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Brief Report

Fibromuscular dysplasia as the substrate for systemic and pulmonary hypertension in the setting of Moya-Moya disease

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Abstract We report the first case, to the best of our knowledge, of a child with the unusual association of Moya-Moya disease and both systemic and pulmonary hypertension. Histological examination revealed fibromuscular dysplasia as the common denominator for a diffuse arteriopathy.

Keywords: Pulmonary arterial stenosis; renal arterial stenosis; cerebrovascular pathology

Moya-Moya disease is a chronic, occlusive, cerebrovascular disorder of unknown pathogenesis. The name "Moya-Moya" comes from the Japanese. It means "puff of smoke", and refers to the typical appearance of the cerebral angiograms of the sufferers of the disease. Indeed, Moya-Moya disease is characterized by spontaneous occlusion of the circle of Willis, associated with an exaggerated development of collateral vascular network at the base of the skull. It is the collateral network that gives the angiographical aspect of "puff of smoke".[1] A few cases of the disease have recently been reported with extracranial arterial lesions, suggesting a diffuse arteriopathy as the underlying cause.[2–6] We report here the details of a child presenting with the disease in the setting of a multisystemic arteriopathy, including renal and pulmonary arterial stenoses. To our knowledge, an association of these three conditions has not thus far been reported. Histological examination revealed fibromuscular dysplasia as the common denominator for the arteriopathy.

Case report

A girl, aged 15 years, was admitted to our department for investigation of pulmonary hypertension, initially considered to be idiopathic. She was known to have Moya-Moya disease, which had been diagnosed at the age of 3 years subsequent for presentation due to recurrent loss of consciousness. They had likely been caused by multiple cerebral infarctions, demonstrated at cerebral magnetic resonance imaging. Cerebral angiography had shown intracerebral arterial occlusions and micro-aneurysms, involving the circle of Willis and the cortical arteries. Numerous collateral vessels had been formed at the base of the skull, giving the classical "puff of smoke" image (Fig. 1a). Surgical treatment of encephalo-duro-arterio-myo-synangiosis, using the superficial temporal artery, had significantly improved the cerebral perfusion, and the patient had been free of neurological symptoms since then. At the age of 4 years, however, she presented with systemic hypertension, shown to be due to stenosis of the right renal artery (Fig. 1b). Treatment consisted of percutaneous balloon angioplasty, followed by surgical revascularization. Histological examination of the renal arteries revealed intimal fibroplasia, characterized by intima hyperplasia and rupture of the internal elastic lamina (Fig. 1c).

Mild pulmonary hypertension had initially been noted at the age of 4 years, and had progressively increased with growth. At the age of 15 years, the systolic pressures in the pulmonary arteries, estimated by Doppler interrogation of tricuspid regurgitation, approached 50 millimetres of mercury. Respiratory disorders, collagen arterial disease, thromboembolic events, intoxications, granulomatous disease, and portal hypertension were all excluded. The chest X-ray revealed enlargement of the pulmonary trunk and its right and left branches. The electrocardiogram was consistent with right ventricular hypertrophy.

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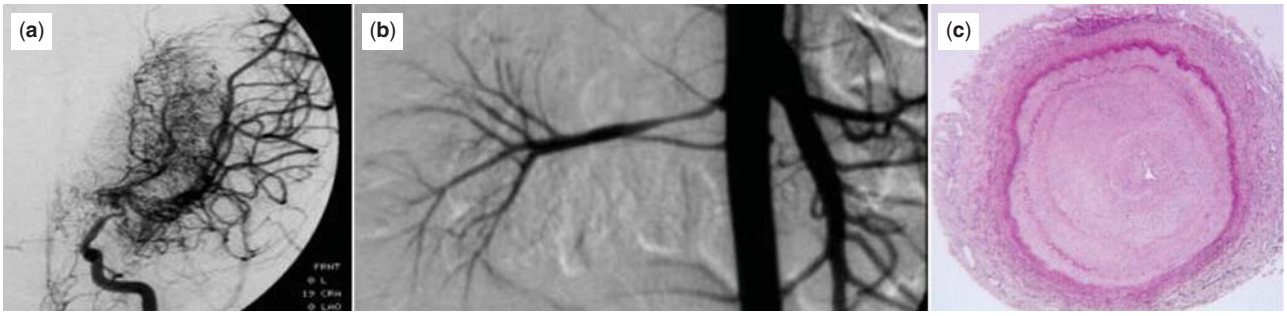

