

Cerebral cavernous malformation in a patient with pontine hemorrhage: A case study

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Abstract

The cerebral cavernous malformations are benign vascular hamartomas, with thin and dilated vascular walls and therefore constantly susceptible to hemorrhage. Clinically, they present with recurrent headaches, acute intracranial hemorrhage and focal neurological deficits. They are considered as *angiographically occult vascular malformations* and the imaging technique of choice for their diagnosis is magnetic resonance tomography. We present the case of a female patient with acute-onset symptomatology, congruent with a lesion in the basal pons. Her medical history included an intracranial hemorrhage due to a cavernoma, which was surgically removed. The magnetic resonance imaging of the brain revealed two new cavernomas, which were not identified in the imaging conducted in the past. In literature, the cases of de novo appearance of cavernomas are considered highly rare, especially in patients with no consistent family history or medical history of radiation therapy. Resultantly, they should be considered as dynamic lesions, regarding their number, size and behavior.

Introduction

The cerebral cavernous malformations (also known as cavernous angiomas, cavernous hemangiomas, or cavernomas) are benign vascular hamartomas, which microscopically consist of abnormally dilated sinusoidal vascular channels, without intervening neural parenchyma, without large feeding arteries or draining veins.¹ The walls of the dilated vascular spaces are composed of a single layer of flattened endothelial cells, without smooth muscle or elastic fibers and are separated from each other by collagenous hyalinized or fibrous tissue. Evidence of prior hemorrhage is a nearly constant feature of cavernous malformations.²

Common clinical manifestations of

cerebral cavernous malformations (CCM) include recurrent headaches, acute intracranial hemorrhage and focal neurological deficits from mass effect.² Intracranial hemorrhage occurs in both the supratentorial and infratentorial varieties of CCMs. A progressive course due to recurrent small hemorrhages within and around the malformation is occasionally seen in the posterior fossa (especially pontine lesions).³ Smaller, non-symptomatic episodes of hemorrhage are thought to contribute to the development of seizures. These smaller hemorrhages result in the progressive deposition of hemosiderin in the cerebral parenchyma surrounding the CCM. Iron, which is present in hemosiderin, is a well-known epileptogenic material. Indeed, seizures are the most common symptom in patients with CCMs, accounting for 40% to 60% of the presenting complaints.²

Before the widespread use of magnetic resonance tomography (MRT), the diagnosis of a cerebral cavernous malformation was very rare. The role of angiography in their diagnosis was always and remains limited; in most cases, a CCM is angiographically occult and, in fact, some earlier literature used the terminology *angiographically occult vascular malformations* to describe these lesions.⁴ The MRT is the modality of choice for the diagnosis of CCMs. Typically they appear on T2 sequences as a reticulated mixed signal center with a surrounding hypointense rim, described as *pop-corn* pattern. Nonetheless, depending on the phase of blood deposition and resorption and the corresponding pathological characteristics, their MRT-appearance is classified in four types, known as Zabramski classification.² Gradient echo or susceptibility sequences increase the sensitivity in detection of smaller CCMs.⁵

Case Report

A 39-years-old female patient presented in our emergency department with acute-onset vertigo, diplopia, weakness and numbness of the left arm and leg. The neurological examination was notable for a right abducens nerve palsy, left hemiparesis and hypoesthesia, with the underlying lesion expected to be located in the basal pons.

The patient had a past medical history of intracranial hemorrhage, which occurred twenty years before and presented with epileptic seizures; a CCM in the area of the left temporal lobe was revealed as the cause of her symptoms and it was subsequently surgically removed. Magnetic resonance imaging (MRI) of the brain was performed

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Consent for publication: The patient gave her written consent to use her personal data for the publication of this case report and any accompanying images.

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on an annual basis after the surgery, for the first three years, and then every two years, with the last one conducted ten years before the current incident, in an 1,5-Tesla magnetic resonance tomograph; none of them revealed any vascular malformations or other lesions except for the expected post-surgical gliosis.

At the present incident, a computer tomography was performed within hours after the symptom onset and revealed an hyperdense lesion in the right pons area, as well as an hypodense lesion at the right parietal lobe, with central hyperdense spots.

