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Reticular Fiber Deficiency in the Intracranial Arteries of Patients with Dissecting Aneurysm and Review of the Possible Pathogenesis of Previously Reported Cases

Katalin Hegedüs

Department of Neurology and Psychiatry, University Medical School of Debrecen, H-4012 Debrecen, Hungary

Summary. The pattern of reticular fibers in the tunica media of the major intracranial arteries was investigated in two patients with dissecting aneurysm. In numerous circumscribed areas, the reticular fibers were absent close to the internal elastic lamina in all major arteries of each patient. It is suggested that the subintimal deficiency in reticular fibers results in insufficient fixing of the tunica intima to the media contributing to their separation when the internal elastic lamina becomes defective. The presumed etiologies of the previously reported cases are reviewed and the possible origin of the deficiency in reticular fibers is discussed.

Key words: Dissecting aneurysm – Intracranial arteries – Reticular fibers

Introduction

Intracranial dissecting aneurysms are rare, although recently it has been recognized more and more as the cause of cerebrovascular diseases, predominantly in younger individuals (< 40 years) [29]. Mostly, the plane of dissection occurs between the internal elastic lamina and the tunica media. This differs from the aorta and other extracranial arteries, where the hemorrhage is commonly found within the media or adventitia. This type of dissection is infrequent in cerebral arteries, it was observed in approximately one-fifth of the reported cases.

The pathogenesis of cerebral dissecting aneurysms is poorly understood. Dissection has been observed within different pathologic conditions. In several reports, however, no definite cause of dissection could be determined [5, 7, 19, 23, 30, 34, 35, 57]. As the amount and distribution of reticular fibers has not yet been investigated in patients with intracranial dissecting aneurysms, we present its pattern in the major intracranial arteries of two patients with subintimal hemorrhage reported previously [21, 30].

Material and Method

All major intracranial arteries of two patients with subintimal dissecting aneurysm were investigated with Gömöri's method for reticulin. One was a 13-year-old boy with dissecting aneurysm of the right carotid and middle cerebral arteries. The other was a 47-year-old man with dissection of the basilar and both vertebral arteries. Case reports have already been published [21, 30].

Samples were taken from the major branching sites and 3 to 5 mm proximal or distal from them. The blocks were serially sectioned, and stained with hematoxylin-eosin, elastic-van Gieson, orcein, trichrome, and PAS.

Results

In the intracranial arteries of the 47-year-old man, various pathologic changes of the internal elastic lamina were observed in the nondissected arteries, especially at the branching points. The findings were similar to those observed in the intracranial arteries of the 13-year-old boy. The degree of intimal proliferation corresponded to the changes considered characteristic of aging.

In contrast to arteries of patients without vascular diseases (Fig. 1), using Gömöri's method for reticulin, numerous areas of various size without reticular fibers were seen next to the internal elastic lamina (Figs. 2 and 3). In the other parts of the muscular layer, the reticular fibers were often irregular and coarser than usual, especially in the arteries of the 47-year-old man. In some places these fibers were also sparse in the outer part of the media (Fig. 4). The changes mentioned above could be found in all major intracranial arteries of each patient. In each artery, however, the segments without reticular fibers alternated with segments with a relatively well-preserved reticulin pattern (Fig. 4).

Discussion

According to Yonas [64] the comparatively rare dissection within the tunica media or adventitia of the arteries supplying the brain may derive from rupture either of vasa vasorum or new vessels which form in the necrotic media. In the absence of necrotizing processes, the vessel lumen is the only source of subintimal hemorrhage in the intracranial arteries, since these arteries generally lack vasa vasorum [54, 64]. However, in severe atherosclerosis the intracranial arteries may also contain vasa vasorum [54].

