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Moyamoya disease and moyamoya syndrome in children – case reports and a literature review

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Summary

Background:

Moyamoya disease is a rare angiopathy (vascular disorder) that leads to a narrowing and occlusion of the distal internal carotid artery and proximal anterior and middle cerebral arteries. The presence of a rich network of collateral blood vessels at the base of the brain is called “moyamoya syndrome”. Moyamoya disease is diagnosed in patients with unidentified risk factors. Moyamoya disease should rather be excluded and moyamoya syndrome diagnosed in patients with conditions and risk factors which may promote these specific vascular lesions.

Case Reports:

Three cases of the disease in pediatric patients have been described in this article. The first one concerns a nine-year-old girl who experienced ischemic stroke and had cerebral vascular abnormalities typical of moyamoya disease. The second case is a seventeen-year-old female patient with a history of subarachnoid hemorrhage history. Also in this patient, clinical features suggested moyamoya disease. The third case report concerns a thirteen-year-old girl with type I neurofibromatosis and a history of transient ischemic attack (TIA), who was diagnosed with moyamoya syndrome.

Conclusions:

Moyamoya disease occurs both in pediatric and adult patients. In pediatric patients, this medical condition should be considered if cerebral ischemia of unknown origin or acute neurological deficits develop.

MeSH Keywords:

Angiography • Moyamoya Disease

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Background

Moyamoya disease is a rare, progressive angiopathy (vascular disorder) that leads to narrowing and occlusion of the supraclinoid portion of the distal internal carotid artery, as well as proximal anterior and middle cerebral arteries. These findings are associated with the development of a network of tiny collateral blood vessels to compensate for decreased blood flow to the brain. Usually, the collateral blood vessels are especially abundant in the basal ganglia which results in a characteristic “puff of smoke” (moyamoya in Japanese) appearance on angiographs [1–4]. Pathogenesis of the disease has not yet been determined. However, genetic background is believed to play the most

important role. In 7–10 percent of all cases, moyamoya disease occurs in other family members [2–7]. This condition is common in Asian populations, and most prevalent in Japan (affects almost 3 per 100,000 children). However, the disease is detected in all geographic regions, including Poland, irrespective of race [3–8]. The peak morbidity is observed in children aged between 6 and 15 years old, and in adults in their 40s. Moyamoya disease is almost twice as common in women as in men [2,3]. Intracerebral and subarachnoid hemorrhages are predominant in adults, and transient ischemic attacks (mainly recurrent paresis) are most common in children [2,3]. Decreased blood flow to the areas of brain that are supplied by internal carotid arteries and their main branches (i.e., frontal, temporal and parietal

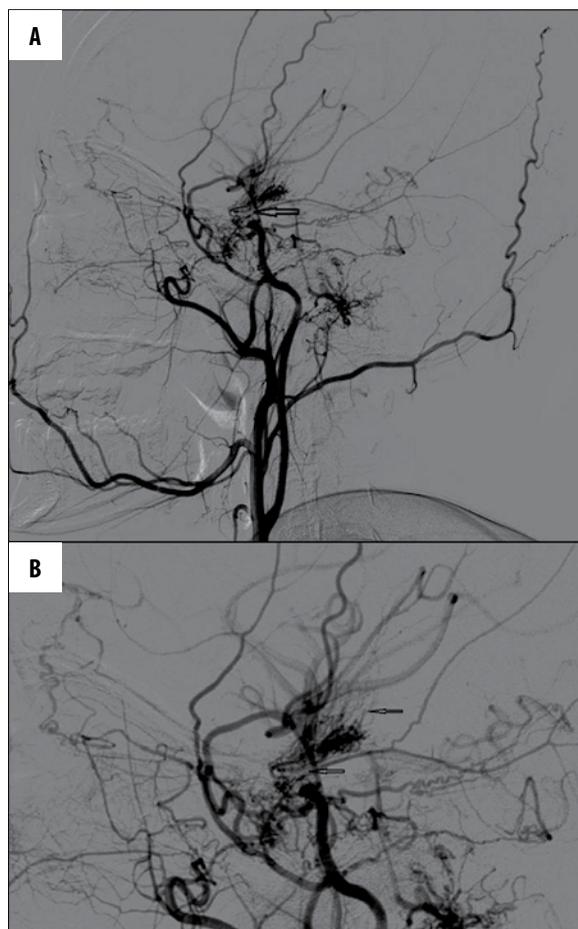


Figure 1. Angiography of the right common carotid artery – lateral projection. (A) Right internal carotid artery occluded in the cavernous segment (arrow). (B) The same image magnification – in the area of obstruction numerous, tortuous collateral vessels are present – symptom of moyamoya (arrows).

