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Cerebral cavernomatosis and epilepsy: treatment and serial imaging follow-up

Catalina Elena Bistriceanu[1,2], Dan Iulian Cuciureanu[1,3]

[1]Neurology Department, Faculty of Medicine, "Gr. T. Popa" University of Medicine and Pharmacy, Iasi, Romania
[2]Elytis Hospital Hope, Iasi, Romania
[3]"Prof. Dr. N. Oblu" Neurosurgery Clinical Emergency Hospital, Iasi, Romania

ABSTRACT

Cerebral malformations, known as cavernomas, are low flow vascular malformations that have a multilobulated appearance. A large percent of cavernous malformations have seizures as initial symptoms. We report a case of a 48 years old patient presented in the neurological department for seizure work-up. We performed serial brain imaging to follow the evolution of bleeding cavernomas and electroencephalography to find epileptogenic cavernomas. Conservative management was decided and the evolution under antiepileptic drugs was good, but with some compliance issues further discussed.

Keywords: cerebral cavernous malformations, epilepsy-related cavernomatosis

INTRODUCTION

Cerebral cavernous malformations (CCMs) are characterized by the presence of endothelium-lined caverns without mature vessel walls and have a multilobulated appearance. There is usually a progressive growth pattern and a repeated hemorrhage in their biology [1]. Cavernomas are estimated to occur in 0.5% to 0.7% of the population [2,3]. Among all vascular malformations, they account for 10–25% of cases [4].

CCMs are benign vascular lesions that can occur anywhere in the brain parenchyma or leptomeninges, but usually in the supratentorial region [5]. 40–70% of supratentorial cavernous malformations tend to have seizures as their initial symptoms; they can manifest as central nervous system bleeding and other neurological problems depending on where they are located. In addition, localization-related epilepsy may be affected by individual predispositions, since lesions of the same type, size, and location may manifest differently in different patients (including seizure disorders of different severity) [5,6].

Cavernomas can be detected more accurately with magnetic resonance imaging (MRI) than with computed tomography (CT). Cavernomas appear as heterogeneous "popcorn-like" lesions with mixed signal intensity cores and a peripheral rim of hypointense signal intensity reflecting hemosiderin zones [3,7].

Symptomatic cavernous malformations can be detected with conventional MR imaging by detecting a ring of hypointensity due to hemosiderin deposits caused by recurring microhemorrhages [8, 9]. As a result of its ability to display hemosiderin-filled brain tissue with a very distinct hypointensity, GRE (Gradient Recalled Echo) MR imaging is a key diagnostic method for cavernous malformations. SWI (susceptibility-weighted imaging) also is useful to detect CCMs due to its sensitivity for deoxyhemoglobin and hemosiderin [10].

According to some authors, epilepsy related to CCMs may have many mechanisms; some structural lesions like the hemosiderin deposit which is a marker that damage happened is noted; a rim of astroglial reaction and leakage of other blood constituents might play a role. Albumin is considered pro-epileptogenic because it influences astrocytic functions [11].

Corresponding author:
Catalina Elena Bistriceanu

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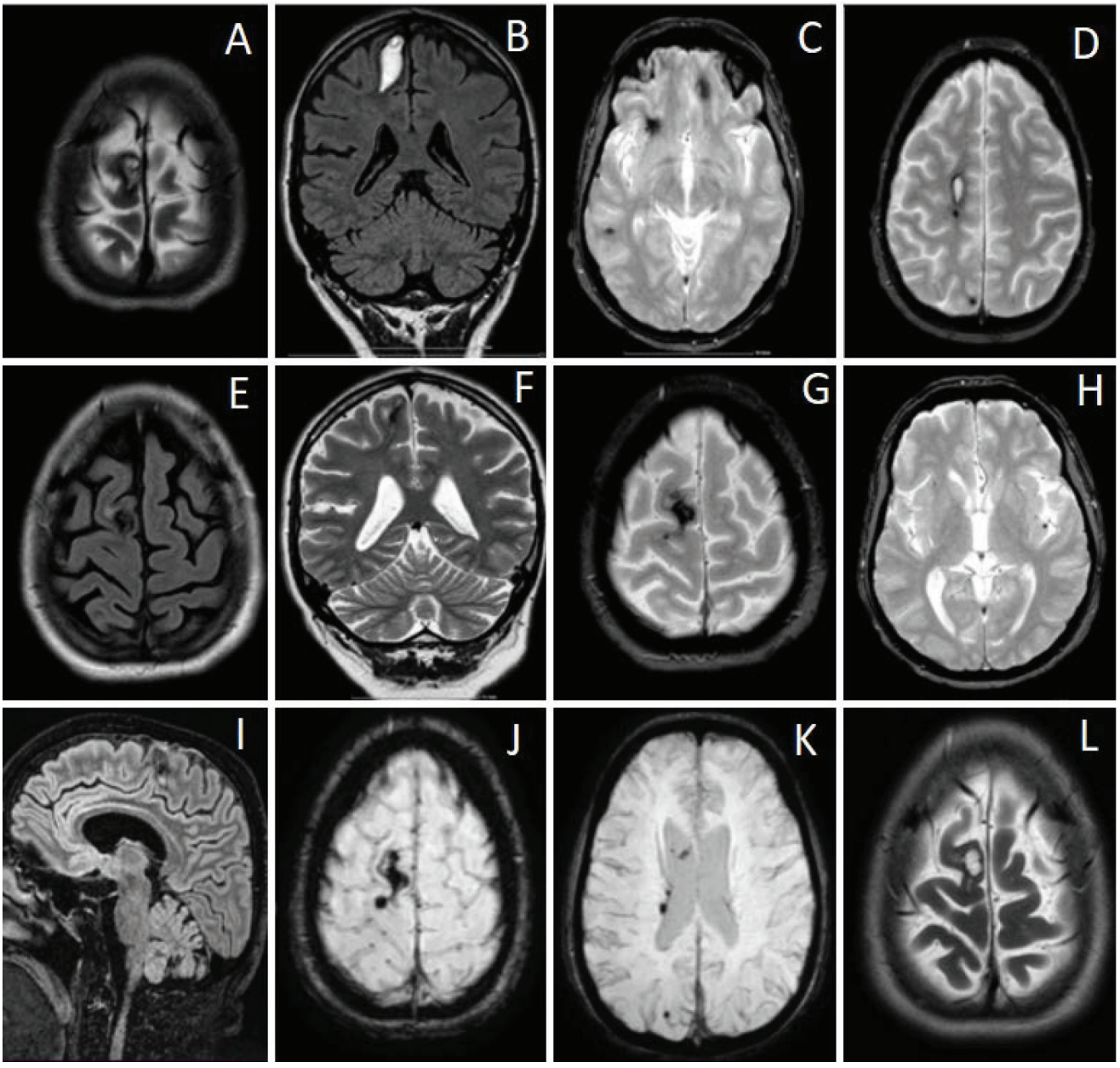

