Pearls & Oy-sters: Moyamoya Vasculopathy and Its Association With Congenital Heart Disease

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Pearls

- Moyamoya vasculopathy (MMV) is characterized by a progressive, usually bilateral narrowing of the terminal segment of the internal carotid artery and/or the initial segments of the anterior/middle cerebral artery leading to an occlusion and formation of a fragile network of abundant collateral vessels with a high risk of stroke.

- Moyamoya syndrome (MMS) is rare and differs from primary idiopathic Moyamoya disease (MMD) as it develops secondary to an underlying acquired or inherited condition, including cranial radiotherapy, Neurofibromatosis Type I, Down’s syndrome, sickle cell disease or congenital heart disease.

Oy-sters

- In addition to embolic stroke, patients with congenital heart disease carry an elevated risk for vascular cognitive impairment, MMS, cerebral aneurysms and intracranial hemorrhage.

- In order to avoid severe cerebrovascular complications, non-invasive arterial imaging offers an option for the early detection and initiation of preventive measures in patients with congenital heart disease.

Methods

Written informed consent was obtained from the patient mentioned in this case study.

Case Report

A 48-year-old man of Caucasian origin presented to our emergency room two hours after acute onset of headache and language abnormalities. The patient had a past medical history of congenital heart disease comprising aortic coarctation (CoA), bicuspid aortic valve and ectasia of the ascending aorta. He had undergone surgical treatment at the age of one year...
with resection of CoA and end-to-end anastomosis. At the age of nine years, an aortic patch plastic was implanted due to aortic restenosis. The subsequent physical and mental development during childhood and adolescence was unremarkable. At the age of 29 years, he underwent replacement of the ascending aorta by a 24mm-Hemashield prothesis and in the later course, implantation of a mechanical aortic heart valve (23mm, SJM). Since then, the patient had been on oral anticoagulation with phenprocoumon. Additional medication included antihypertensive treatment with metoprolol and ramipril. Blood pressure readings were taken on a daily basis showing normotension during the months ahead of the event. The patient had a history of smoking (10 pack years) but quit at the age of 28 years. He did not abuse any other drugs. Prior to the current symptom onset, the patient reported a good state of health and worked full-time employed as a salesperson. Neurological examination at the time of admission revealed moderate global aphasia (NIHSS Score 4). An initially performed cranial CT scan showed a temporal intracerebral hematoma of 18 ml (3.3 x 3.0 x 3.6 cm) in the left hemisphere (Figure A). In addition, old lacunar infarcts in the areas of the caudate nucleus and basal ganglia were visible and a cranial CT angiogram (CTA) revealed a weak anterior circulation bilaterally. On admission, blood pressure measurement unveiled only slight hypertension (140/90mmHg) and the INR measured 2.9. For anticoagulation reversal, the patient received 3000 IU of 4-factor-PCC intravenously (INR dropped to 1.1). A digital subtraction angiography performed two days after admission showed a bilateral high-grade stenosis of the terminal carotid arteries including the proximal segments of the medial cerebral arteries and a surrounding network of small collaterals (Figure C1-4) with no signs of cerebral aneurysms. The analysis of cerebrospinal fluid was normal. There was no evidence for cerebral or systemic vasculitis, rheumatic or infectious disease by clinical examination and diagnostic testing. On echocardiography, the function of the left ventricle and the mechanical aortic valve prosthesis appeared normal. The clinical course was uneventful, oral
anticoagulation was reinitiated 12 days after admission. On discharge (day 15) the patient had mild anemia and continued in rehabilitative care.