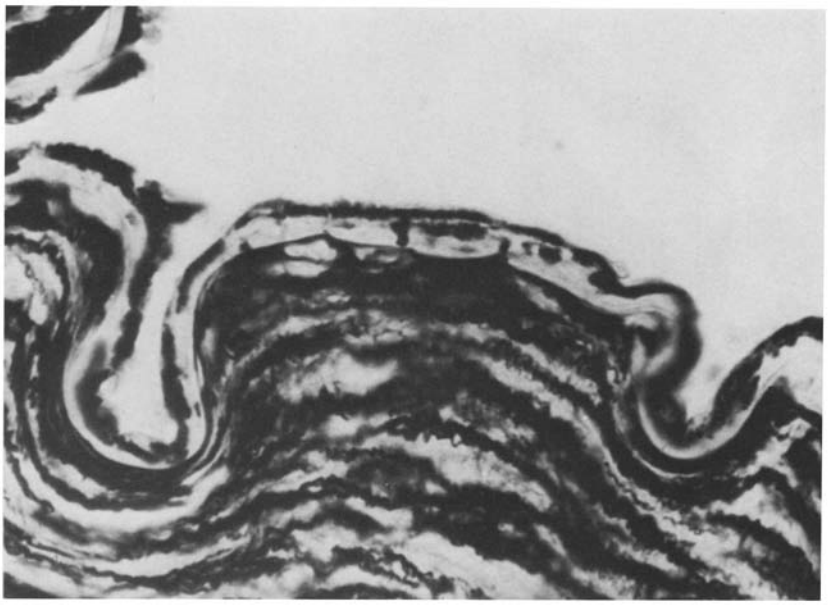

Fig. 1. The basilar artery of a 39-year-old man without vascular disease. Normal pattern of reticular fibers. The reticular fibers accompanying both sides of the elastic lamina are interconnected through the fenestrae. Gömöri's method for reticulin × 400

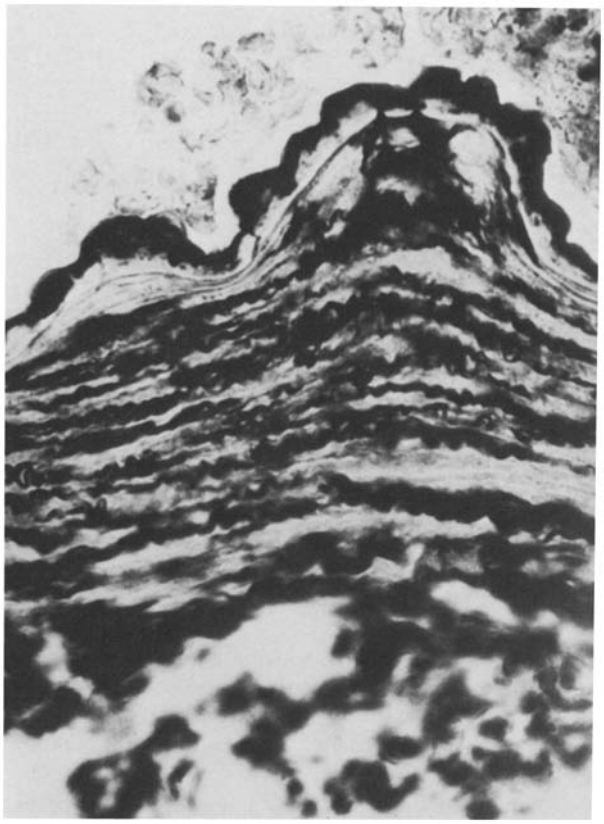

Fig. 2. The basilar artery of a 13-year-old boy with dissecting aneurysm of the right internal carotid and middle cerebral arteries. In small areas the reticular fibers are absent close to the medial side of the internal elastic lamina. Gömöri's method for reticulin × 400.

In cases of medial dissection of intracranial arteries mucoid or cystic medial degeneration [20, 29], idiopathic medial necrosis [42], and nonspecific arteritis [17, 64] have been identified as underlying disorders. In other cases atherosclerosis [1, 3, 43] and surgical trauma [6, 46] have been considered to be responsible for the development of intramural hemorrhage.