lobes), leads to typical symptoms such as hemiplegia, dysarthria, aphasia, and cognitive disorders. Visual field loss, disturbances of consciousness and personality changes are also common and may be misdiagnosed as mental disorders. Typical childhood activities or behaviors such as singing, running, crying or eating hot foods, that may be associated with hyperventilation, increase the risk of TIAs [4]. Vascular lesions, that comprise typical features of moyamoya disease (moyamoya syndrome), can be found also in other medical conditions such as brain tumors, congenital malformations, meningitis, hematological diseases, atherosclerosis, traumatic and radiation-induced brain injuries. This can significantly hinder diagnosis. Patients should be diagnosed with moyamoya syndrome if they have conditions and risk factors which may promote these specific vascular lesions [4,7].

Case Reports

Case 1

A 9-year-old obese girl with moderate mental retardation and generalized chorea, who has been previously treated at

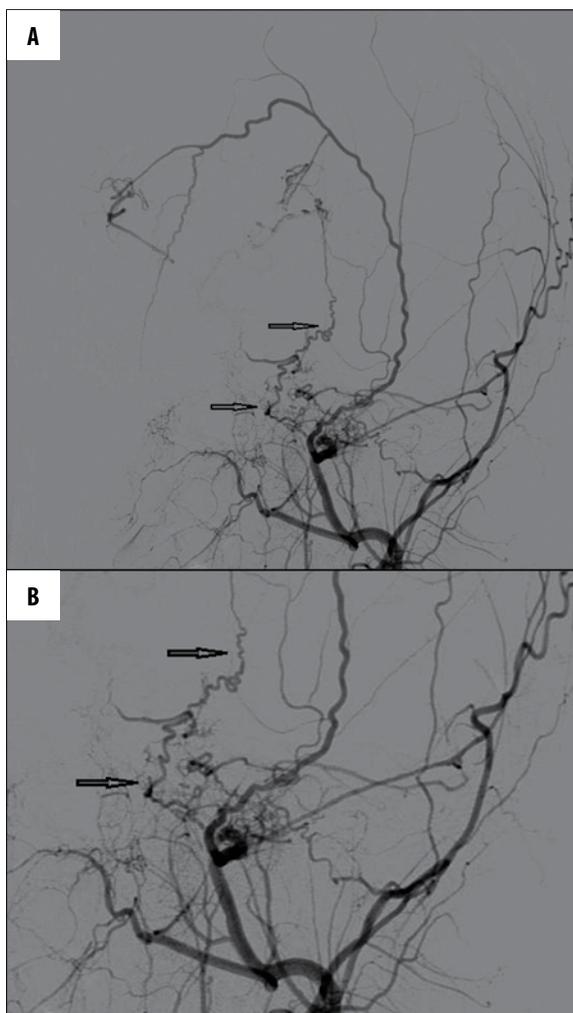


Figure 2. Angiography of the left common carotid artery – lateral projection. (A) Total occlusion of the left internal carotid artery both in extracranial and intracranial sections. Collateral vessels from the left external carotid artery branches supplying brain parenchyma (arrows). (B) The same image magnification (arrows).

the Pediatric Neurology Outpatient Clinic for Sydenham's chorea, was admitted to the Department of Pediatric Neurology after she had experienced right hemiplegia associated with positive right Babinski reflex, and central right 7th cranial (facial) nerve palsy. The girl was conscious and could carry out simple orders on presentation to the hospital. Laboratory tests did not reveal any signs of infection or abnormal findings in CSF analysis. Brain CT scans showed two hypodense focal lesions in the deep structures of the left hemisphere that could represent focal cerebral ischemia. The patient was also found on angiography to have occlusion of the main arteries to the brain. The right internal carotid artery was occluded both in its intracranial and extracranial portion, and collateral vessels developed to supply the brain with blood via cerebral branches of the right external carotid artery (Figure 1). The left internal carotid artery was occluded in its cavernous portion (Figure 2). Numerous tiny, tortuous collateral blood vessels were present in the occluded areas of both internal carotid arteries (moyamoya phenomenon). Moreover,

