Spontaneous Reduction of Diverticular Outpouchings and Multiple Dissecting Aneurysms of Cervicocranial Arteries with Fibromuscular Dysplasia — The Relation to Alpha-1-Antitrypsin Deficiency —

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ABSTRACT. The authors experienced a patient with fibromuscular dysplasia and multiple dissecting aneurysms of the cervicocranial arteries due to an alpha-1-antitrypsin deficiency. This 48-year-old woman presented with gait disturbance and hypalgesia of the right extremities. Magnetic resonance imaging revealed a small infarction of the left lateral part of the medulla oblongata. Angiography revealed dissecting aneurysms of the right internal carotid artery and the left vertebral artery near the infarction, and demonstrated multiple diverticular outpouchings of the cervical vertebral arteries bilaterally and the typical "string of beads" appearance in the bilateral brachial arteries. Her alpha-1-antitrypsin plasma level was 173 mg/dl (normal range 184-243 mg/dl) on the first admission. Angiography one year later revealed diminishing of the size of the dissecting aneurysms and diverticular outpouchings, and the patient's alpha-1-antitrypsin plasma level had normalized (223 mg/dl). The plasma level of alpha-1-antitrypsin may be useful for following this disease.

Key words: dissecting aneurysm — fibromuscular dysplasia — alpha-1-antitrypsin

Recent studies suggest that a deficiency of alpha-1-antitrypsin (α1-AT) may be a risk factor for the bevelopment of intracranial aneurysms[1,2] and fibromuscular dysplasia (FMD).[3,4] Little is known about the natural history of FMD and no reports of spontaneous disappearance of aneurysms due to the FMD have been found in the English literature. To the best of our knowledge, we present the first case of spontaneous diminishing of aneurysms due to FMD with normalization of the α1-AT plasma level.

CASE REPORT

This 48-year-old woman, who was a heavy smoker, presented with gait disturbance, diplopia and hypalgesia of the right extremities.

Examination: Neurological examination revealed a miotic pupil and blepharoptosis of the left side, nystagmus on left lateral and upward gaze, and hypalgesia of the right extremities. Magnetic resonance (MR) imaging disclosed a small infarction of the left lateral part of the medulla oblongata (Fig 1). Angiography showed dissecting aneurysms of the left vertebral artery near the

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infarction of the medulla oblongata (Fig 2A) and the right internal carotid artery (Fig 3A), and demonstrated multiple diverticular outpouchings of the cervical vertebral arteries bilaterally (Fig 4A, 5A) and the typical "string of beads" appearance in the bilateral brachial arteries (Fig 6). These angiographic findings were diagnostic of FMD. We concluded that the couse of the infarction of the medulla oblongata was dissection of the left vertebral artery. The bilateral renal arteries were angiographically normal. The patient's α1-AT plasma level was 173 mg/dl (normal range 184-243 mg/dl) on first admission.

Conservative treatment (pentoxifylline 300 mg/day and bifemelane HCl 150 mg/day orally) for the cerebral infarction was started and she was instructed to stop smoking. Eye signs slowly improved, but the hypalgesia of the left extremities remained. Three and six months later, angiography revealed gradual diminishment of the dissecting aneurysms and the diverticular outpouchings.

Angiography one year later revealed diminishing of the size of the dissecting aneurysms and diverticular outpouchings and disappearance of one of the diverticular outpouchings (Fig 2B, 3B, 4B, 5B). The α1-AT plasma level had normalized (223 mg/dl).

