 4 healthy, age-matched controls.

Author Affiliations: Departments of Neurological and Behavioural Sciences (Drs Rufa, Dotti, Federico, and De Stefano) and Ophthalmology and Neurosurgery (Drs Caporossi and Frezzotti), Medical School, University of Siena, Siena, Italy.

METHODS

PATIENTS AND CONTROLS

A first group of 9 eyes of 5 patients with genetically confirmed CADASIL (5 men; 3 symptomatic, 2 asymptomatic; mean age, 38.8 years; range, 27-50 years) and a second group of 8 eyes of 4 healthy age- and sex-matched, nonsmoker control subjects (3 men, 1 woman; mean age, 40 years; range, 29-55 years) were enrolled in the study. None of the subjects had any other systemic, vascular, or ocular pathologic features or had under-