Article received on June 24, 2019 and accepted for publishing on December 3, 2019.

CLINICAL PRACTICE

Clinicopathological evaluation of Moyamoya disease. Case report and review of literature

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Abstract: *Moyamoya disease is a rare affliction, which progressively affects cerebral arteries, more frequently those in the circle of Willis and the internal carotid arteries. This condition has a genetic component, but the cause of the disease is unknown. It usually affects children but can affect adults as well, representing a health issue due to its mortality. Not in a few cases, Moyamoya disease has been difficult to recognize as a cause of ischemic or hemorrhagic strokes. In this article, we present the case of a young patient, with a medical history of cerebral hemorrhage, which was diagnosed with Moyamoya disease after clinical and cerebral angiographic corroboration in a specialized vascular center. The patient entered the Emergency Receiving Unit with a sudden comatose state. Paraclinical tests revealed massive intraparenchymal hemorrhage, with movement in the medial line and ventricular flooding.*

Keywords: *Moyamoya disease, stroke, cerebral death*

INTRODUCTION

Moyamoya disease is a rare progressive blood vessel disease characterized by progressive stenosis of cerebral arteries, more frequently those in the circle of Willis and the internal carotid arteries. A collateral blood flow is formed around the blocked arteries to compensate for the lack of blood flow, but those collateral vessels are small and fragile, thus increasing the risk of bleeding, aneurysm and thrombosis [1].

The name of Moyamoya disease comes from the Japanese language, where it means "cloud of smoke". This disease was discovered in 1957 as an internal carotid artery hypoplasia of the tunica intima [2].

This condition has a genetic component, but the cause of the disease is unknown. Patients may present chorea, headache, seizures, or cognitive impairment expression of transient ischemic attacks or ischemic stroke and a large proportion of patients, mostly adults presenting with intracerebral hemorrhage. Two age peaks are recognized: one during childhood and one in young adults [1, 3]. In most regions, women are more frequently affected than men [3].

Although Moyamoya is a vascular disease, it is associated with other medical conditions like autoimmune disease, Down syndrome, arteriosclerosis, neurofibromatosis type 1 or other multiple tumors developing in the spinal cord [4, 5, 6].

In this article we present the case of a young patient, with a medical history of cerebral hemorrhage, who was diagnosed with Moyamoya disease after clinical and cerebral angiographic corroboration in a specialized vascular center and we review the literature on this disease.

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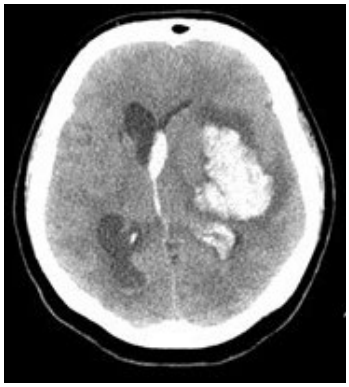
CASE PRESENTATION

We present the case of a patient aged 39, from an urban environment, known with having a medical history of cerebral hemorrhage in the previous year (twice in 6 months). The patient was investigated in a specialized vascular center in western Romania, where she was diagnosed with Moyamoya disease and was recommended a course of treatment. She is brought into the Emergency Clinical County Hospital in Oradea, Romania, with a sudden comatose state which had come on several hours before. On physical examination, neurological testing reveals asymmetric mydriasis, bilateral flexion in the plantar cutaneous reflex, symmetrical dropping of the arms and feet on the bed and a Glasgow score of 3. Other examinations (skin, extremities, abdomen, musculoskeletal system) were within normal limits.

A cranial CT scan shows massive localized hemorrhage in the left temporoparietal region, of 5.6/4/1 cm, with ventricular flooding in the third and lateral ventricles and mass effect with movement in medial line of 8 cm (Figure 1).

