Collagen Deficiency in Cerebral Aneurysms

To the Editor:

It has been suggested that some patients with cerebral aneurysms may have a relative deficiency of type III collagen.\(^1\) Such a deficiency would suggest that cerebral aneurysms are genetically determined. If type III collagen deficiency is important in the etiology of cerebral aneurysms, such deficiency should be demonstrable in patients with a clear family history of cerebral aneurysms and in patients with multiple aneurysms. To test this hypothesis, we established skin fibroblast cell cultures of four female patients who had a total of 12 cerebral aneurysms. Patient 3’s mother had two cerebral aneurysms, and one of her sisters had one cerebral aneurysm. The secreted procollagen chains were analyzed and quantified by sodium dodecyl sulfate-polyacrylamide gel electrophoresis.\(^4\) Studies were performed in duplicate on two separate cultures. Three control cell lines, as well as cell lines from a patient with Ehlers-Danlos type IV (E-D IV) syndrome, were analyzed simultaneously and in duplicate. Visual inspection of medium proteins labeled with \(^{3}H\) proline (LKB ultrascans XL microdensometer) revealed no difference between controls and aneurysm patients, whereas the E-D IV patient had a clear deficiency of pro-\(\alpha(Ill)\). These observations were confirmed by the quantitative data shown in Table 1.

Our data do not support the hypothesis that the familial or multiple cerebral aneurysms in our patients were caused by a genetically determined deficiency of type III collagen and therefore cast doubt upon the necessity of invoking such a deficiency genetically determined. If type III collagen deficiency is important in the etiology of cerebral aneurysms, such deficiency should be demonstrable in patients with a clear family history of cerebral aneurysms and in patients with multiple aneurysms. To test this hypothesis, we established skin fibroblast cell cultures of four female patients who had a total of 12 cerebral aneurysms. Patient 3’s mother had two cerebral aneurysms, and one of her sisters had one cerebral aneurysm. The secreted procollagen chains were analyzed and quantified by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. Studies were performed in duplicate on two separate cultures. Three control cell lines, as well as cell lines from a patient with Ehlers-Danlos type IV (E-D IV) syndrome, were analyzed simultaneously and in duplicate. Visual inspection of medium proteins labeled with \(^{3}H\) proline (LKB ultrascans XL microdensometer) revealed no difference between controls and aneurysm patients, whereas the E-D IV patient had a clear deficiency of pro-\(\alpha(Ill)\). These observations were confirmed by the quantitative data shown in Table 1.

Our data do not support the hypothesis that the familial or multiple cerebral aneurysms in our patients were caused by a genetically determined deficiency of type III collagen and therefore cast doubt upon the necessity of invoking such a deficiency to account for the formation or rupture of sporadic aneurysms. This is further supported by the paucity of reports of cerebral aneurysms in patients with E-D IV, who often have a marked deficiency of type III collagen.\(^5\) Our data do not exclude the presence of posttranslational collagen defects.

It has been suggested that measuring type III collagen content in cultured skin fibroblasts may be an alternative to angiography for detecting relatives at risk for the presence of familial cerebral aneurysms. Our data (Patient 3, Table 1) show that familial cerebral aneurysms can coexist with normal type III collagen levels and with a normal collagen type III:I ratio. We, therefore, conclude that skin biopsy for collagen analysis is not an adequate screening procedure by which to exclude the presence of cerebral aneurysms in family members at risk. This can be achieved only by four-vessel cerebral angiography.

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