FIGURE 1. A: axial T2-Weighted TSE: 2cm AP/3cm CC/1,2cm LL sub-acute right superior frontal hemorrhagic lesion; B: coronal FLAIR: hyper intensity of the same frontal lesion; C: axial T2 FFE right temporal hypo intensity that corresponds to a right cavernoma; D: axial T2 FFE right frontal and parietal hypo intensities; E: axial FLAIR: 12x7mm right superior frontal cavernoma with a mild perirolandic expansion (resorption of the intralesional hemorrhagic component comparing with the images from 2021); F: coronal FLAIR: hypo intensity of the same frontal lesion with mild surrounding hyper intensity corresponding to gliosis; G: axial T2 FFE nodular hypo intense lesions that corresponds to residual hemosiderin deposits; H: T2 FFE left insular cavernoma; I: sagittal FLAIR: right superior frontal cavernoma with hemoglobin degradation compounds at interior and perilesional gliosis; J,K: axial SWI: supratentorial nodular lesions compatible with right frontal and parietal cerebral cavernomas; L: axial T2 right frontal cavernoma

When patients present focal neurologic deficit or cerebral hemorrhage, they have a 4%-6% risk of developing seizures in the first 5 years after diagnosis. For patients who had a first seizure related to a cavernoma, the risk for developing a second seizure within 5 years is 94% [12].

The management of cavernoma related epilepsy can be initiated with antiepileptic drugs. After presurgical epilepsy workup, selected patients can be referred to microsurgical resection [12]. Another option is represented by real-time MR thermography-guided stereotactic laser ablation (SLA), which is a minimally invasive alternative to open microsurgery, but it still requires larger case-controlled long-term studies [13]. An alternative for inoperable highly eloquent lesions is stereotactic radiosurgery, but there isn't enough evidence for this method in difficult cases with intracranial cavernous malformations [14].

CASE REPORT

We report the case of a right-handed 48 years old patient presented in the neurology department for seizure management. From case history, the patient was born at term, without any problem in early childhood and a negative familial history for neurologic disorders. He had long term alcohol consumption and a toxic liver disorder.

He had a first seizure in 2021, with subsequent cranio-cerebral trauma and subarachnoid hemorrhage. The seizure semiology was: contracture of left lower limb and secondary generalized tonic-clonic seizure. The neurological exam was unremarkable. The routine laboratory tests revealed mild elevated liver transaminase level.

Conservative management was decided and an antiepileptic drug with Levetiracetam 1500mg/day was started, with a good tolerance and seizure-free period. The brain MRI with contrast revealed multiple cavernomas, with a recent right superior frontal bleeding (Figure 1 A-D).

After a few months, the patient interrupts the antiepileptic treatment and this determines the recurrence of the seizures. Another brain MRI was performed (in 2022) and the resorbtion of hemorrhagic bleedings and the stationary other cavernomas described at previous brain imaging was observed (figure 1 E-H). Under Carbamazepine 600mg/day, the patient was seizure-free another few months. He interrupted again anti-seizure treatment and had 2 generalized seizures. The interictal EEG revealed mild left temporal dysrhythmias (Figure 2). We considered that a left temporo-insular cavernoma described on brain MRI (figure 1 H) could be responsible for the EEG findings. However, a long EEG monitoring was needed to find electro-clinical correlations and further presurgical work-up was needed because the seizure semiology didn't correspond with this brain region. The patient postponed the epileptological work-up. The brain MRI with contrast (in 2023) revealed the brain cavernomas previously described, without any recent bleeding (Figure 1 I-L). Under Levetiracetam 1500mg/day, the evolution was good, but still with unknown patient's adherence.

