



# Familial Cerebral Cavernous Malformations: A Case Report

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## *Authors' contributions*

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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**Case Report**

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## **ABSTRACT**

**Aims:** Describe the main imaging findings of familial cerebral cavernous malformations.

**Presentation of Case:** This is the clinical case of a 68-year-old woman with a history of type 2 diabetes mellitus and long-standing systemic arterial hypertension. She presents to the neurology outpatient clinic reporting dizziness, temporal-spatial disorientation, episodes of amnesia, and chronic insomnia. Based on the clinical presentation, a diagnosis of cognitive impairment, likely of vascular origin. The MRI reveals multiple supratentorial and intraxial lesions with heterogeneous components, exhibiting a hypointense ring on T1 and T2-weighted sequences with images

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demonstrate a "blooming" effect on the T2\*/GRE sequence, characteristic of cerebral cavernomas, displaying a "popcorn" appearance.

**Discussion:** In the presented case, a patient with multiple cerebral cavernomas showing classic features on MRI was discussed. Clinical manifestations commonly involving seizures, hemorrhage, and focal neurological deficits. Genetic factors play a role, with familial cases following an autosomal dominant inheritance pattern. Imaging studies, particularly MRI with susceptibility-weighted imaging, aid in diagnosis, revealing characteristic "popcorn" appearance lesions. Other differential diagnoses for cerebral hemorrhages should be considered, including vascular brain malformations and conditions like cerebral amyloid angiopathy and hypertensive encephalopathy. Management involves a multidisciplinary approach, with surgical resection being the gold standard for symptomatic cases.

**Conclusion:** Cerebral cavernous malformations (CCM) present varied symptoms, diagnosed through MRI showcasing characteristic appearances. Accurate determination of familial or sporadic origin is crucial for tailored treatment, involving medical therapy, surgical resection, or radiosurgery. Multidisciplinary collaboration among specialties ensures personalized management for patients with CCM.

*Keywords: Cavernoma; familial cerebral cavernous malformations; hemorrhage; magnetic resonance imaging; cerebral vascular anomalies.*

## 1. INTRODUCTION

Within cerebral vascular malformations, there are four main types: cavernous malformations (cavernoma), arteriovenous malformations, venous developmental anomalies, and capillary telangiectasia, each one of these presents its own pathological features [1,2,3]. Among these, arteriovenous malformations and cavernous cerebral malformations are the most common, with a prevalence of cavernomas estimated at 0.5 to 0.7% of the population [1,4].

Cerebral cavernous malformations (CCM) are intracranial flow lesions histologically characterized by abnormally dilated endothelial channels (known as caverns), with a single endothelial layer lacking mature vascular wall characteristics, leading to increased permeability predisposing to focal hemorrhages and various neurological manifestations [5,6].

Patients with cerebral cavernomatosis can be classified into 2 groups:

1. Familial form: considered when there is more than one affected individual in the family or a single individual with multiple lesions (multiple cavernomatosis).
2. Sporadic form: characterized by a single cavernous malformation and often associated with a developmental venous anomaly [4,7].

## 2. PRESENTATION OF CASE

This is the clinical case of a 68-year-old female patient known to have type 2 diabetes mellitus and long-standing systemic arterial hypertension under treatment. In her family history, it is noted that she has a son with similar symptoms. With no other significant pathological or surgical history.

She presents to the neurology outpatient clinic of the General Hospital of Morelia with complaints of dizziness, temporal-spatial disorientation, episodes of amnesia, and chronic insomnia. Physical examination does not reveal significant findings.

Laboratory studies, including complete blood count and blood chemistry, are unremarkable. Given the clinical presentation, a diagnosis of cognitive impairment with amnesic features, likely of vascular origin, is made, prompting a request for a simple brain magnetic resonance imaging (MRI).

MRI images reveal multiple supratentorial and intraxial lesions with heterogeneous components with reticulated mixed-signal intensity cores with a hypointense rim on T1 and T2-weighted sequences (Fig. 1) with increased signal intensity on FLAIR sequence suggestive of vasogenic edema (Fig. 2). Additionally, the images display a "blooming" effect on the T2\*/GRE sequence (Fig. 3), characteristic of cerebral cavernomas, with a "popcorn" appearance, and evidence of subarachnoid hemorrhages on the convexity.