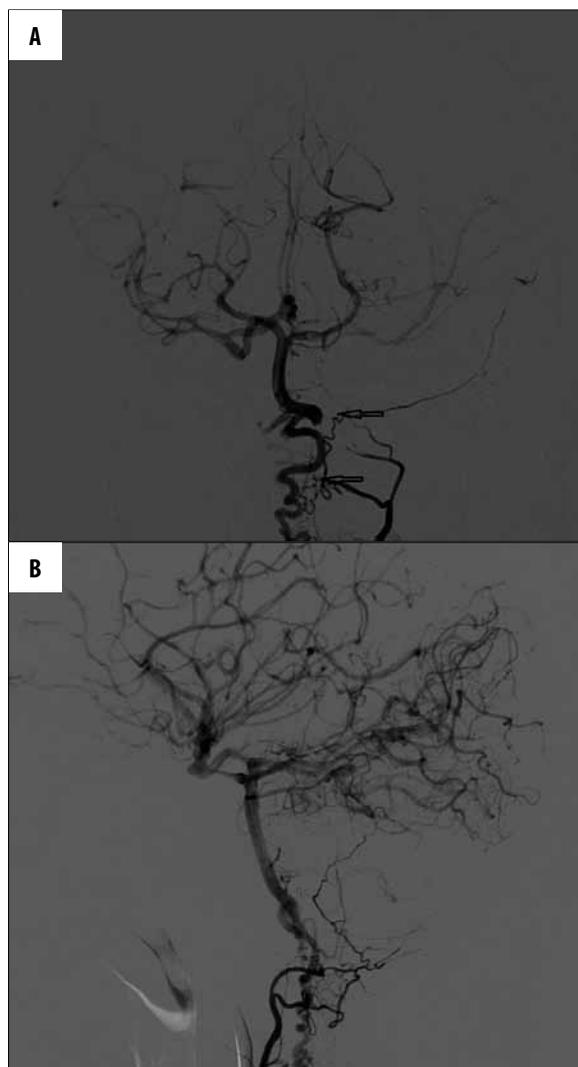


Figure 3. Angiography of the left vertebral artery. (A) Anteroposterior projection. Occlusion of the left vertebral artery (LVA) in the middle of the cervical segment. Its final segment fills from wide, winding collateral vessels (arrow). (B) Lateral projection.

occlusion of the right terminal vertebral artery was found, as well as occlusion in the mid-portion of the left cervical vertebral artery. However, blood flow was restored in the terminal left vertebral artery and basilar artery through the wide, tortuous collateral vessels (Figure 3). These vessel collaterals provided blood to the areas supplied by the main cerebral arteries, that is to the right internal carotid artery with the right anterior and middle cerebral arteries, and also to the left anterior and middle cerebral arteries via the anterior communicating artery. The patient was diagnosed with moyamoya disease based on the overall clinical picture and additional tests. Then, the drug therapy was initiated, as well as motion physical therapy and logopedic treatment. The girl's general condition gradually improved. After about one month of treatment, she was referred to the Department of Neurosurgery and underwent cortical revascularization surgery using the multiple burr hole technique (MBH). The surgical procedure was performed bilaterally and involved fronto-temporo-parietal area. A



Figure 4. CT unenhanced scan of the brain, axial plane – subarachnoid hemorrhage.

follow-up arteriography did not reveal significant differences compared to baseline at about four months after surgery. Currently, the Pediatric Neurology Outpatient Clinic provides care for the patient.

Case 2

A 17-year-old female patient was admitted to a hospital for a severe headache associated with nausea and vomiting which occurred while she was swimming in a swimming pool. She had a history of recurrent headaches for the past 2 months, which occurred mainly in the afternoon and resolved spontaneously. Neurological examination revealed decreased superficial (exteroceptive) sensation in the left arm and leg, and pronounced neck stiffness on admittance to the hospital. Brain CT scans showed extravasation of blood along the path of the middle cerebral artery and in the sellar area on the left side which would indicate the evidence of subarachnoid hemorrhage (Figure 4). Therefore, a computed tomography angiography (CTA) examination was performed. Both the left middle cerebral artery and its branches exhibited significant decrease in contrast enhancement on CTA scans, which could suggest arterial constriction due to subarachnoid hemorrhage. On the third day of hospitalization, paresthesias abated. The headache gradually resolved and serum electrolyte levels returned to normal. Cerebral arteriography was performed on Day 14 and revealed proximal occlusion of the middle cerebral artery associated with the development of the extensive network of tiny collateral blood vessels (moyamoya phenomenon) (Figure 5). The patient was diagnosed with moyamoya disease and referred to the Department of Neurosurgery for additional diagnostic tests and further treatment. To date, follow up tests have not demonstrated any difference in the structure of her blood vessels. Currently, the Neurology Outpatient Clinic provides care for the patient.