Figure 1: Cranial CT image shows the hemorrhagic accumulation with fresh blood; intraparenchymatous temporo-parietal densities with 5.6/4.1 cm axial diameters; slight perilesional edema, ventricular flooding in the bilateral lateral and third ventricles, and mass effect, the median line is shifted to the right by approximately 8 cm.



Laboratory results on admission showed hydro-mineral imbalance (hypokalemia and hypomagnesemia), which were corrected and remained within normal limits for the short duration of the patient's hospital visit. Complete blood cell count and examination of the peripheral smear showed normocytic anemia with normal leukocyte and platelet counts. Coagulation tests (D dimer, fibrinogen, partial thromboplastin time, prothrombin time, and thrombin time) were within normal limits.

The patient is then transferred to the Intensive Care Unit, where she receives orotracheal intubation and mechanical ventilation. Depletive and neurotrophic cerebral treatment is instituted, along with antibiotic therapy and acid-base and electrolytic balancing. The neurological state of the patient remains unchanged, with a Glasgow score of 3, fixed bilateral mydriasis and no cerebral reflexes. A control cranial CT scan is undertaken within another 48 hours, which shows the same collection of temporoparietal hemorrhage and no other modifications. The lateral ventricles have increased in size compared to the previous CT scan, with erased subarachnoid spaces (Figure 2). The suspicion of cerebral death is raised. After 72 hours, the suspicion of cerebral death was raised and the protocol in declaring cerebral death is followed, which is then confirmed by 2 EEG's, 2 apnea tests, ICU doctor, neurologist, neurosurgical assessment (Figure 3).

Figure 2: Cranial CT Image: the temporal-parietal intraparenchymal massive hemorrhagic left collection with ventricular intrusion in the right-side ventricle and ventricle 3 and relatively unchanged mass effect. The lateral ventricles have increased in dimension compared to the previous examination, bilaterally. Deleted subarachnoid spaces. Hypodensity of the cerebral parenchyma with deletion of the differentiation between the white subset and the newly developed gray substance which may suggest hypoxic ischaemia.

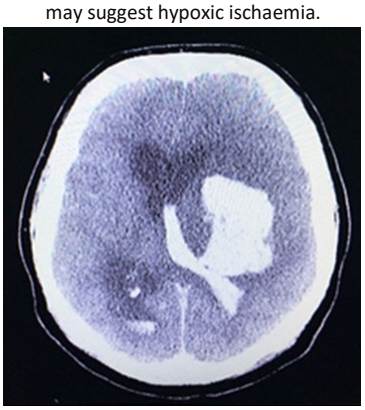
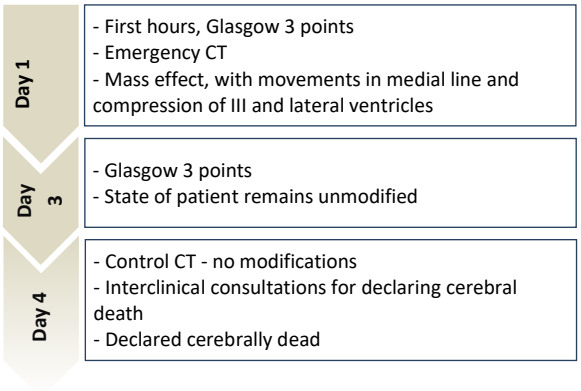


Figure 3: Evolution of patient



In the case we presented, the patient suffered a profound left cerebral vascular hemorrhagic accident, with three

ventricular flooding and mass effect, as well as movement in the medial line by 8 cm, which made her comatose. Despite proper treatment, no signs of improvement were recorded. The family grants permission for transplant and investigations begin to facilitate organ transplantation. In the subsequent necrotic examination, a massive 7/6/3 intraparenchymal hemorrhage is observed, with erased channels and flattened circumvolutions, as well as reddish cerebrospinal fluid.