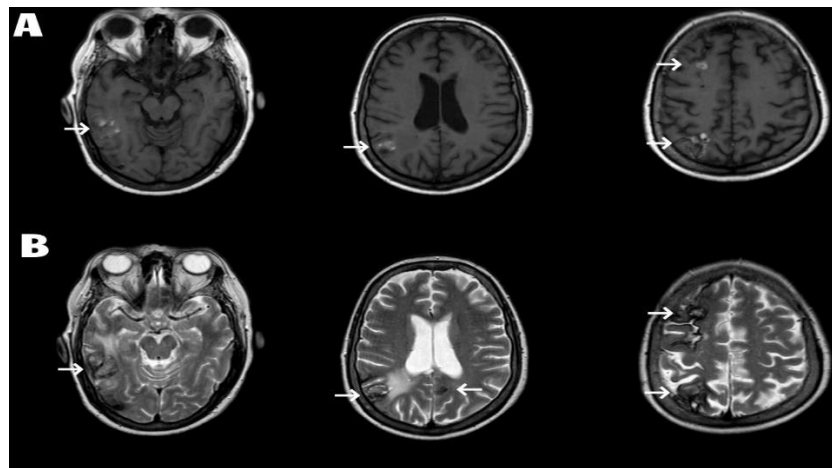


Fig. 1. MRI images axial T1 (a) and T2 (b) sequence revealing multiple heterogeneous signal intensity lesions (white arrows), with a hypointense rim

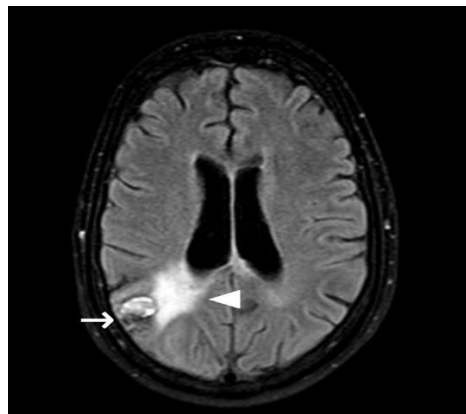


Fig. 2. MRI images in axial FLAIR sequence showing vasogenic edema (arrowhead) adjacent to the cavernoma (white arrow)

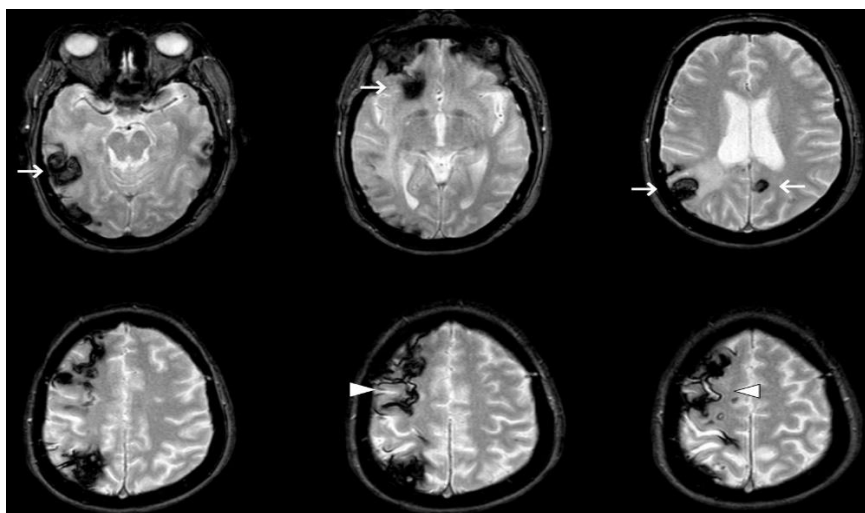


Fig. 3. MRI images in axial T2\*/GRE sequence demonstrating multiple caverns (white arrows), with heterogeneous signal intensity showing "blooming" effect and, associated with subarachnoid hemorrhages of the convexity (white arrowhead)

### 3. DISCUSSION

In the previous case, we presented a patient with multiple cerebral cavernomas exhibiting classic features on magnetic resonance imaging (MRI). Clinical presentation typically occurs between the 2nd and 5th decades of life, with an average age of onset around 30 years [5,8]. The most common clinical manifestations include seizures (20-40%), hemorrhage (30-40%), and focal neurological deficits (25-30%), with less frequent symptoms such as chronic headache (10-30%). Additionally, systemic vascular lesions like hepatic hemangiomas, vertebral angiomas, renal angiomas, and cutaneous capillary malformations may be present [8]. Despite this, up to 25-50% of cases remain asymptomatic, with the condition being incidentally discovered on MRI [5].