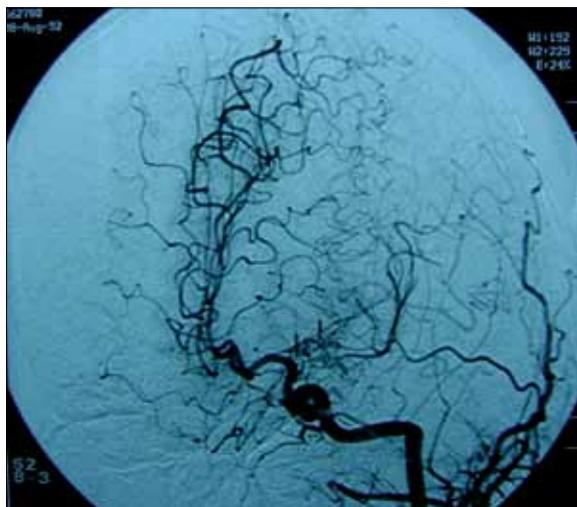


Figure 5. Angiography of the left internal carotid artery – oblique projection. Occluded left medial cerebral artery with adjacent collateral circulation (arrows).

Case 3

A 13-year-old girl with von Recklinghausen's disease was admitted to the Department of Neurology after she had experienced a transient (lasting for about 5 minutes) left-sided hemiplegia associated with speech disorders. Neurological examination did not reveal any focal symptoms or meningeal signs on admittance to the hospital. However, numerous café au lait macules (CALMs) and single cutaneous nodules were found on her torso and limbs on physical examination. Findings from laboratory tests were normal. Magnetic resonance imaging of the brain revealed lesions typical of neurofibromatosis type 1 (NF-1). The computed tomography angiography (CTA) showed critical stenosis of the left distal internal carotid artery just before its terminal bifurcation and short-length narrowing of arteries that comprise the circle of Willis, namely the left and right proximal anterior and proximal middle cerebral arteries, and right posterior cerebral artery. Tiny, tortuous collateral blood vessels were also present in the area of stenosis (moyamoya phenomenon). The above-described CTA findings were further confirmed on arteriography (Figure 6). Therefore, the patient was diagnosed with moyamoya disease in view of a previous history of von Recklinghausen's disease.

Discussion

Moyamoya disease was first described as "bilateral internal carotid artery hypoplasia" in 1957 [5]. The name of the disease originates from a Japanese word "moyamoya" which means a "puff of smoke". The disease was first described in Japanese literature in 1965, and in English literature in 1969 [3,7]. Since that time, an increasingly growing number of cases has been reported in the North America and Europe. Moyamoya disease has become a worldwide problem, even though initially it seemed to occur only in the West Asian region [5,7]. In 1997, the Japanese Ministry of Health and Welfare proposed to introduce a kind of a clinical guide on diagnosis and treatment of moyamoya disease. The main diagnostic criteria include narrowing