Discussion

Moyamoya vasculopathy (MMV) is characterized by a chronic and progressive occlusion of the terminal carotid arteries and/or the initial segments of the anterior/middle cerebral arteries, evoking a fragile network of surrounding collateral vessels at the base of the brain. A characteristic finding on vascular imaging is the eponymous smoke-like formation of blood vessels and the first describers therefore entitled the condition “Moyamoya” (Japanese for “puff of smoke”). The occurrence of MMV shows relevant regional differences with a comparably high incidence in East Asia and a low incidence in Europe and North America. It’s prevalence in Japan has been estimated up to 3/100,000, that is ten times higher than the one observed in Europe. Whereas underlying mechanisms of MMV remain to be entirely elucidated, a genetic predisposition of the disease has been recognized early. Recent studies were able to identify RNF213 as an important susceptibility gene and associated gene loci on chromosome 3, 6, 8 and 17 have been found in a chromosomal search for familial MMV. Patients with symptomatic MMV commonly present with transient ischemic attacks, ischemic stroke or intracerebral hemorrhage (ICH). Other neurological symptoms include migraine-like headaches, seizures or cognitive dysfunction. Cerebral angiography is considered the gold standard for the diagnosis of Moyamoya vasculopathy and the system most commonly used for classification is the Suzuki staging system. After diagnosis of MMV, a thorough investigation of precipitating factors is necessary - In absence of these factors, MMV is classified as idiopathic (Moyamoya disease, MMD), while the term Moyamoya Syndrome (MMS) applies to only 10-20% of cases where an underlying acquired or inherited condition is associated with the cerebral vascular occlusion phenomenon. The most common associated disorders are Neurofibromatosis Type 1, Down’s syndrome, sickle cell disease and cranial radiotherapy. Another, albeit rare, cause of MMS is congenital heart disease, as illustrated
in the presented case. While the association of MMV with CoA has been reported earlier, it remains unsolved until today, to what extent the hemodynamic changes with long-lasting hypertension restricted to the upper body typically seen in patients prior to surgical repair of CoA, contribute to the cerebrovascular occlusion. Likewise, both findings could also result from a systemic vasculopathy or systemic congenital malformation. A novel hypothesis proposes that defects of neural crest cells during embryogenesis could contribute to a simultaneous occurrence of cardiac and cephalic pathologies. Along with MMV, the association of cardio- and cerebrovascular diseases has also been reported in PHACE syndrome and ACTA2 mutations syndrome. Apart from MMV, patients with CoA are exposed to an elevated risk for cerebral aneurysms. Vascular imaging prior to the occurrence of neurologic symptoms offers an option to identify underlying conditions early and evaluate primary preventive measures. Optimal treatment of hypertension, cessation of smoking and reduction of alcohol consumption should be initiated. In addition, endovascular or neurosurgical interventions might be indicated for primary treatment in patients with cerebral aneurysms. In case of MMV, evaluation in a specialized neurovascular center is recommended. Symptomatic progression has been estimated to occur in up to two thirds of patients with MMV over a 5-year period and although the risk of intracerebral bleeding or stenosis associated symptoms is high, therapeutic options remain limited. There is no evidence-based medical treatment with proven benefit. The use of antithrombotic medication consisting of antiplatelet agents or anticoagulation are discussed controversially. In the patient presented in this report, the mechanical aortic valve demanded the use of phenprocoumon for oral anticoagulation, which was re-established twelve days after ICH onset. Otherwise, the use of vitamin K antagonists would hardly be justifiable in symptomatic MMS with prior ICH. Surgical treatment of MMV constitutes a therapeutic option for selected patients at a low level of scientific evidence: A smaller randomized trial as well as a recent meta-analysis suggest a marginal preventive benefit with neurosurgical
revascularization, while the effect was more pronounced among patients with hemorrhagic MMV\textsuperscript{10,11}. The most common surgical technique is direct revascularization with the superficial temporal artery to ACA/MCA anastomosis. Indirect revascularization procedures rely on the use of well-blood-supplied tissues to induce neovascularization of the cortical surface\textsuperscript{2}. In the future, deeper insights into the pathophysiologic mechanisms and the genetic background of MMV might be the prerequisite for new, causal treatment options and individualized preventive measures.

References

Figure 1: Brain imaging consistent with lobar ICH and Moyamoya vasculopathy

(Aa.-A.c) CT showing a well-defined, hyperattenuating temporal lesion with a volume of 18 ml in the left hemisphere. (B) Axial view of a CT Angiogram demonstrating weak anterior circulation. (C.a-C.d) Cerebral Angiogram exposing bilateral occlusion of the terminal carotid arteries and proximal segments of the medial cerebral arteries as well as a fine anastomotic network of collateral vessels.
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