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Case Report

Frontoparietal cavernous malformation in a 39-year-old woman: a case report

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Abstract: Cerebral cavernous malformation (CCMs) is an angiographically occult, low-flow neurovascular disease resulting from capillary dilatation of cerebral blood vessels that may also occur in the spinal cord, causing extravasation of blood cells from the affected vessel that leads to multiple repercussions in the patient's life. This condition's clinical characteristics include recurrent bleeding, seizures, persistent neurological deficits, epilepsy, and death. In this study, we describe the clinical course of a patient with a Cavernous Malformation and its prognosis regarding the association between clinical progression and therapeutic perspectives. It's relevant to elucidate possible lack of studies that may urge further research on this theme and new learning pathways should be opted for to increase awareness of this condition in order to improve its prognosis.

Keywords: Cerebral cavernous malformation; Angiographically occult; Low-flow neurovascular disease; Neurological deficits.

1. Introduction

Cavernous angioma (CA), cavernoma or cerebral cavernous malformation (CCMs), is an angiographically occult, low-flow neurovascular disease resulting from capillary dilatation of cerebral blood vessels that may also occur in the spinal cord, causing extravasation of blood cells from the affected vessel [1-3]. It has an incidence in the general population of 0.2-0.5% with risk of intracerebral hemorrhages and with focal neurological deficits that begin between 30- 50 years of age and, although it can occur throughout the life course, there is an age- related increase in prevalence with higher risk in the fourth decade of life [4, 5].

The advent of advances in molecular biology as well as nuclear magnetic resonance imaging (MRI) scans have led to increased diagnosis of symptomatic lesions and incidental findings, allowing for a better understanding of the disease and its natural history [1, 2, 6-8]. The disease has two distinct biological forms. The sporadic form, which is more common, usually with a single lesion and no hereditary transmission spectrum, and the

familial form, also called familial cavernomatosis, in which the patient has multiple lesions that may be distributed throughout the neuroaxis and has an autosomal dominant pattern with incomplete penetrance. Three protein-coding genes associated with the familial form have already been identified, *CCM1 (KRIT1)*, *CCM2 (MGC 4607)*, and *CCM3 (PDCD10)* [9-11].

Although rare, accounting for 5 to 13% of all CNS vascular anomalies, CA are reported to be the second most common cerebral vascular malformation, with specific associated risks including the occurrence of recurrent bleeding, persistent neurological deficits, epilepsy, and death. Lesion size, location, familial form, early age group, patient lifestyle, the intrinsic psychological burden, and follow-up care may define case management [11-13]. Current knowledge of the natural history of the disease shows that the risk of bleeding is 0.08% patient-years among asymptomatic patients, but after bleeding the annual risk increases considerably, with an estimated risk of 42% of new bleeding event in 5 years [13, 14]. Considering the review of recent studies and cases reported in the current literature regarding the ideal management and effective therapeutic interventions, it is evident the need to describe CA in this case report, as it is an infrequent disease with a complex and challenging clinical picture.

2. Case Report

A 39-year-old female patient, with no medical history, was admitted to the hospital's emergency room with motor deficit in the left upper limb, associated with constant headache for 15 days. Cranial MRI was performed, which showed a hemorrhagic lesion in the frontoparietal transition on the right, with perilesional edema (Figure 1A). After conservative medical management and observation of the evolution of the condition, he returned to the emergency room because of the worsening of the headache and an episode of convulsive crisis with consequent hospitalization of the patient.

