EPILEPTIC SEIZURES AS THE FIRST MANIFESTATION OF THE FRONTOPARIETAL ARTERIOVENOUS MALFORMATION OF THE BRAIN

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Abstract: Introduction: Arteriovenous malformations of the brain include a group of congenital disorders in the early development of arterial-venous blood vessels of the brain. Their clinical presentation is most common in the form of a brain hemorrhage, epileptic seizures, and headaches.

Case report: We showed a man who at the age of 28 early in the morning after breakfast had the first generalized tonic-clonic seizure. After the second unprovoked epileptic seizure, antiepileptic therapy was introduced. The brain scanner showed the existence of arteriovenous malformations in the right frontoparietal region. As the size of the malformation was less than 30mm, it was decided that the patient should be treated with Gamma knife radiosurgery. After the successful radiosurgery together with the antiepileptic drugs treatment, the patient is in a stable 1.5 year-long remission of epileptic seizures without neurological failures.

Conclusion: Epileptic seizures can be the initial clinical manifestations of arteriovenous malformations of the brain. With an early diagnosis, adequate antiepileptic drugs therapy and neurosurgery, radiosurgery (Gamma Knife), which is often necessary, many symptomatic epilepsies enter a stable remission of epileptic seizures.

Key words: arteriovenous malformations, brain, epileptic seizures, radiosurgery, gamma knife.

INTRODUCTION

Symptomatic epilepsies constitute a significant percentage of epilepsies in both the early and adult stages of human development, with vascular diseases of the brain (arteriovenous malformations, cavernomas, and aneurysms) being particularly significant. Arteriovenous malformations (AVM) of the brain represent a congenital disorder in the early differentiation of the development of arterial and venous blood vessels of the brain by establishing direct contact between the arteries and veins without the presence of capillaries (1). An AVM structurally consists of the pathological vascular web, the “nest”- nidus, which is composed of one or more supply arteries that continue on the main drainage vein and its collector branches. Because of this, an AVM shows a pathological tendency of frequent hemorrhages with deposits of hemosiderin in the surrounding brain tissue, which creates potential conditions for epileptogenesis, or the occurrence of epileptic seizures (2). By localization, AVMs are classified into supratentorial and infratentorial, superficial (cortical) and deep (subcortical) malformations. The main predictor factors for the assessment of operational risk for each AVM are localization, size and type of venous drainage (3). The most common effects of an AVM on surrounding brain structures are circulatory disorders in terms of microhemorrhage, the “steal” phenomena, the “mass” effects caused by the AVM size and its compression on adjacent structures with possible obstruction of the flow of liquor and the development of hydrocephalus (4). In the pathophysiological sense, an AVM among other things, causes “blood steal” (“the steal phenomena”) in the adjacent regions of the brain, because normal blood flow is diverted within the AVM, thus bypassing the surrounding brain structures. This type of “blood steal” from the surrounding brain, with consequent hypoperfusion, carries a high risk of epileptic seizures (5, 6). The predominant clinical manifestation of an AVM is brain hemorrhage (subarachnoidal, intracerebral, and intraventricular, or any combination thereof) (7). It is thought that about 50-70% of patients with an AVM experience brain hemorrhage. An average of 8% of subarachnoid hemorrhage (SAH) is caused by an AVM. AVM hemorrhage carries a risk of death in 10-15% of cases. It is thought
that 15-20% of all sudden deaths are caused by an AVM (8, 9, 10). Crawford et al. 1986 (11), in their study of monitoring AVM patients for 20 years, found that the risk of hemorrhage was 42%, epilepsy 18%, neurological deficiency 27% and fatal outcome 29%. The mortality rate in the initial hemorrhage of people with an AVM ranges from about 10%-15%, and in aneurysm ruptures is about 50% (10). Epileptic seizures represent the second most common clinical manifestation of an AVM, more commonly seen in patients with severe malformations. Epileptic seizures are an initial symptom in 24-47% of patients with an AVM (11). The most common type of seizure is generalized motor seizures, ie focal seizure with generalization (55.8%), then focal seizures without secondary generalization (12, 13). A superficially localized AVM is mainly clinically manifested by epileptic seizures, while the deep ones have a greater tendency to bleed (14). The dominance of focal seizures with generalization is the consequence of chronic cerebral hypoxia around the AVM and hemosiderin deposits caused by micro-hemorrhages. Headache is also a common clinical manifestation, and it appears as an initial symptom in the range of 5-35% of cases and results in an increase in pressure in the venous sinuses (15). Neurological deficiency occurs in about 27% of cases (11). The natural history of an AVM is that the patient has an annual risk of bleeding of 3%, with a risk of developing an accompanying neurological deficiency of 35% and a fatal outcome of 10% (16).

AVM diagnostics is most commonly performed via computerized brain tomography (CT, MSCT), magnetic resonance imaging (MRI, MRA), and cerebral angiography (17). Computerized brain tomography, magnetic resonance imaging, and transcranial doppler (TCD) are considered to be basic non-invasive diagnostic methods for AVMs. There is a tendency in modern neurosurgery towards using non-invasive methods in AVM diagnostics, although the use of angiography is still dominant. The treatment of a brain AVM with antiepileptic drugs (AED) gives good results in more than 68% of cases and the refractoriness of epileptic seizures to AED was present in about 32% of cases. Generalized motor seizures are dominant in 94.7% of cases and focal seizures occur in 5.3% of cases. Good medication control of epileptic seizures supports the view that there is no need for emergency surgical treatment of an AVM. Treatment of an AVM with palliative methods is often ineffective in terms of reducing morbidity and healing (18). The surgical procedure leading to complete healing is complete excision of the AVM with no remaining residue (19, 20). Other neurosurgical methods are embolization and radiosurgery (focused gamma radiation-Gamma Knife) (21, 22). Post-operatively, in an AVM there is a decrease in the frequency of seizures in 14-54% of cases, while in 7-22% of patients de novo epilepsy develops postoperatively (23). Patients who are deemed to carry a high risk of neurosurgical treatment of an AVM (resection, embolization or radiosurgery) are subject to drug treatment.

