

MOYAMOYA DISEASE IN A PATIENT WITH BRAIN TUMOR: CASE REPORT

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SUMMARY – A 40-year-old male presented to emergency room with epileptic grand mal seizure. He had untreated hypertension, and prior diagnostic investigation showed duplex renal arteries of the right kidney with hyperreninemia in the left renal vein. He was nonsmoker, with moderate alcohol intake. Neurologic examination was normal except for high blood pressure and tongue bite. Electroencephalogram was nonspecific. Nuclear magnetic resonance (NMR) showed vascular lesions in the white matter and infratentorially an expansive lesion with no postcontrast imbibition in the right cerebellar hemisphere. Neurosonography revealed hypoplasia of both internal carotid arteries (ICA), mean diameter <2 mm, subtotal stenosis at the origin of both ICA, and development of collateral path, typical for moyamoya disease. Magnetic resonance angiography (MRA) and digital subtraction angiography (DSA) confirmed the neurosonography diagnosis. Immunologic tests for vasculitis were negative, while hematologic examination showed 4G allele for PAI-1. Serum lipids were elevated. We recommended neurosurgical operation of brain tumor. Histopathologic finding showed meningioma. This case is interesting because of the rare complex cerebrovascular disease, i.e. coexistence of hypoplasia of both ICA, bilateral subtotal stenosis of ICA, intracranial moyamoya disease, and brain tumor.

Key words: *Brain neoplasms – diagnosis; Brain neoplasms – ultrasonography; Moyamoya disease – diagnosis; Moyamoya disease – etiology; Moyamoya disease – pathology; Case report*

Introduction

Moyamoya disease is a specific chronic cerebrovascular occlusive disease, first reported by Japanese surgeons in 1957. It is characterized by progressive stenosis and occlusion of the terminal portions of bilateral internal carotid arteries and abnormal vascular network in the vicinity of the arterial occlusion¹. There are 4 types: transient ischemic attack (TIA), ischemic, hemorrhagic, and epileptic². In infants,

children and adolescents it presents with ischemic attacks or seizures. It rarely occurs in adults, usually in the third or fourth decade of life. Subarachnoid hemorrhage is the most common initial manifestation in adults. There are two peaks, at the age of 5 years and around the age of 40 years. Approximately 6000 cases of moyamoya disease have been reported across the world. The highest prevalence is in Japan, with a higher female to male ratio. In Asian patients, moyamoya mostly presents with cerebral hemorrhage, while in nonAsians it usually presents with ischemic stroke. Fifteen percent of all cases in Japan have familial occurrence, and recent studies suggest some responsible genetic foci on chromosomes 17 and 6^{3,4}. The symptoms include weakness of an arm, leg or both, headache, convulsions, impaired mental development,

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visual and speech disturbance, sensory impairment, involuntary movements or unsteady gait. The epileptic type of moyamoya disease is characterized mostly by focal seizures. Once the process of vascular occlusion begins, it tends to continue despite any known medical management. It leads to recurrent stroke and severe impairment of daily living functions. Moyamoya disease is rarely asymptomatic.

Moyamoya disease should be distinguished from moyamoya syndrome, which is associated with neurofibromatosis⁵, cranial irradiation⁶, Down's syndrome⁷, morning glory anomaly⁸, systemic lupus erythematosus (SLE)⁹, prothrombotic disorder¹⁰, or a congenital heart disease¹¹, such as coarctation of aorta, ventricular septal defect, aortic and mitral valve stenoses, tetralogy of Fallot, and stenosis of coronary arteries. All this suggests that moyamoya disease might be an intracranial manifestation of systemic arterial disorder.

The diagnosis of moyamoya disease includes characteristic angiographic findings together with clinical criteria. Nuclear magnetic resonance (NMR) and magnetic resonance angiography (MRA) should be performed for the diagnosis and follow up of moyamoya disease. Often, nuclear medicine studies such as single photon emission computerized tomography (SPECT) are used to demonstrate the decreased blood and oxygen supply to the brain areas involved in the pathologic vascular process.

The treatment of moyamoya disease is still unsatisfactory. Cases with milder symptoms are usually treated conservatively, while more severe symptomatic cases are treated by revascularization procedures. Multiple revascularization procedures such as pial synangiosis, superficial temporal artery to middle cerebral artery bypass direct anastomosis are considered to be justified. Its efficacy for hemorrhagic type of disease remains uncertain. While symptoms may seem to improve immediately after the revascularization procedure, it takes about 6-12 months before new vessels develop.