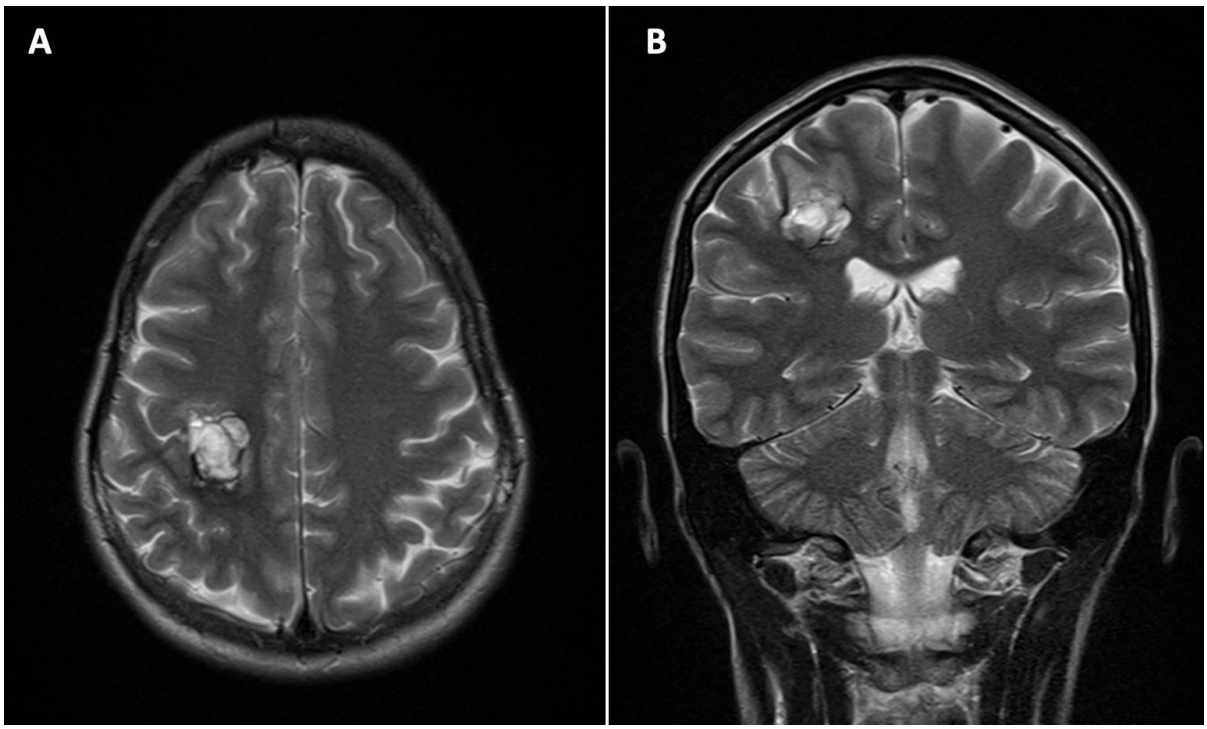

Figure 1: A. Axial T2 and B. Coronal T2 showing heterogeneous and hyperintense lesion in the right frontoparietal region of the "*popcorn*" type surrounded by hemosiderin. There is no surrounding edema.

Due to results of the MRI and CT, a CT scan of the chest, abdomen and pelvis was requested, associated with a cranial angioresonance, with the intention of investigating an arteriovenous malformation (AVM), a primary tumor of the CNS with or without metastases. In this context, the patient remained with the symptomatology of loss of motor strength in the left hand associated with paresthesia in the forearm and lower limb, in addition to constant headache. On physical examination, he presented left hand paresis grade III and Glasgow Coma Scale 15/15.

In view of the exams collected and the MRI result indicating a lesion in the right side in the motor area of the CNS, the diagnosis of cavernoma was confirmed, with evidence of hemorrhage in reabsorption in the motor region (Figure 1B). The patient presented mild symptoms, the neuroaxial MRI examination showed no evidence of other vascular lesions, and the angioresonance was innocent, thus excluding potential familial cavernomatosis. With improvement of the clinical condition, he was discharged with medical advice.

3. Discussion

3.1 Causes and Repercussions of CCMs

The cavernous malformation can occur as sporadic, single, or familial lesions. Patients with the familial form present multiple lesions, each with risk, with no dependence with growth or bleeding. Generally, it is kwon that the CCMs associated with venous anomalies are the result of recurrent micro-hemorrhages, which trigger the liberation of several growth factors, promoting the CCM formation, a process called hemorrhagic angiogenic proliferation [5, 12].

This condition may present incidentally seizures or focal neurological symptoms. In this sense, the formation and growth of these lesions, associated with iron deposits that result from local bleeding led to the clinical manifestations of this disease. Therefore, many surgical procedures for cavernous have demonstrated good results in operative management, with minimal surgical morbidity or mortality among patients with lesion in the cerebral hemispheres [5, 8, 13]. In this context, it is worth noting that, initially, the patients who have seizures are treated with drugs, while the surgical resection is more often used if seizures increase or become refractory to the pharmacological treatment. Thus, surgery is the most chosen treatment for cavernous malformation or for lesions that cause non- treatable symptoms, differing, however, from radiosurgery, which is more used in deeper lesions with a more morbid neurosurgical access [6].