Subintimal dissection has also been observed in several pathologic processes of cerebral arteries including syphilis [55, 56, 58], nonspecific arteritis [11, 51], cystic medial degeneration [60, 61], fibromuscular dysplasia [26, 32, 40, 44], and Moya Moya disease [63]. Its association with Marfan syndrome [4] and homocystinuria [10, 18] have also been noted.

In many cases with subintimal dissection, various changes of the internal elastic lamina such as splitting, fraying, reduplication, focal absences, and irregular thickening have been described [2, 5, 10, 16, 21, 23, 31, 33, 40, 61, 62]. Several authors have assumed that alterations of the elastic lamina play an important role in the development of subintimal bleeding [4, 16, 21, 38, 41, 63].

The so-called congenital defects in the media are thought to be the morphologic basis of dissection by Wolman [62] and Nedwich [30]. However, medial discontinuities and various changes of the internal elastic lamina are common at the bifurcation and branching sites of the cerebral arteries, especially with increasing age [54]. Atherosclerosis has also been implicated in the pathogenesis of subintimal dissecting aneurysm [9, 12, 48]. It is well-known intramural hemorrhage or rupture of atheroma frequently occurs in atherosclerotic arteries [54]. Nevertheless, these circumscribed intramural hemorrhages only rarely develop into dissecting aneurysm [28].

Besides the morphologic changes of the vessel wall, the dissection has often been related to mechanical factors. The possible pathogenetic role of trauma [13, 14, 15, 25, 32, 37, 45, 47, 59], surgical trauma [24, 49], and strenuous physical exertion [36, 39, 50] is discussed most frequently in the literature. The relationship between dissecting aneurysm and migraine has been suggested by Alexander et al. [3], Sinclair [52], and Spudis et al. [53].

In both of our patients the reticular fibers were absent in circumscribed areas close to the internal elastic lamina. In some places they were also more sparse in the outer part of the tunica media. The circumscribed subintimal deficiency in reticular fibers was observed in all major intracranial arteries of each patient. Similar patterns of reticular fiber deficiency have sometimes been seen in patients with berry aneurysms [22]. However, in this condition the reticular fibers are diffusely reduced in number in the intracranial arteries or they