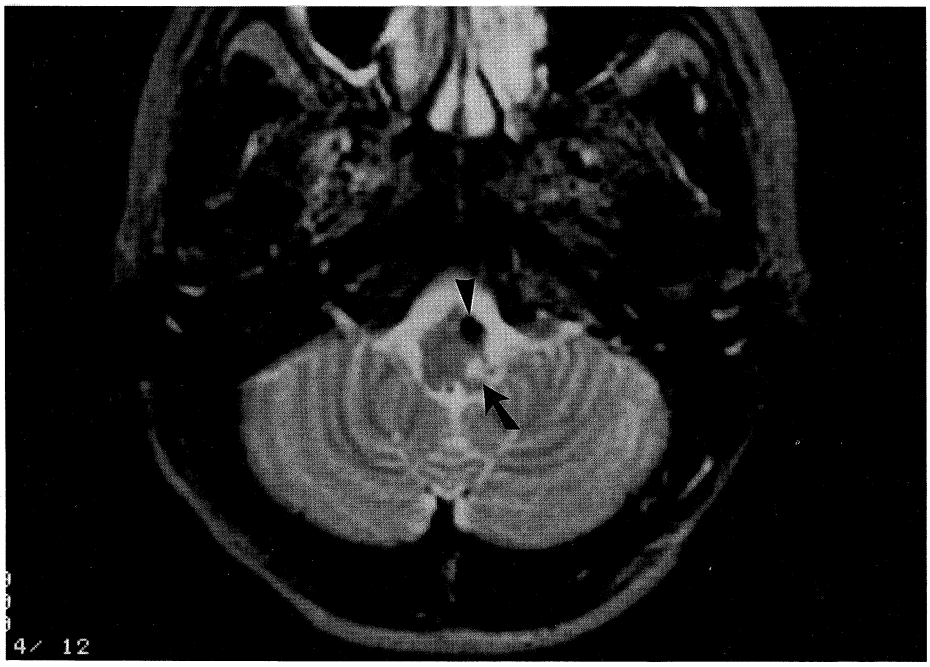

Fig 1. T2-weighted magnetic resonance image showing a small infarction of the left lateral part of the medulla oblongata (arrow) and a dissecting aneurysm of the left vertebral artery (arrowhead).

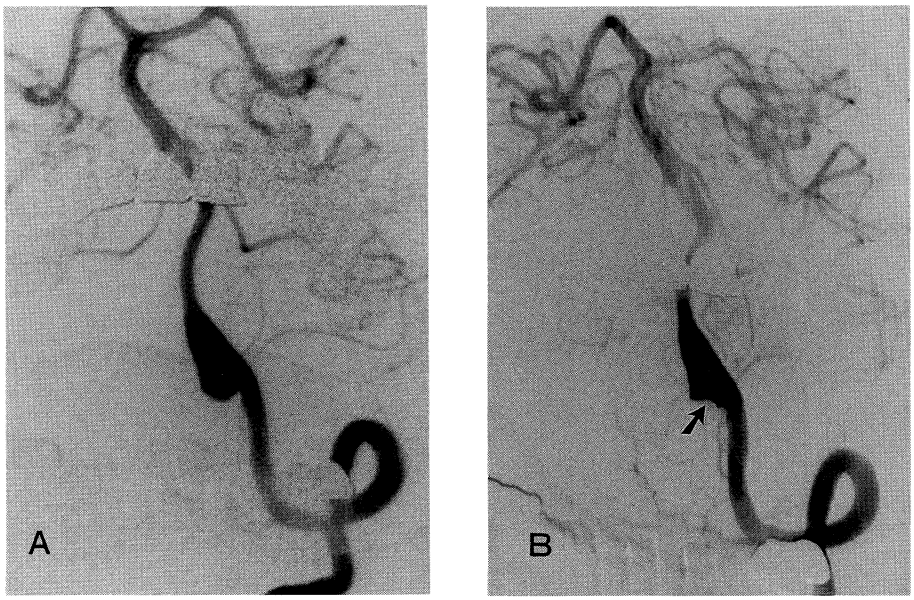

Fig 2. A : Left vertebral angiogram showing dissecting aneurysm of the vertebral artery. B : Left vertebral angiogram one year later showing diminishing of the bottom of the dissecting aneurysm (arrow).