3.2 Radiological Aspects and Differential Diagnosis of MCCs

Imaging tests are an important tool for the differential diagnosis of MCCs, which commonly present appear in isolation and are located above the tent of the cerebellum in 80% of cases [15]. The imaging resource widely recommended for the investigation of this brain malformation is the RMI. The *American College of Radiology (ACR) Appropiateness Criteria* provide an expert consensus recommendation for acute neurological symptoms, including headache, focal neurological deficits and altered consciousness. When intraparenchymal hemorrhage is diagnosed, follow-up imaging with contrast-enhanced MRI is indicated to evaluate an underlying vascular lesion. Whether symptomatic or accidentally detected, most MCCs are diagnosed with MRI, which has been shown to heave nearly 100% sensitivity. MRI is particularly valuable in the identifying multiple lesions in the case of familial MCC. T2-weighted MRI tipically demonstrates a "popcorn" core of characteristic mixed signal with a hypointense border [16, 17].

MCC can present on non-contrast skull CT as amorphous calcifications, but further MRI imaging is needed to confirm the dyagnosis unless if it is contraindicated. The main role of NCCT is the identification of hemorrhage in symptomatic patients. Diffusion tensor imaging (DTI) plays an increasingly important role in the management of MCCs and has been used to identify critical white matter tracts in preoperative planning for MCC. Functional MRI techniques, such as blood oxygen level dependent (BOLD), task activation

mapping of language function, are highly accurate and non- invasive tools that have been shown to be useful in the preoperative workup of MCC. Emerging work using high field strength (SWI) can provide detailed information about the angioarchitecture of the MCC, potentially identifying lesions at risk [18, 19].

4. Conclusion

Cavernous malformations are common vascular lesions that present a high degree of suspicion in patients with intraparenchymal hemorrhage and clinical symptoms such as seizures and focal neurological deficits. Under this bias, MRI becomes essential for the differential diagnosis of CCM's and thus improves the patient's prognosis.

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Conflicts of Interest: None.

Supplementary Materials: None.

