Pathogenesis of cervical artery dissections: association with connective tissue abnormalities.


Department of Neurology, University of Heidelberg, Germany. tobias_brandt@med.uni-heidelberg.de

BACKGROUND: The etiology of spontaneous cervical artery dissection (CAD) is largely unknown. An underlying connective tissue disorder has often been postulated. OBJECTIVE: To further assess the association of CAD with ultrastructural abnormalities of the dermal connective tissue. METHODS: In a multicenter study, skin biopsies of 65 patients with proven nontraumatic CAD and 10 control subjects were evaluated. The ultrastructural morphology of the dermal connective tissue components was assessed by transmission electron microscopy. RESULTS: Only three patients (5%) had clinical manifestations of skin, joint, or skeletal abnormalities. Ultrastructural aberrations were seen in 36 of 65 patients (55%), consisting of the regular occurrence of composite fibrils within collagen bundles that in some cases resembled the aberrations found in Ehlers-Danlos syndrome type II or III and elastic fiber abnormalities with minicalcifications and fragmentation. A grading scale according to the severity of the findings is introduced. Intraindividual variability over time was excluded by a second biopsy of the skin in eight patients with pronounced aberrations. Recurrent CAD correlated with connective tissue aberrations. In addition, similar connective tissue abnormalities were detected in four first-degree relatives with familial CAD. CONCLUSION: CAD is associated with ultrastructural connective tissue abnormalities, mostly without other clinical manifestations of a connective tissue disease. A structural defect in the extracellular matrix of the arterial wall leading to a genetic predisposition is suggested. The dermal connective tissue abnormalities detected can serve as a phenotypic marker for further genetic studies in patients with CAD and large families to possibly identify the underlying basic molecular defect(s).

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