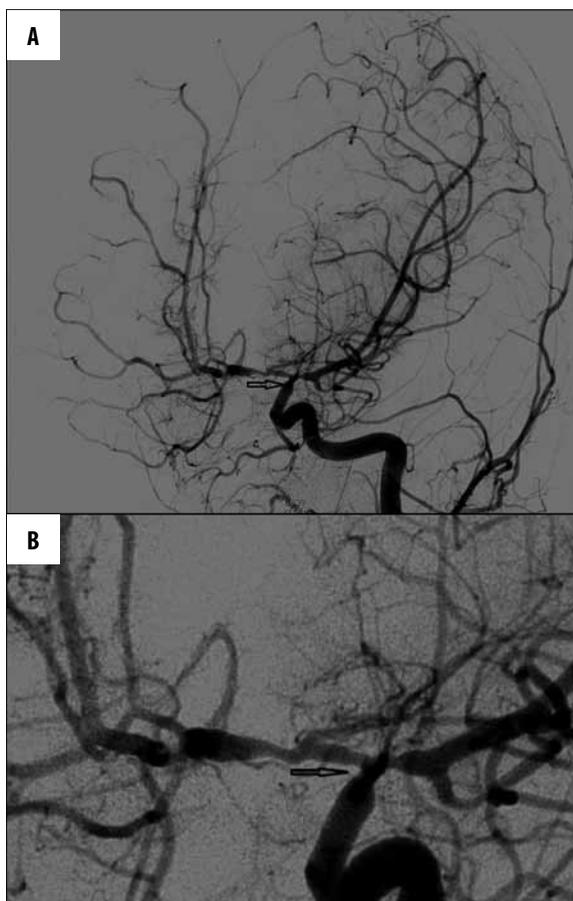


Figure 6. Angiography of the left internal carotid artery. (A) Critical stenosis of the left internal carotid artery just before division (arrow). (B) The same image magnification (arrow).

or occlusion of the distal internal carotid artery or proximal anterior and middle cerebral arteries, associated with a network of abnormal small collateral blood vessels. A definite diagnosis can be made only if bilateral lesions occur [7], while patients with unilateral lesions can be diagnosed as probably having moyamoya disease [1,7]. An unknown etiology is another very important diagnostic criterion. Moyamoya disease should rather be excluded and moyamoya syndrome diagnosed in patients with conditions or risk factors which may promote these specific vascular lesions [7]. These include: autoimmune diseases (e.g., systemic lupus erythematosus), hematological diseases (e.g., aplastic anemia), malignant tumors, birth defects (e.g., neurofibromatosis type I, Down syndrome), infectious diseases (e.g., tuberculosis), metabolic diseases (e.g., type IIa hyperlipoproteinemia), vascular diseases (e.g., arteriovenous malformations) and many others, e.g. drug abuse or traumatic brain injury [7]. One of our patients (Case 1) with moyamoya disease was previously diagnosed as having Sydenham's chorea, which is considered an autoimmune disorder. However, there are no reports in the available literature to indicate that the disease may cause a vasculopathy. Reports on the natural history vary with regard to the course of the disorder. Moyamoya disease is incurable and progressive in nature in the vast majority of patients, including those with no symptoms [4,7]. In one of our patients (Case 2), follow-up tests did not show any

evidence of progression of the disease. However, the period of observation was short. Usually, ischemic stroke, which is the most common clinical sign of underlying moyamoya disease in European patients, affects the area of the brain supplied by the internal carotid artery. In the majority of patients ischemic stroke produces various focal symptoms such as aphasia, hemiplegia and dysesthesia. Cognitive and behavioral disorders are less common. It may happen that patients, who experience these symptoms, are misdiagnosed as having schizophrenia, depression or personality disorders [4,9,10]. The digital subtraction angiography (DSA) is still considered a "gold standard" diagnostic test in moyamoya disease. However, due to their common use and availability, computed tomography (CT) and magnetic resonance imaging (MRI) are becoming the first-line diagnostic modalities in patients with suspected moyamoya disease [4]. There is no need to perform DSA if patient shows all signs of the disease in computed tomography angiography (CTA) or magnetic resonance angiography (MRA). The common use of non-invasive diagnostic imaging technologies in clinical practice increased the chance for identification of asymptomatic patients [1,3]. So far, there is no effective treatment for moyamoya disease. Surgical treatment

is the only effective method to improve cerebral circulation and prevent further ischemic events. The superficial temporal-to-middle cerebral artery bypass represents the mainstay of surgical treatment for moyamoya disease. Other indirect or combined revascularization procedures are less common [1,4]. The non-invasive treatment involves antiplatelet therapy, whereas anticoagulant drugs are rarely used. Calcium channel blockers may also be useful in the treatment of headaches, which are common in moyamoya patients [1].

Conclusions

Moyamoya disease affects both children and adults. It should be considered in pediatric patients with acute neurological deficits or cerebral ischemia of unknown etiology. Patients with diagnosed or suspected moyamoya disease should be referred directly to clinical centers experienced in diagnosis and treatment of this medical condition, as delayed diagnosis and treatment can increase the risk of permanent disability due to ischemic stroke. Early diagnosis and surgical revascularization may significantly improve clinical outcomes [4,7,9].

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