Figure 1.
*(**a**) shows the characteristic "puff of smoke" image at the base of the skull, with (**b**) showing stenosis of the right renal artery, shown by histology (**c**) to be produced by intimal fibroplasia with intimal hyperplasia and rupture of the internal elastic lamina.*

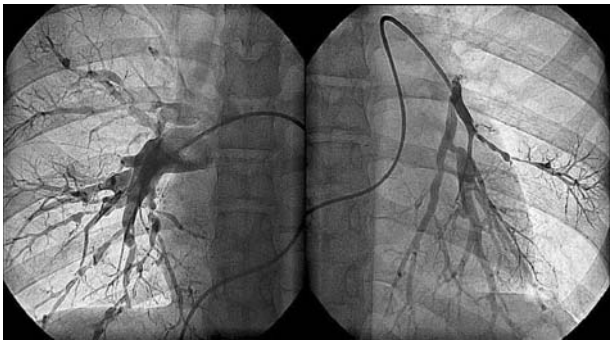

Figure 2.
Multiple stenoses of the distal pulmonary arteries, giving the characteristic "string of beads" image of fibromuscular dysplasia.

Catheterization of the right heart showed that the systolic, diastolic, and mean pressures in the pulmonary arteries were 100, 14, and 54 millimetres of mercury, respectively. The pulmonary venous capillary wedge pressure was normal, at 12 millimetres of mercury. Saturations in the cavities of the right heart were also normal, at 65%, and there was no step-up in saturations of oxygen, suggesting normal cardiac output and no left-to-right shunting. Pulmonary angiography revealed multiple stenoses of the distal pulmonary arteries, giving a "string of beads" appearance on both sides (Fig. 2). Hence, the pulmonary hypertension, initially thought to be idiopathic, was the consequence of the distal pulmonary arterial stenoses.

Discussion

Some recent reports have described the involvement of extracranial vessels in patients with Moya-Moya disease. For example, the association with renal arterial stenosis, giving the complication of systemic hypertension, is now well-recognized.[2] The association of Moya-Moya disease with pulmonary hypertension, in contrast, is unusual, with but few case reports in the literature.[3–5] Investigation in the first case associated with idiopathic pulmonary hypertension, reported by Kapusta et al.,[3] revealed hypertrophy of the media layer of small branches of pulmonary arteries on histological examination. The authors had suggested a common vascular denominator for both diseases although they were not able to prove this hypothesis.

To the best of our knowledge, our patient is the first to exhibit the association of Moya-Moya disease with both renal and pulmonary arterial stenoses. As previously suspected,[3,4] our observation confirms that the systemic vasculopathy known as fibromuscular dysplasia can be the underlying cause of the damage to the end-organs. In our patient, histological examination of the renal arteries clearly showed arterial fibrodysplasia. We could not prove the nature of the cerebral vascular pathology, because we did not perform a cerebral operation, only a palliative procedure to improve cerebral perfusion. Also, although we have no direct histological proof of the nature of the pulmonary arterial changes, fibromuscular dysplasia is highly likely, as the "string of beads" appearance on pulmonary angiography is known to be characteristic of fibromuscular dysplasia (Fig. 2). Our findings demonstrate that the pulmonary hypertension, previously thought to be idiopathic in the setting of Moya-Moya disease,[3] at least in our patient was a complication of multisystemic fibromuscular dysplasia.

Fibromuscular dysplasia is a rare non-atherosclerotic and non-inflammatory arterial disease that primarily involves arteries of small and medium size. The scheme for its classification is based on the arterial layer, intima, media, or adventitia, in which the lesion predominates.[6] Although genetic and hormonal factors have been suspected, its aetiology remains unknown.[6–9] Clinical manifestations vary from the involved patients being asymptomatic to a multisystemic disease, the level of expression then depending on the vessels involved. Classically, therapeutic options include percutaneous intervention and surgical revascularization.[6] Interestingly, our patient encapsulated the different strategies regarding treatment.

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As previously reported,[10] our experience confirms that surgical treatment for the impaired cerebral perfusion with encephalo-duro-arterio-myo-synangiosis is a good therapeutic option for children with Moya-Moya disease. Treatment for renal stenosis, however, was more difficult. Balloon angioplasty of the renal artery was unsuccessful, so surgical revascularization was required. Our experience demonstrates, therefore, that fibromuscular dysplasia can be the common denominator for vascular disease when Moya-Moya disease is associated with extracranial occlusive arteriopathies. Hence, diffuse vascular lesions should be always be searched for in patients known to have Moya-Moya disease.

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