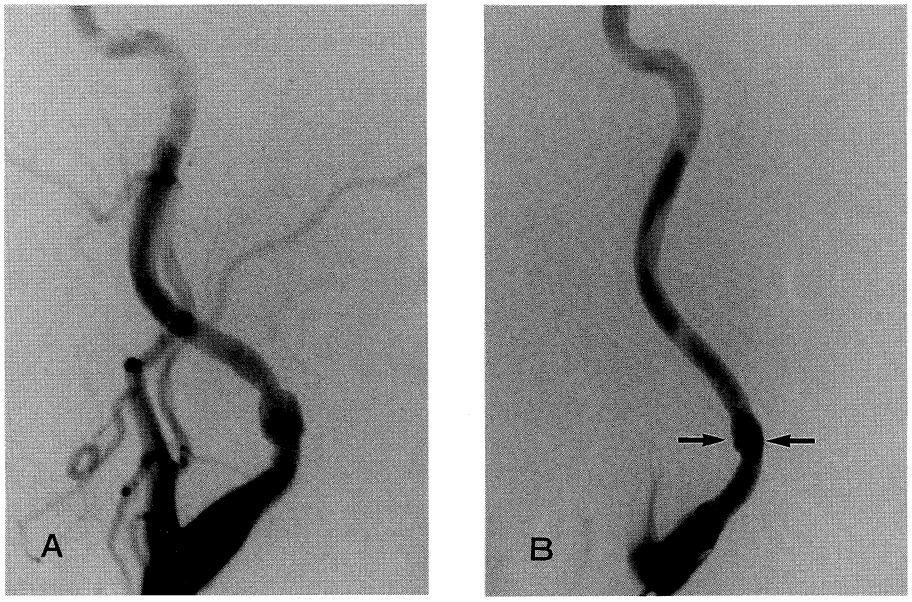

Fig 3. A : Right internal carotid angiogram showing a dissecting aneurysm of the internal carotid artery. Double contours are visualized. B : Right internal carotid angiogram one year later showing diminishing of the width of the dissecting aneurysm (arrows).

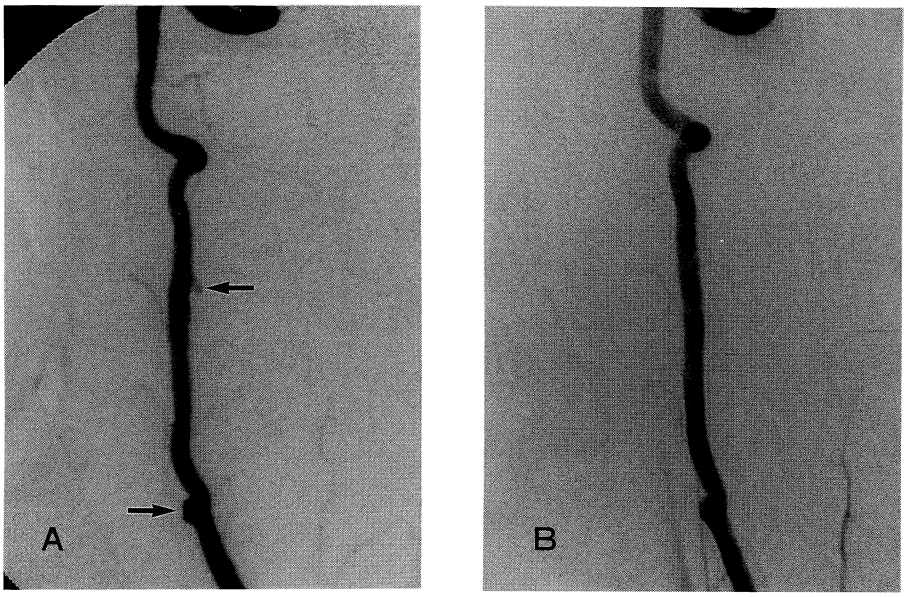

Fig 4. A: Left vertebral angiogram (lateral view) showing two diverticular outpouchings (arrows). B: Left vertebral angiogram one year later (lateral view) showing disappearance of the distal diverticular outpouching.

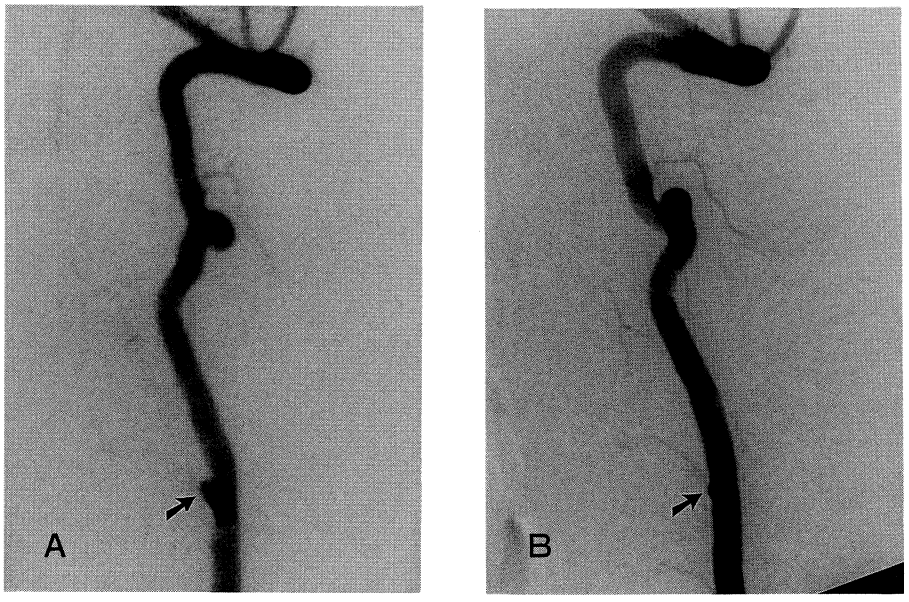

Fig 5. A: Right vertebral angiogram (lateral view) showing a diverticular outpouching (arrow). B: Right vertebral angiogram one year later (lateral view) showing diminishing of this outpouching (arrow).

