Cerebrovascular disease in Ehlers-Danlos syndrome

K Hegedus

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Letter to the Editor

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Cerebrovascular Disease in Ehlers-Danlos Syndrome

To the Editor:

Schievink et al[1] describe two patients who suffered from Ehlers-Danlos syndrome type IV. One patient developed spontaneous dissection of the internal carotid artery and the other subarachnoid hemorrhage from rupture of an aneurysm. Collagen type III analysis in cultured skin fibroblasts revealed partial deficiency in both patients. The authors suggest that collagen type III deficiency plays a role in the pathogenesis of both saccular and dissecting aneurysms, while emphasizing that associated carotid artery dissection has not been reported previously.

I have previously observed[2-4] a partial lack of reticular fibers, considered to consist of type III collagen,[5-7] in the major intracranial arteries of patients with saccular, fusiform, and dissecting aneurysms. In cases of intracranial dissecting aneurysm, the reticular fiber deficiency was most pronounced close to the internal elastic lamina[4]; in the other cases, the partial lack of reticular fibers was diffuse or restricted to the outer part of the muscular layer.[2,3] Ostergaard et al[8] also confirmed that the arteries of patients with berry aneurysms are more deficient in reticular fibers in the intracranial than in the extracranial arteries. Using computerized densitometric investigation (unpublished observations), we found that the amount of reticular fibers in the major intracranial arteries of patients without vascular disease is 76.2±6.2% (mean±SD). The intracranial arteries of patients with berry aneurysms contain 50.5±5.9% reticular fibers, and those with dissecting aneurysms 52.3±5.1%. The difference between these and patients without cerebrovascular diseases is strongly significant ($p<0.001$, Student's t test).

It is noteworthy that the intracranial arteries of patients with cerebrovascular disease associated with bleeding also contain reduced amounts of reticular fibers. In addition to patients with aneurysms, this group includes patients with unexplained subarachnoid hemorrhage[9] and premature[10] as well as mature[11] newborns with intracranial hemorrhage.

On the basis of these observations, we have already suggested that the partial lack of reticular fibers, that is, the collagen type III deficiency, is an important predisposing factor in the development of saccular, fusiform, and dissecting aneurysms,[2-4] as well as in the occurrence of unexplained subarachnoid hemorrhage[9] and intracranial hemorrhage of premature[10] and mature[11] newborns. We believe that these vascular diseases are various manifestations of the same underlying structural disorder.

Simultaneous use of the silver impregnation method and collagen type III analysis is needed to answer the question of whether collagen type III entirely corresponds to the reticular fibers. The silver impregnation method is easy to perform and can be made quantitative so that it is also appropriate for early detection of vascular anomalies.

Katalin Hegedüs, MD
Department of Neurology and Psychiatry
University Medical School
Debrecen, Hungary

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