References

1. Awad IA, Polster SP. Cavernous angiomas: deconstructing a neurosurgical disease. J Neurosurg. 2019 Jul 1;131(1):1-13. doi: 10.3171/2019.3.JNS181724. PMID: 31261134; PMCID: PMC6778695.
2. McKerracher L, Shenkar R, Abbinanti M, Cao Y, Peiper A, Liao JK, Lightle R, Moore T, Hobson N, Gallione C, Ruschel J, Koskimäki J, Girard R, Rosen K, Marchuk DA, Awad IA. A Brain-Targeted Orally Available ROCK2 Inhibitor Benefits Mild and Aggressive Cavernous Angioma Disease. Transl Stroke Res. 2020 Jun;11(3):365-376. doi: 10.1007/s12975-019-00725-8. Epub 2019 Aug 24. PMID: 31446620; PMCID: PMC7036327.
3. Flemming KD, Kumar S, Brown RD Jr, Lanzino G. Predictors of Initial Presentation with Hemorrhage in Patients with Cavernous Malformations. World Neurosurg. 2020 Jan;133:e767-e773. doi: 10.1016/j.wneu.2019.09.161. Epub 2019 Oct 9. PMID: 31605843.
4. Zafar A, Quadri SA, Farooqui M, Ikram A, Robinson M, Hart BL, Mabray MC, Vigil C, Tang AT, Kahn ML, Yonas H, Lawton MT, Kim H, Morrison L. Familial Cerebral Cavernous Malformations. Stroke. 2019 May;50(5):1294-1301. doi: 10.1161/STROKEAHA.118.022314. PMID: 30909834; PMCID: PMC6924279.
5. Flemming KD, Kumar S, Brown RD Jr, Lanzino G. Predictors of Initial Presentation with Hemorrhage in Patients with Cavernous Malformations. World Neurosurg. 2020 Jan;133:e767-e773. doi: 10.1016/j.wneu.2019.09.161. Epub 2019 Oct 9. PMID: 31605843.
6. Batra S, Lin D, Recinos PF, Zhang J, Rigamondi D. Cavernous Malformations: Natural history, diagnosis and treatment. Nature Rev Neurol, v. 5, n. 12, p. 659-670, Dez. 2009.
7. Flemming KD, Kumar S, Brown RD Jr, Lanzino G. Predictors of Initial Presentation with Hemorrhage in Patients with Cavernous Malformations. World Neurosurg. 2020 Jan;133:e767-e773. doi: 10.1016/j.wneu.2019.09.161. Epub 2019 Oct 9. PMID: 31605843.
8. Shervin Taslimi, MD, MPH Amirhossein Modabbernia, MD Sepideh Amin- Hanjani,MD, Fred G. Barker II, MDR. Loch Macdonald, MD.: Natural history of cavernous malformation: Systematic review and meta-analysis of 25 studies Neurology 2016;86:1984–1991.
9. Torres G, Kini AT, Al Othman B, Lee AG. Familial Cavernous Hemangioma. J Neuroophthalmol. 2020 Jun;40(2):262-264. doi: 10.1097/WNO.0000000000000778. PMID: 30893269.
10. Labauge P, Denier C, Bergametti F, Tournier-Lasserve E. Genetics of Cavernous Angiomas. Lancet Neurol, v. 6, n. 3, p. 237-244, Mar. 2007.
11. Zafar A, Quadri SA, Farooqui M, Ikram A, Robinson M, Hart BL, Mabray MC, Vigil C, Tang AT, Kahn ML, Yonas H, Lawton MT, Kim H, Morrison L. Familial Cerebral Cavernous Malformations. Stroke. 2019 May;50(5):1294-1301. doi: 10.1161/STROKEAHA.118.022314. PMID: 30909834; PMCID: PMC6924279.
12. Dalyai RT, Ghobrial G, Awad I, et al. Management of incidental cavernous malformations: a review. Neurosurg Focus. 2011;31(6):E5. doi:10.3171/2011.9.FOCUS11211.
13. Al Barbarawi MM, Asfour HA, Qudsieh SM, et al. Isolated tectal cavernomas: A comprehensive literature review with a case presentation. Heliyon. 2022;8(4):e09244. Published 2022 Apr 5. doi:10.1016/j.heliyon.2022.e09244

14. Chen CJ, Ding D, Derdeyn CP, Lanzino G, Friedlander RM, Southerland AM, Lawton MT, Sheehan JP. Brain arteriovenous malformations: A review of natural history, pathobiology, and interventions. Neurology. 2020 Nov 17;95(20):917-927. doi: 10.1212/WNL.0000000000010968. Epub 2020 Oct 1. PMID: 33004601.
15. Blitstein M & Tung G. MRI of Cerebral Microhemorrhages. AJR Am J Roentgenol. 2007;189(3):720-5. doi:10.2214/ajr.07.2249
16. Expert Panel on Neurologic Imaging: Salmela MB, Mortazavi S, Jagadeesan BD, Broderick DF, Burns J, Deshmukh TK, Harvey HB, Hoang J, Hunt CH, Kennedy TA, Khalessi AA, Mack W, Patel ND, Perlmutter JS, Policeni B, Schroeder JW, Setzen G, Whitehead MT, Cornelius RS, Corey AS. ACR Appropriateness Criteria®Cerebrovascular Disease. J Am Coll Radiol. 2017 May;14(5S):S34-S61.
17. Gross BA, Lin N, Du R, Day AL. The natural history of intracranial cavernous malformations. Neurosurg Focus. 2011 Jun;30(6):E24.
18. Petersen TA, Morrison LA, Schrader RM, Hart BL. Familial versus sporadic cavernous malformations: differences in developmental venous anomaly association and lesion phenotype. AJNR Am J Neuroradiol. 2010 Feb;31(2):377-82.
19. Dammann P, Wrede K, Zhu Y, Matsushige T, Maderwald S, Umutlu L, Quick HH, Hehr U, Rath M, Ladd ME, Felbor U, Sure U. Correlation of the venous angioarchitecture of multiple cerebral cavernous malformations with familial or sporadic disease: a susceptibility-weighted imaging study with 7-Tesla MRI. J Neurosurg. 2017 Feb;126(2):570-577.