Familial multiple cerebral cavernomatosis follows an autosomal dominant inheritance pattern with incomplete clinical and neuroradiological penetrance. The three most commonly affected genes are CCM1/KRIT1, CCM2/MGC4607, and CCM3/PDCD10, which are evaluated in specific molecular genetic testing [8,9]. However, in symptomatic patients with multiple cerebral cavernomas like our case, genetic screening may not provide significant utility for clinical management [8].

Imaging studies for evaluation typically include computed tomography (CT) and MRI, with the latter being more precise for cerebrovascular pathology. The use of 3T MRI with susceptibility-weighted imaging (SWI) is recommended over gradient-echo (T2\*/GRE) or T2 fast spin echo (FSE) sequences, as it can detect a higher number of lesions, especially in familial cases [5,7].

Cerebral cavernous malformations can be classified into different types based on pathological and imaging features, according to the Zabramski classification where type 2 lesions are the most characteristic of the FCCM [8]. On CT, these lesions appear as poorly defined with calcifications. MRI typically reveals the "popcorn" appearance, demonstrating caverns with heterogeneous signal due to blood in various stages, calcification, and a hemosiderin ring. T1-weighted sequences show a mixed signal core, T2-weighted sequences show a reticulated mixed signal core with a hypointense rim (hemosiderin ring), and T2\*/GRE sequences demonstrate the "blooming" effect of

hemosiderin, increasing sensitivity for cavernoma visualization [5]. And the use of SWI sequences demonstrate the number of lesions 1.7 higher than that seen in T2\*/GRE and 8 times higher than that in T2 FSE images [10].

Despite the imaging features of the FCCM, other causes of cerebral haemorrhages are to be considered as other types of vascular brain malformations consist of capillary telangiectasias, aneurysms, and arteriovenous malformations.

Sporadic cerebral cavernous malformations (SCCM), is typically characterized by a single cavernous malformation and often associated with a developmental venous anomaly (DVA); CCM can occur in the sporadic form, but they are always situated around or near a DVA. Some series indicate that up to 30% of sporadic CCMs are associated with a DVA. In a study using 7 Tesla MRI imaging, 100% of individuals with sporadic CCMs were found to have abnormal venous output from the cavernous malformation. Of note, DVAs are rarely seen in individuals with FCCM [7,11].

Another conditions like cerebral amyloid angiopathy, numerous small foci may have a similar imaging appearance, with a predilection, however, for the peripheral subcortical white matter. There may also be a history of prior (larger) lobar haemorrhage or superficial siderosis. (Chronic) hypertensive encephalopathy has a predilection for the region of the basal ganglia. And in diffuse axonal injury, there is a history of severe trauma, and the lesions have a typical distribution at the borders between the cortical grey matter and the underlying white matter [12].

Management of cerebral cavernous malformations involves a multidisciplinary approach. depending on whether the patient is asymptomatic or presenting with symptoms [7]. Medical management with the aim of reducing the risk of hemorrhage is based on the use of statin, beta-blocker, and/or antithrombotic medication. In a study patients with FCCM present a probability of rehemorrhage during a 5-year follow-up (FU) similar to that in patients with sporadic CCM. Additionally, although the relationship was not significant, they noted a tendency toward a decreased risk of rebleeding in patients with antithrombotic and statin intake during FU [13]. Surgical resection is considered the gold standard of interventional treatment, with common indications including first

hemorrhage with accessible cavernomas, recurrent hemorrhage, intractable seizures, or mass effect with declining neurological function [7][14]. Radiosurgery is an option for surgically inaccessible lesions with a high risk of bleeding. In areas where traditional surgery or radiosurgery is challenging, minimally invasive techniques such as stereotactic laser ablation have been implemented, showing reduction in lesion size without neurological sequelae [14].

#### 4. CONCLUSION

Cerebral cavernous malformations (CCM) present a wide range of symptoms, including seizures, focal neurological deficits, and hemorrhages, with the possibility that some patients may remain asymptomatic. The diagnosis of FCCM is based on imaging studies, with magnetic resonance imaging (MRI) being the preferred method for evaluation. The characteristic "popcorn" appearance on T2\*/GRE or SWI sequences is typical of cerebral cavernomas. Determining whether the FCCM is familial or sporadic is crucial for treatment planning and may require specific genetic evaluation. In terms of management, therapeutic options include symptomatic medical therapy, surgical resection, and radiosurgery, with the choice depending on the location and number of lesions, as well as the patient's symptoms. Multidisciplinary collaboration among neurology, neuroradiology, neurosurgery, and rehabilitation is essential for comprehensive and personalized management of patients with FCCM.

#### ETHICAL APPROVAL

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

#### CONSENT

All authors declare that written informed consent was obtained from the patient for publication of this case report and accompanying images.

#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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