DISCUSSION

Antiepileptic drugs are recommended as an initial conservative approach in cerebral cavernomatosis patients with a single seizure rather than surgery [6,15]. Some investigators have reported seizure control in 60% of patients using this approach [15,16].

A retrospective study on 163 patients with cavernoma-related epilepsy, evaluating the outcome of microsurgical "pure" lesionectomy in patients with supratentorial cavernous angiomas presented with seizures found that 68.7% were seizure-free, 10.1% presented less frequent seizures and 17.1% remained unchanged; the follow up was at 48 months on average, range 0.5-14 years [17].

In our case, the patient's compliance was the main problem, because the seizure recurrence was mainly due to the suddenly stopped medication. Under adequate treatment, he needs an epileptological monitoring.

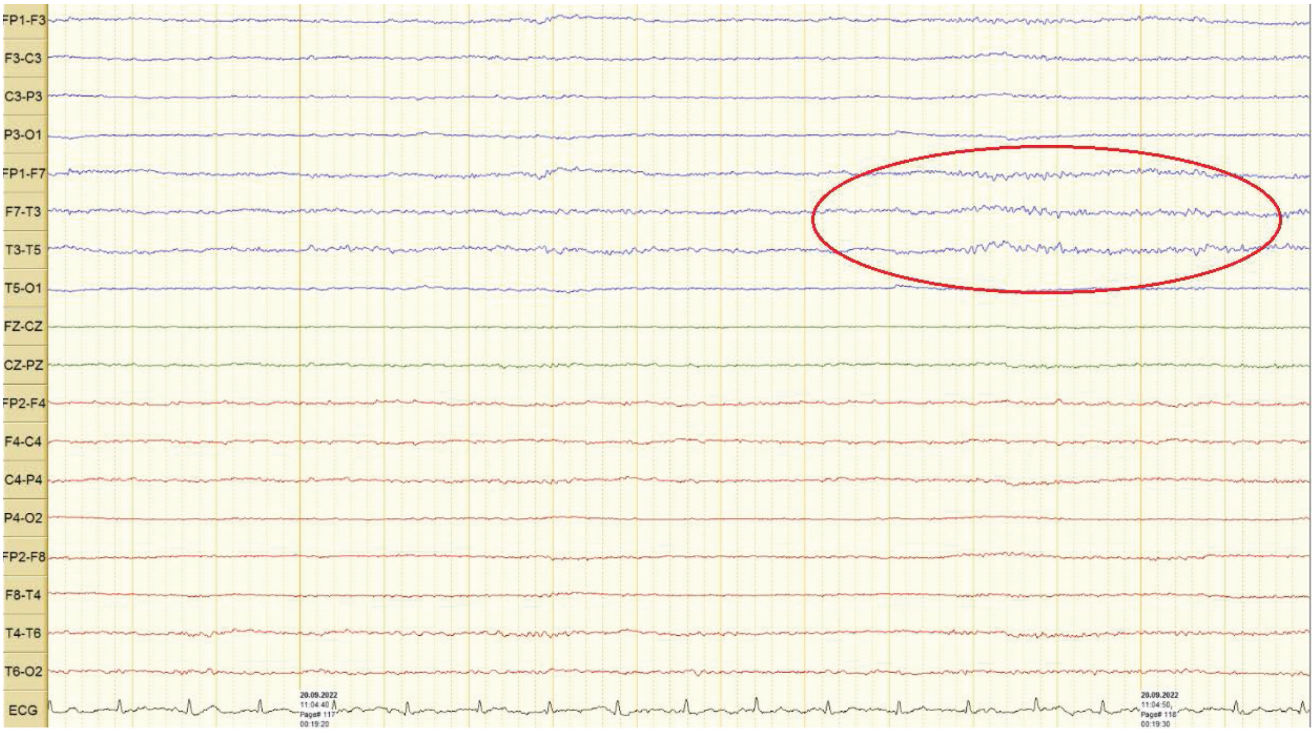

FIGURE 2. EEG bipolar montage: interictal pattern with mild left temporal dysrhythmias

Some authors recommend that patients with cavernomas who present with seizures should be managed conservatively at first. When pharmacotherapy fails to control seizures, or antiepileptic drugs have too severe adverse effects, or the patient does not comply well with treatment, surgical intervention is considered [15].

CONCLUSION

Epilepsy-related cerebral cavernomatosis represents a challenge for neurologists and neurosurgeons. This disorder requires proper monitoring and also an individualized treatment strategy for each patient. For every patient, the clinicians must decide when and what lesions require a different management and when is the appropriate time to pass from conservative management to surgical treatment.

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