Eleven days later, a new MRI was performed (in an 1,5-Tesla magnetic resonance tomograph), which revealed two CCMs; one in the pons, responsible for the current hemorrhage, and a second one in the right parietal lobe. Both of them had not been identified in the MRI conducted ten years ago. The patient was thoroughly asked for the presence of family history, regarding the detection of CCM in imaging studies or the presence of epileptic seizures, intracranial hemorrhage or recurrent headaches, which was negative. Hence the radiological and consequently the clinical diagnosis is that these CCMs are *de novo* cerebral cavernomas (Figures 1-7).

Discussion

The histogenesis of CCMs is actually unknown. In 1963, Russel and Rubinstein classified vascular malformations of the central nervous system into four types: arteriovenous malformations (AVMs), cavernous angiomas, capillary telangiectases, and venous angiomas.^{6,7} In 1968, McCormick *et al.* reported that 16% of all intracranial vascular malformations found in autopsy were cavernous and that the majority of them had been *cryptic*.⁸ With the advent of MRI techniques that render the detection and diagnosis of these lesions easy and accurate, there has been a substantial increase in the number of patients diagnosed with these lesions.⁹ CCMs are common, with a prevalence of 0.16%, based on incidental MRI findings,¹⁰ and as high as 0.5% based on autopsy studies,¹¹ with increasing prevalence of detection at older ages. The population-based annual detection rate of CCM has been estimated at 0.56 per 100,000 per year for adults >16 years of age.¹²

The CCMs are more often associated with epileptic seizures than all other vascular malformations⁵ and they are considered to be responsible for 20% to 40% of all cases of intracranial hemorrhage of non-hypertensive cause.

They occur as solitary or multiple lesions, as sporadic or familial cases. Approximately 20% of the cases present with multiple CCMs, the majority of them with positive family history. An autosomal-dominant inheritance, with variable penetrance appears and three gene loci have been identified: CCM1 (KRIT1) in the

chromosome 7q21-22, CCM2 (MGC4607) in the chromosome 7p15-13 and CCM3 (PDCD10) in the chromosome 3q25.2-27.⁴

In the literature, cases of patients with *de novo* appearance of CCMs are considered rare; the rate of it is calculated at about 0.4% per patient/year for the familial form of the disease.¹³ An exception consists of the patients that have developed new, often multiple CCMs after radiation therapy; the

majority occurs in the pediatric population and is rare in adults, occurring only in those who have received greater than 30Gy of radiation. The pathophysiological mechanisms of radiation-induced CCM formation are not clearly understood but the literature supports the suggestion that radiation therapy can result in vascular wall necrosis and vascular wall changes including cell edema, dilation of their lumen, hyalinization, fibro-

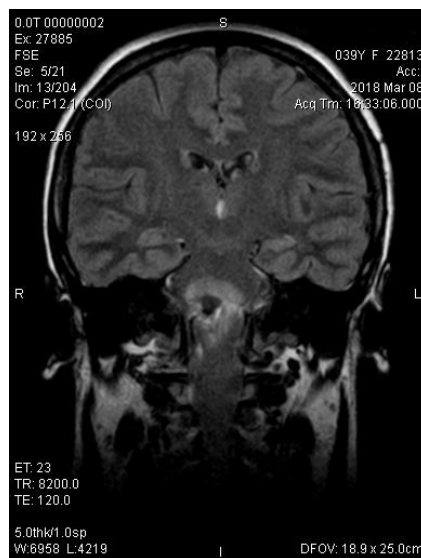


Figure 1. Magnetic resonance imaging (MRI) of the brain: Coronal fluid attenuated inversion recovery (FLAIR) image, depicting a roundish hemorrhagic lesion in the right inferior pons, with an hypointense center and hyperintense peripheral.



Figure 2. Axial T2-MRI image of the right pontine lesion, with the typical popcorn-like appearance.

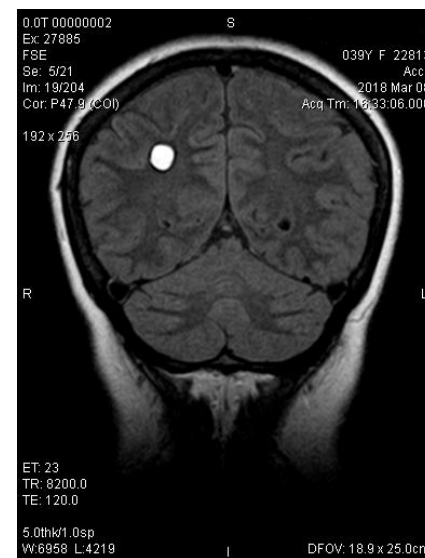


Figure 3. MRI FLAIR coronal view of an hypertensive round lesion in the right parietal lobe, suggestive of a new hemorrhagic lesion.