**CASE REPORT**

We showed a patient, aged 28, who reported to the neurologist due to the onset of the first epileptic generalized tonic-clonic (GTK) seizure. The seizure took place in the morning after breakfast and was not followed by prodromes or focal symptomatology. There was a sudden loss of consciousness with a fall and occurrence of GTK spasms and urination. After 2-3 minutes of the seizure, the patient regained his consciousness, felt heaviness in his body, exhaustion and nausea. He was healthy in the previous few days, he did not have headaches, and did not suffer from nervousness or insomnia. The vital signs upon admission were: blood pressure 120/80 mmHg, cardiac frequency 80/min, body temperature 36.7 °C. There were no abnormalilities in the neurological findings. The values of routine biochemical and laboratory analyses of serum (glycemia, Er, Hgb, Le, ESR, urea, creatinine, bilirubin, transaminases, total proteins, albumin, Na, K, Mg, Ca) and urine were within reference limits. There was no evidence of previous epileptic seizures or hereditary epilepsy. Electroencephalography (EEG), which was performed on the day of the seizure, resulted in normal findings, ie epileptiform graft elements were not registered. Since it was the first unprovoked seizure with normal EEG findings, antiepileptic therapy was not included. A month after the onset of the first GTK seizure, a second epileptic seizure occurred, the same clinical manifestation lasting 3-5 minutes. An EEG recording was performed and did not register epileptic activity. The patient then had a CT, CTA of the brain that showed the presence of a 25 mm arteriovenous malformation in the right frontoparietal region (Clinic of neurosurgery in Belgrade, Serbia). The therapy includes AED valproate at an initial dose of 0 + 0 + 250 mg/day, with a gradual increase in the dose of 250 mg per week, to an effective dose of 500 + 0 + 500 mg/day. The patient was subjected to neurosurgical treatment and then, due to the size of the AVM (<30 mm), it was decided to carry out a Gamma Knife radiosurgery (Acibadem hospital in Istanbul, Turkey). On the first day after radiosurgery, another GTK seizure occurred during sleep, and the EEG recorded focal spikes and theta waves on the right frontoparietal without propagation to the homologous region of the opposite hemisphere. The dose of valproate was increased to 500 + 0 + 1000 mg/day after which there were no further seizures. The patient is in a stable 1.5-year remission of epileptic seizures,
DISCUSSION

Arteriovenous malformations of the brain represent a congenital disorder in the early differentiation in the development of arterial and venous blood vessels of the brain. Due to their size, bleeding tendency and supratentorial localization often cause symptomatic epileptic seizures of the generalized or focal type. Epileptic seizures are treated with AED, but since they are symptomatic seizures associated with an AVM, they are usually drug-resistant (24). When an AVM is proven to cause epileptic seizures, neurosurgery, i.e., radiosurgery is indicated. Gamma Knife is stereotactic radiosurgery for the treatment of tumors and brain metastases (benign and malignant) which are smaller than 30mm and well limited. It is performed without general anesthesia, without opening the skull, lasting from 30 minutes to 2h, and after the treatment, the patient can go home the same day or the next day. Gamma Knife directs radiation to a focussed pathological spot in the brain that is computer-determined so that gamma rays destroy the tumor tissue with the maximum sparing of surrounding healthy tissue. Earlier, since there was no Gamma Knife, even in the case of a small tumor, the whole brain was radiated. Our case report shows that epileptic seizures can be the first symptom of a brain AVM and that Gamma knife treatment together with AED (before and after treatment) leads to a complete remission of epileptic seizures. Our case report confirms works from the literature that Gamma Knife neurosurgery may be a prominent alternative to the treatment of brain AVM (25, 26). Most neurological studies indicate that the main predictor of post-radiation epileptic seizures is the existence of an AVM nidus residue after the treatment (27). Thus, the primary goal of stereotactic radiotherapy is the complete obliteration of the AVM nidus, which ensures the conditions for a complete remission of epileptic seizures and gradual elimination of anti-epileptic drugs (28).

CONCLUSION

Epileptic seizures can be the initial clinical manifestations of arteriovenous malformations of the brain. With an early diagnosis (CT, MRI, EEG), adequate antiepileptic drugs therapy and Gamma Knife radiosurgery, which is often necessary, a complete remission of epileptic seizures is established in most patients, and the use of antiepileptic drugs is stopped. Using this procedure and treatment, many symptomatic epilepsies enter a stable remission of epileptic seizures.

Abbreviations

AVM — arteriovenous malformations
SAH — subarachnoid hemorrhage
GTC — generalized tonic-clonic
AED — antiepileptic drug
EEG — electroencephalography
CT — computed tomography
MSCT — multi-slide computer tomography
MRI — magnetic resonance imaging
MRA — magnetic resonance angiography
TCD — transcranial doppler

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misiji epileptičkih napada i bez neuroloških ispada. **Zaključak:** Arteriovaskularne malformacije mozga mogu se manifestovati epileptičkim napadom kao inicijalnim kliničkim znakom. Ranom dijagnozoj, adekvatnom antiepileptičkom medikamentoznom terapijom i često nepodnim neurohiruškim, odnosno, radiohiruškim tretmanom (gama noz), mnoge simptomatske epilepsi-je ulaze u stabilnu remisiju epileptičkih napada.

**Ključne reči:** arteriovaskularne malformacije, mozak, epilepsija, napadi, radiohirurgija, gama noz.

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