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Abstract

BACKGROUND: Mutations in the Notch3 gene are the cause of CADASIL, a hereditary small vessel disease leading to stroke and vascular dementia. The disease is characterized by ultrastructural granular deposits within small arterial vessels and degeneration of vascular smooth muscle cells. Yet, little is known about endothelial function in CADASIL. Vasoreactivity induced by L-arginine, which is the substrate for endothelial nitric oxide synthase, is a parameter of endothelial function and has been shown to be altered in patients with cerebrovascular disease.

METHODS: To assess endothelial function in CADASIL, L-arginine-induced vasoreactivity was studied in 25 CADASIL subjects and 24 non-CADASIL control subjects without previous history of cerebrovascular disease by transcranial Doppler sonography of the middle cerebral artery.

RESULTS: Resting mean flow velocity was significantly reduced in patients (43.7 +/- 14.5 cm/s) compared to controls (57.0 +/- 10.4 cm/s) [p < 0.001]. Patients exhibited a significantly higher pulsatility index (PI = 0.94 +/- 0.19) than control subjects (PI = 0.79 +/- 0.11) [p < 0.01]. L-arginine-induced vasoreactivity was significantly increased in patients (36.1 +/- 15.5 %) versus controls (27.9 +/- 8.5 %) [p < 0.05]. In patients, there was a significant reduction of the PI following L-arginine application (PI = 0.86 +/- 0.13) compared to resting PI [p < 0.01].

CONCLUSIONS: Our results may indicate a pathogenic role of impaired cerebral hemodynamics and endothelial dysfunction in CADASIL. Our finding of enhanced L-arginine vasoreactivity might have therapeutic implications for CADASIL and sporadic small vessel disease.

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