Case Report

A 40-year-old male was admitted to the Intensive Care Unit at University Department of Neurology, Sestre milosrdnice University Hospital, due to a grand mal epileptic seizure for the first time in his life. He



Fig.1. Subtotal stenosis of the right internal carotid artery.

had arterial hypertension since childhood, but did not take antihypertensive drugs. In 1991, he was hospitalized at University Department of Medicine, Zagreb University Hospital Center, for high blood pressure and nephrologic investigation including renal angiography. Renal angiography revealed duplex renal arteries in the right kidney and elevated renin in the left renal vein. He was taking lisinopril for a few months, but the medication was stopped because of side effects. He suffered from chronic low back pain with exacerbation two weeks before admission. He was a nonsmoker with moderate alcohol intake.

Neurologic examination at admission was normal except for high blood pressure (190/100) and a tongue bite. Laboratory blood and urine results were normal

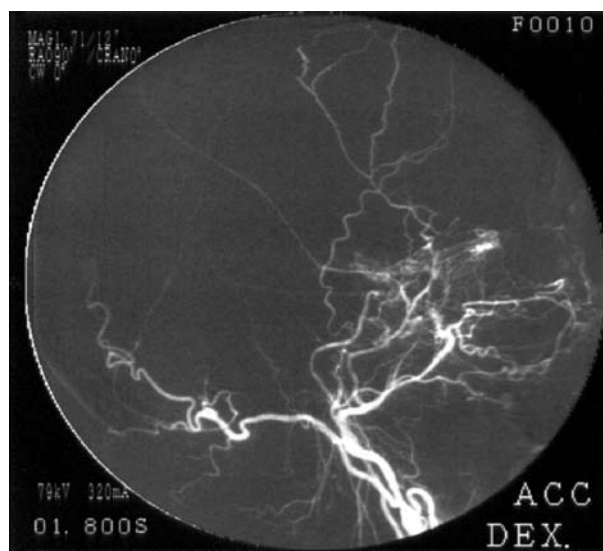


Fig.2. Carotid angiogram with a network of small anastomotic vessels at the base of the brain, rete mirabile.



Fig.3. Nuclear magnetic resonance showing expansive lesion in the right cerebellar hemisphere.

except for elevated serum cholesterol and triglycerides. Electrocardiogram showed signs of left ventricular hypertrophy. Electroencephalogram was nonspecific. Computed tomography scan revealed chronic vascular lesions. Neurosonography revealed hypoplasia of both internal carotid arteries (ICA), mean diameter <2 mm, subtotal stenosis of both ICA with attenuated hemodynamics and development of collateral path, typical for moyamoya disease. Both vertebral and basilar arteries had normal hemodynamic spectrum. Transcranial Doppler sonography showed attenuated hemodynamics in the circle of Willis. Digital subtraction angiography (DSA) confirmed the diagnosis of moyamoya disease. Carotid angiogram showed typical rete mirabile, confirming suspicion of moyamoya disease.

NMR showed T2 hyperintense vascular lesions in the white matter and a T2 hyperintense homogeneous lesion 2.5 cm in diameter infratentorially in the right cerebellar hemisphere, with no postcontrast imbibition. Morphological characteristics of this expansive process in the posterior cranial fossa were indicative of meningioma. Immunologic tests for vasculitis were negative, while hematologic examination showed 4G allele for plasminogen activator inhibitor-1 (PAI-1), what implies a higher risk of deep vein thrombosis and myocardial infarction. Neurosurgeon recommended neurosurgical removal of the brain tu-

mor. The patient recovered fully and was advised to take antihypertensive, antiaggregation and antiepileptic drugs. Histopathology of the brain tumor that was removed completely showed it to be a meningioma.

After 5-year follow up, the patient was free from any new ischemic events and seizures. Control NMR and MRA were unchanged.