DISCUSSIONS

Moyamoya disease is a rare pathology, but its seriousness needs to make us aware of the risks that can appear. This disease is a medical problem from a variety of standpoints because it can appear in both children and adults, it progressively affects cerebral arteries through stenosis and occlusion and can lead to cerebral vascular accidents or repetitive transient ischemic attacks, which can kill the patient by themselves. Usually, children present symptoms attributed to slowly progressive cerebral hypoperfusion and repetitive ischemic symptoms, while adults have hemorrhagic or ischemic events [7-8].

The cause of Moyamoya disease is unknown, but it is believed that there is a genetic component involved [9]. According to some studies, this disease could be autosomal dominant, with incomplete penetration, depending on age and genomic factors [10]. Another study shows that the RNF213 gene is the main gene associated with Moyamoya disease [11]. In some studies, arterial stenosis was found to occur in not only the intracranial arteries but also renal, pulmonary, coronary, and pancreatic arteries. Renal artery stenosis is the most frequently reported associated with Moyamoya disease and the consequence is renovascular hypertension [12].

The walls of blood vessels have three layers in their structure: tunica intima, media and adventitia. From a morpho-pathological point of view, Moyamoya disease is characterized by the thickening of the tunica intima in internal carotid arteries bilaterally, which, at this level, can contain lipid deposits. The most frequently affected arteries are the anterior, middle and posterior cerebral arteries, which form the circle of Willis and can present with different degrees of stenosis and occlusion because of thickening in the tunica intima, curling in the internal elastic lamina and thinning of the tunica media.

The transversal sectioning of a basal artery in a patient with Moyamoya disease, with hematoxylin-eosin staining shows fibrosis and thickening of the tunica intima and proliferation of the smooth muscle cells (white arrows), as well as the folding and chronic contraction of the internal elastic lamina (blue arrows) and absence of inflammatory or atherosclerotic changes [13].

The incidence of the disease is greater in children around the age of five and adults around the age of 40. The condition is more frequent in women than in men, with a higher incidence in Asian population and a lower one in the European population. Women can present with transient ischemic attacks or cerebral hemorrhages in their medical history, or they can be asymptomatic. The recurrence in cerebral vascular accidents can be higher in these patients [14]. Clinically, patients with Moyamoya disease may present seizures, transient ischemic attacks, ischemic and hemorrhagic strokes. Headache, speech disturbances, visual deficits, intellectual deterioration, cranial nerve paralysis can also be seen in both children and adults. Mental retardation can be seen in children having Moyamoya disease.

Moyamoya disease is an important diagnosis to consider in children or young adults presenting stroke. Cerebrospinal fluid results of a lumbar puncture or electro-encephalography can be abnormal but are usually nonspecific. This pathology can be most frequently diagnosed in a quick fashion by using modern cerebral imaging methods such as an angio-CT, angio-MRI or 3D-DSA (rotational digital subtraction angiography), in a disease that is sometimes asymptomatic. Knowing all the radiological signs have a major influence on placing early and correct diagnosis, which can lead to prompt treatment and a possible increase in life expectancy in these patients.

Unfortunately, the therapeutic options are limited or inappropriate. Treatment in the acute phase is symptomatic for maintaining cerebro-vascular perfusion. Anticoagulant and antiplatelet agents, corticosteroids have shown no remarkable benefit. Surgical treatment procedures have been used to manage the hemorrhagic and ischemic consequences of Moyamoya disease to restore and maintain adequate cerebral perfusion, but there are serious adverse effects including cerebrovascular infarct or hemorrhage, motor or sensory dysfunction, cognitive decline, and death [15].

CONCLUSION

This pathology needs to be taken seriously because it presents a significant risk factor in creating cerebral vascular accidents, both ischemic and hemorrhagic, in young adults. Surgery can be beneficial, particularly if the diagnosis of moyamoya disease is made early. In patients with a history of cerebral accidents, angio-CT or angio-MRI and/or obtaining a protein RNF213 dosage would be

recommendedto confirm or exclude Moyamoya disease in its early stages and institute proper specialized treatment.

Conflict of interests
None.

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