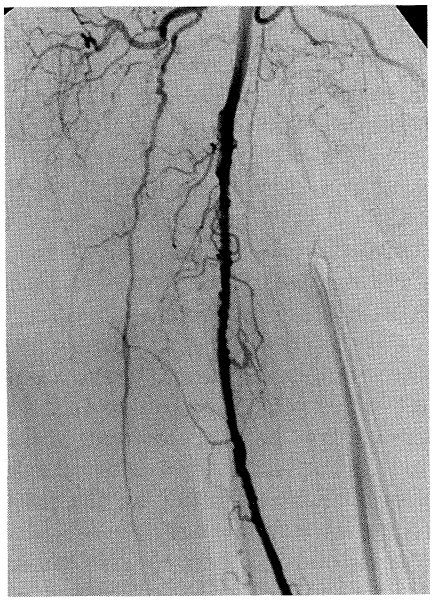

Fig 6. Angiogram of the right brachial artery showing the typical "string of beads" appearance. This angiographic finding is diagnostic of fibromuscular dysplasia.

DISCUSSION

Since Palubinskas and Ripley suggested that FMD represented a general arterial dysplasia rather than a lesion limited to the renal arteries,[5] an increasing number of patients with cervicocranial FMD have been reported.[6-11] Osborn and Anderson reported the angiographic spectrum of cervical and intracranial FMD, and demonstrated three characteristic angiographic patterns associated with cephalocervical FMD from a review of the literature and their series.[14] The most common finding has been the so-called "string of beads" appearance (type 1). A second angiographic pattern is characterized by unifocal or multifocal tubular stenosis (type 2), and a third angiographic type of FMD is characterized by a diverticulum-like outpouching (type 3). In our patient, angiograms revealed the typical "string of beads" appearance in the bilateral brachial arteries (type 1), multiple diverticular outpouchings of the bilateral cervical vertebral arteries (type 3), and dissecting aneurysms of the right internal carotid artery and the left intracranial vertebral artery.

A prevalence of cervicocranial saccular and/or dissecting aneurysms in patients with FMD has also been reported,[12-22] but no report of spontaneous disappearance of aneurysms due to the FMD has been found in the English literature. Several authors found angiographic evidence of progression of cervicocranial FMD.[8,9,12,16] Manninen *et al* reported a patient with dissecting aneurysms of the cervicocranial arteries in FMD, and they treated these aneurysms with self-expanding endovascular stents because of their enlargement in a short time.[22] In our patient, on the other hand, the dissecting aneurysms of the right internal carotid artery and the left intracranial vertebral artery

became smaller, one of the diverticular outpouchings of the left cervical vertebral artery disappeared, and a diverticular outpouching of the right cervical vertebral artery became smaller during a one year period. Another diverticular outpouching of the left cervical vertebral artery was unchanged.

We consider that there is a relation between the disappearance or diminishing of aneurysms and normalization of the α1-AT plasma level. Alpha-1-AT is the most abundant proteinase inhibitor in human plasma, and it is an important guardian of vascular tissue.[23] Schievink *et al* reported that arterial FMD was found in 2 of 6 patients with α1-AT deficiency (33.3%) in comparison with 23 of 6690 patients without α1-AT deficiency (0.3%), and they concluded that these findings provided further evidence for an underlying arteriopathy in patients with α1-AT deficiency.[3] Some reports have suggested that α1-AT deficiency is a genetic risk factor for the bevelopment of intracranial aneurysms or arterial dissection,[1,2,4] and cigarette smoking decreases the biologic effect of α1-AT.[1,3] It is interesting that the dissecting aneurysms and diverticular outpouchings in our patient diminished in size with normalization of the α1-AT plasma level after she was instructed to stop smoking. Since it may be difficult to follow up the subsequent angiography of a patient over a short interval of time, the α1-AT plasma level can serve as a good marker for the condition of a patient with cervicocranial saccular and/or dissecting aneurysms due to FMD.

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