Discussion

This case of a 40-year-old male patient with complex cerebrovascular disease and brain tumor as a coincidental factor presenting with seizure is specific because of a combination of the epileptic and ischemic types of moyamoya disease. The seizure was obviously caused by multiple vascular ischemic lesions due to stenotic lesions of intracerebral arteries. Carotid angiogram showed extensive basal cerebral rete mirabile – a network of small anastomotic vessels at the base of the brain, around and distal to the circle of Willis, along with segmental stenosis or occlusion of the terminal parts of both internal carotid arteries. Six angiographic stages have been described^{1,12,13}: stage 1 shows narrowing of the carotid forks, stage 2 means moyamoya vessels at the base, stage 3 is characterized by more apparent moyamoya changes, stage 4 means reduced basal moyamoya vessels, in stage 5 reduction is more prominent, and in the last stage 6 moyamoya vessels disappear and collateral circulation is produced from external carotid arteries. According this staging, it was stage 3. The characteristic histopathologic features are fibrocellular thickening of the intima containing proliferated smooth muscle cells and prominently tortuous and often duplicated internal elastic lamina. There is usually no atheromatous plaque in the arterial wall nor there are inflammatory signs. The etiology of moyamoya disease is still unclear. Even though several linkage studies showed relations with gene loci, no specific locus has yet been identified. Investigations undertaken to better understand this rare condition have shown involvement of the cerebrospinal fluid (CSF) basic fibroblast growth factor (b-FGF) with receptor up-regulation and tumor growth factor beta 1 in altering cerebral vasculature. Intimal thickening has also been postulated resulting from altered permeability due to enhanced prostaglandin release from the arterial smooth muscle^{14,15}. The first conclusion

was that infratentorial meningioma is an independent factor, but there are several cases of moyamoya disease described in the literature where moyamoya was associated with different types of cranial tumors such as arteriovenous malformations, benign intracranial tumors in neurofibromatosis, cystic tumor of vermis, optic glioma and pituitary adenoma¹⁶. Meningioma could be part of neurofibromatosis type II, a hereditary disorder that is connected with moyamoya disease. A study of the presence of numerical chromosome aberrations in meningioma tumors as revealed by fluorescence in situ hybridization¹⁷ showed an overall incidence of 76%. The most common abnormalities were found in chromosome Y and chromosome 22. Chromosome 17 was affected in 23% of patients. Deletion of a p17 chromosome leads to mutation of tumor suppression gene p53 and tumor transformation of normal meningoendothelial cells^{3,18,19}. On the other hand, changes on chromosome 17 are mostly found in moyamoya disease. The coincidence of solitary intracranial tumor and moyamoya disease could be connected with chromosome 17 aberrations.

The case presented is interesting because it suggests that not only neurofibromatosis type II as an inherited disease characterized by multiple multifocal tumors, mainly neurinoma, schwannoma and meningioma, but solitary intracranial tumors could also be associated with moyamoya disease. The coexistence of these two diseases could have a genetic origin connected with gene mutation located on chromosome 17.

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Sažetak

BOLEST MOYAMOYA U BOLESNIKA S TUMOROM MOZGA: PRIKAZ SLUČAJA

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Muškarac u dobi od 40 godina pregledan je u hitnoj ambulanti zbog epileptičnog napada tipa grand mal. Bolovao je od neliječene hipertenzije, ranijom dijagnostičkom obradom verificirana je dvostruka bubrežna arterija desno i hiperenemija u lijevoj bubrežnoj veni. Bio je nepušač s umjerenom konzumacijom alkohola. Neurološki pregled je bio uredan osim povišenih vrijednosti krvnog tlaka i traga ugriza jezika. Elektroencefalogram je bio nespecifičan. Magnetskom rezonancijom mozga nađene su vaskularne lezije u bijeloj tvari te infratentorijalno u desnoj cerebelarnoj hemisferi ekspanzivni proces bez postkontrastne imbibicije. Neurosonološkim ispitivanjem potvrđena je hipoplazija obiju unutarnjih karotidnih arterija (ACI) s prosječnim promjerom <2 mm, subtotalna stenoza polazišta obiju ACI i razvoj kolateralnog puta, što je tipično za bolest moyamoya. Magnetska angiografija (MRA) i digitalna subtrakcijska angiografija (DSA) su potvrdile neurosonološku dijagnozu. Imunološki testovi za vaskulitis su bili negativni, dok je hematološkom obradom nađen 4G alel za plazminogen aktivator inhibitor-1 (PAI-1). Serumski lipidi su bili povišeni. Preporučili smo mu operaciju tumora mozga. Histopatološki nalaz je ukazivao na meningeom. Ovaj slučaj je zanimljiv zbog rijetke složene cerebrovaskularne bolesti, odnosno supostojeće hipoplazije obiju ACI, bilateralne subtotalne stenoze obiju ACI, intrakranijske bolesti moyamoya te tumora mozga.

Cljučne riječi: Novotvorine mozga – dijagnostika; Novotvorine mozga – ultrazvuk; Bolest moyamoya – dijagnostika; Bolest moyamoya – etiologija; Bolest moyamoya – patologija; Prikaz slučaja