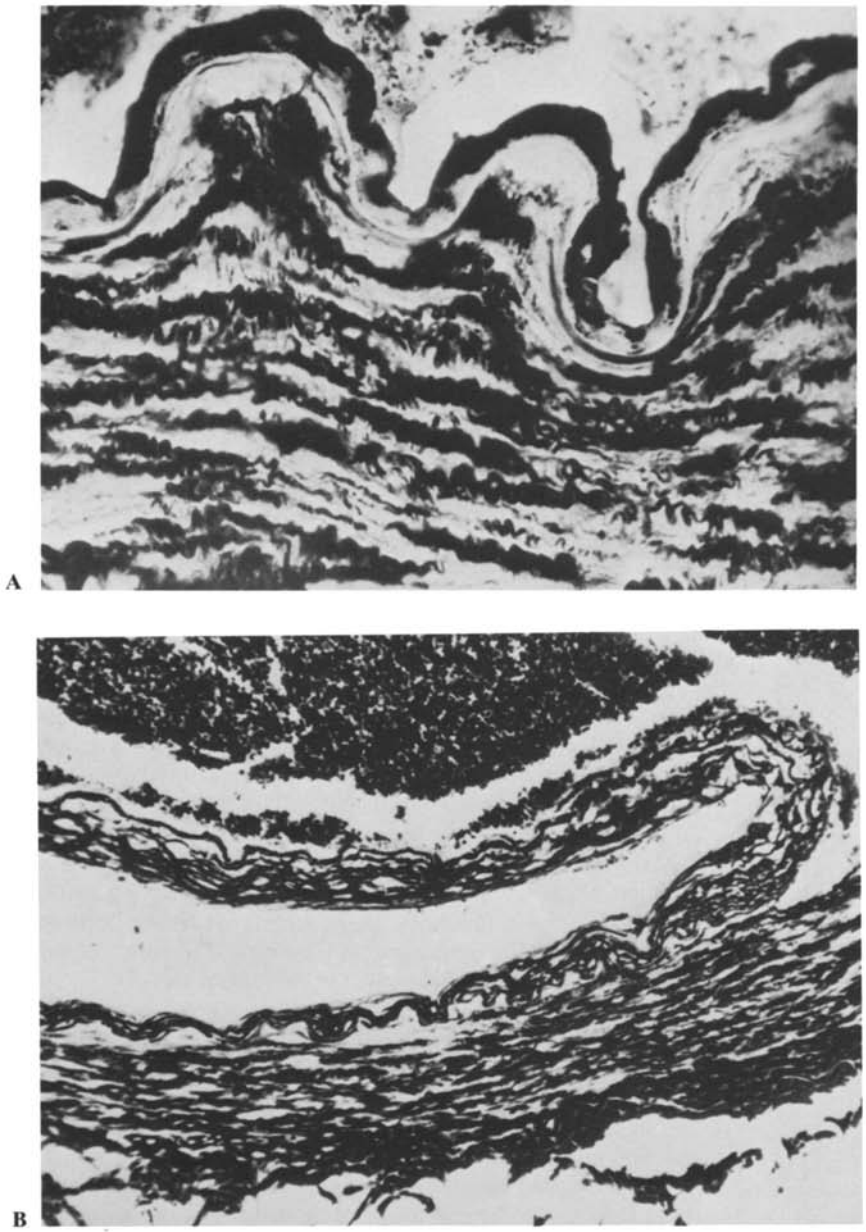

Fig. 3. A The anterior cerebral artery of a 47-year-old man with dissecting aneurysm of the basilar and both vertebral arteries. The reticular fibers are missing almost entirely in the muscular layer next to the internal elastic lamina. **B** The basilar artery of the same patient with subintimal dissection shows similar changes. Gömöri's method for reticulin **A** × 400, **B** × 100.

are sparser mainly in the outer part of the tunica media. In patients without vascular diseases these fibers show a fairly regular distribution within the media surrounding the individual muscle cells [22]. They also form layers on the luminal and medial sides of the internal elastic lamina and are interconnected with each other through the fenestrae. It seems reasonable to presume that in the absence of subintimal reticular fibers, the attachment of the tunica intima to the tunica media is insufficient so that the blood can separate it easily from the media if the elastic lamina becomes defective. Similarly, the partial lack of reticular fibers in the outer part of the media may be a predisposition to dissection between the medial and adventitial layers. The occurrence of bilateral [2, 11] and multiple [40, 44] cerebral dissecting aneurysms can also be explained by our findings.

The reason for the subintimal lack of reticular fibers is still unknown. Its amount and distribution has proved to be independent of age [22], and the atherosclerotic process does not influence the pattern of reticular fibers in the media (unpublished data). The only way by which atherosclerosis can contribute to the occurrence of medial dissection is the reactive development of vasa vasorum in the arteries having subadventitial reticular fiber deficiency from other, still unknown causes.

It is likely that the inflammatory and necrotizing processes of the arterial wall destroy the reticular fibers. In other cases the deficiency in reticular fibers may be the result of both congenital and some other acquired lesions. In some instances an inborn error of collagen metabolism has been proposed concerning the pathogenesis of dissecting aneurysm [10, 16]. On the other hand, swelling of the subintimal collagen was observed to occur in spontaneously hypertensive rats and in animals under chronic estrogen/progesterone treatment [8]. Therefore, Bugiani et al. assumed that the use of oral contraceptives and hypertension predispose to dissection [8]. The pathogenetic role of the latter two factors can be neglected in our cases and in the majority of the reported ones. The occasionally observed simultaneous occurrence of dissecting and