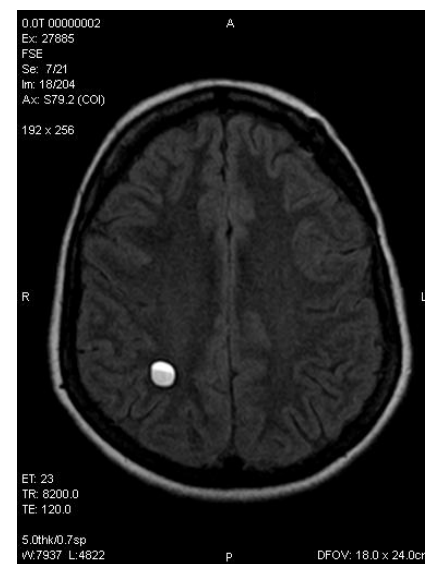


Figure 4. Axial T2-MRI image with the characteristic popcorn appearance of the parietal cerebral cavernous malformation (CCM), with a rim of signal loss due to hemosiderin deposition.

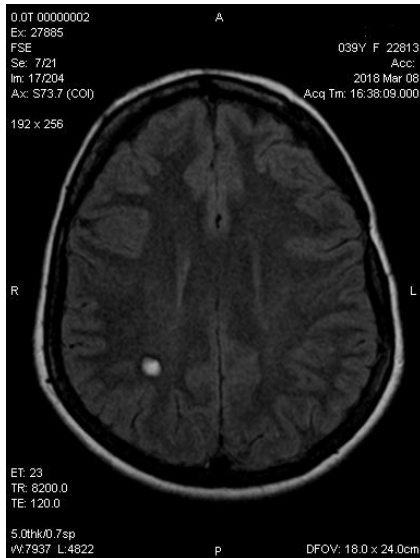


Figure 5. Axial FLAIR MRI image of the brain, showing the hemorrhagic lesion in the subcortical area of the right parietal lobe.



Figure 6. Coronal T2-weighted MRI image depicting the post-surgical gliosis of the left temporal lobe.

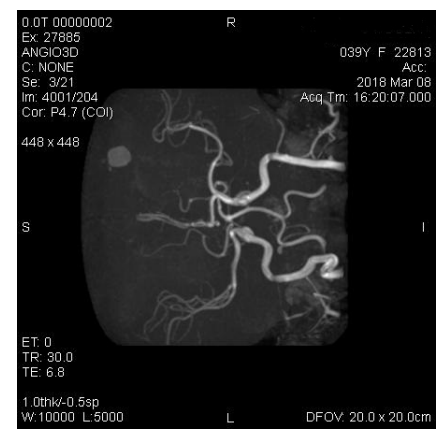


Figure 7. Magnetic resonance angiography (MRA) of the brain: No anomaly of the large intracranial vessels was detected.

sis and mineralization predispose to CCM formation.¹⁴ Viral infections may also play a role in producing or triggering the formation of CCM; in immunodeficient rats, the polyoma virus has been used to induce the formation of multiple intracranial CCMs.¹⁵ The fact remains, that *de novo* formation of CCM, as in the case of our patient, sporadic, without any clues of a positive family history of CCMs, and no history of receiving radiation for therapeutic cause, is considered very rare. To our knowledge, only seven cases have been reported so far in the literature.¹⁶

Conclusions

Although in the case of the patient we present, a thorough examination, including genetic testing, was not possible to be performed, the clinical and radiological evidence, in combination with negative family history suggest, that it is a rare case of sporadic *de novo* formation of CCM. On the other hand, the case of an underlying genetic cavernous malformation with reduced penetrance cannot be thoroughly rejected, as these can occasionally present with variable expressivity, and therefore should not be ignored. The presentation of this case, along with a brief review of the current literature, allows several important conclusions to be drawn: first of all, CCMs should come under differential diagnostic consider-

ation in cases of hemorrhagic lesions or lesions causing epileptic seizures; their diagnosis and follow-up examinations should always include magnetic resonance imaging techniques. Last but not least, CCMs should be considered as dynamic lesions, as far as their size, behavior and *de novo* appearance are concerned, not only in the familial cases, as until recently thought, but also in their sporadic form.

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