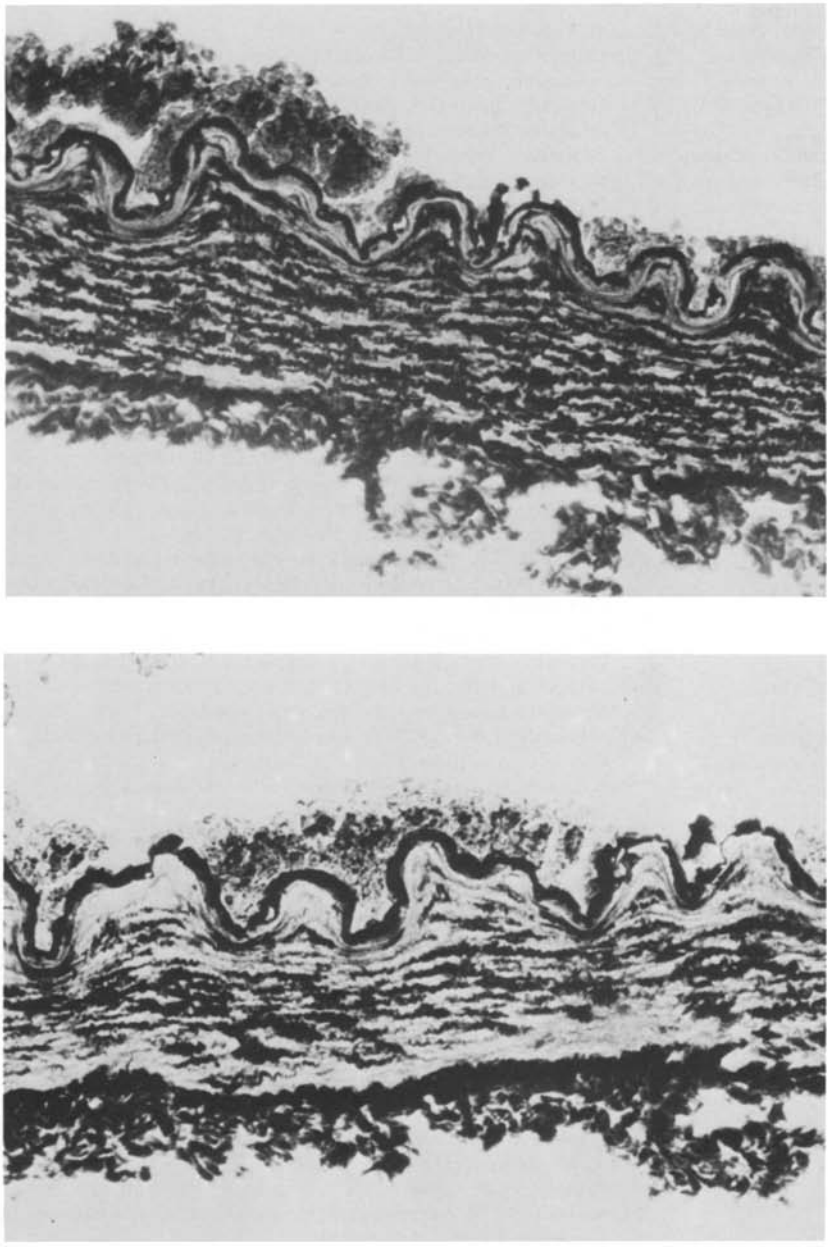

Fig. 4 A, B. The basilar artery of a 13-year-old boy. Gömöri's method for reticulin × 160. **A** A portion with an almost normal pattern of reticular fibers. **B** Another portion with deficient reticular fibers confined mainly to the inner and outer parts of the muscular layer

berry aneurysms [6, 8, 27, 62] and the similar pattern of reticular fibers in both diseases suggest that both pathologic conditions may be different manifestations of the same underlying disorders.

Finally, the direct role of mechanical factors in the production of dissecting aneurysms appears to be easy to understand when reticular fiber deficiency and defective elastic lamina are present together in the intracranial arteries of an individual.

Further investigations are necessary in order to elucidate the exact origin of the partial lack of reticular fibers which are thought to be identical with type III collagen [22].

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