Brain cavernomas. Case report and literature review

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Case Report

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Abstract: Cerebral cavernous malformations are a cerebral vascular disorder characterized by abnormal vascular spaces lined by a single layer of endothelium without intervening neural parenchyma. Its clinical course is variable between asymptomatic, seizures or neurological deficit, previously classified as idiopathic seizures or occult angiographic vascular malformations. Currently with MRI they are detected in T2 gradient-echo sequences (GRE). We present a clinical case of a patient with seizure episodes with CT and brain MRI studies with findings of brain cavernomas, surgical intervention is performed with excision, the histopathological study confirms the diagnosis of brain cavernoma.

KEY WORDS
Cerebral cavernoma, cavernous malformation, epilepsy, magnetic resonance.

Introduction

Cerebral cavernomas are low-flow malformations, their prevalence in the general population is close to 0.1 to 0.5% based on necropsies and MRI studies(1), they can develop sporadically or due to autosomal dominant hereditary disorders. They can be solitary or multiple, most usually remain asymptomatic in adulthood and when they present clinical manifestations seizures and cerebral hemorrhage is the most common(2). We present a case of a male patient with convulsive syndrome of 9 years of evolution with previous diagnosis of brain tumor, given persistence of symptoms, new imaging studies were performed with evidence at supratentorial level in the right parietal region of an image highly suggestive of brain cavernoma diagnosed and confirmed by biopsy.

Case report

Male patient, 27 years old, pathological history of seizures for 9 years, previously diagnosed with an unspecified brain tumor with surgical indication, without receiving treatment of his own free will, he does not bring attached documentation. Currently with multiple hospitalization requirements due to decompensation of seizure episodes, persisting with constant seizures since 2 months ago; heredofamiliar history of mother with DM and arterial hypertension. Transfusional: negative. Allergic: negative. Traumatic: negative. Toxic: negative.

Admitted to the institution for clinical symptoms of 2 months of evolution consisting of tonic-clonic convulsive episodes approximately 3 disorientation. Relatives report that the frequency of the seizures has increased 2 days before, presenting 2 episodes per day. Prior to his admission he presented seizures, he was empirically managed with phenytoin 100 mg with slight improvement, however, without regaining consciousness, so he was taken to a health center where he was stabilized and referred for specialized management. On admission, the patient was alert, conscious, oriented, with reactive pupils, he started treatment with phenytoin and sodium valproate, imaging studies were performed with simple cranial CT (**figure 1**) and contrasted (**figure 2**), findings in relation to right parietal heterogeneous tumor in probable relation to meningioma associated with hyperdense area in the left thalamus by probable hemorrhagic focus.

Due to the tomographic findings, MRI of the skull contrasted with 1.5 T equipment in multiple sequences and planes was performed (**figure 3**), the findings found in the study suggest a high probability of cavernomas, with diffuse distribution and Zabramski type 2 classification.

In view of the MRI findings, diagnostic cerebral angiography was performed without finding arteriovenous malformations, so arteriovenous alteration was ruled out, and the diagnostic probability of carvernoma was maintained. Surgical resection was scheduled, procedure was performed with evidence in the inner frontal gyrus at the junction with the precentral sulcus of a violaceous lesion, with venous tributaries and hemosiderin halo, coagulation and extraction of the lesion was performed (**figure 4**), the procedure was completed without complications.

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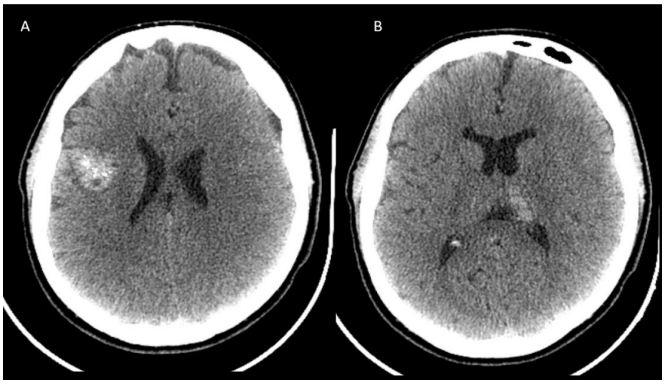

Figure 1. A. Simple skull CT: Image located in the right parietal lobe, in the gray-white substance junction, heterogeneous, with calcifications in its interior and hypodense areas, with loss of grooves and fissures at this level, measuring approximately 3 x 2.5cms. **B**. Image of similar characteristics located in the left thalamus, measuring 2.3cms.

Patient with good postoperative evolution; neurologically conscious, alert, cooperative, mobilizes all limbs, simple control cranial tomography was performed (**figure 5**).

The pathology report shows macroscopic evidence of the surgical specimen with granular surface, yellowish brown, firm consistency, solid when cut (**figure 6**).

Given the adequate clinical evolution the patient was discharged without complications, in postoperative controls with a decrease in seizures, he presented an isolated episode 3 weeks after surgery with a clonic episode in the right arm, continued management with levetirazetam 750 mg per day and phenytoin 300 mg per day.

Discussion

The Cavernous angioma also called cavernous malformations (CM), cavernous hemangiomas or cavernomas was described by Rudolf Virchow in 1863, it is one of the four vascular malformations of the central nervous system (CNS) (3).This type of intracranial vascular malformation presents its origin in development (4), characterized by abnormal vascular spaces lined by a single layer of endothelium without intermediate neural parenchyma or identifiable elements of the vascular wall (5). There is almost always evidence of previous hemorrhage, characterized by hemolytic debris in different stages of degradation, marginalized by a pseudocapsule of hemosiderin-laden gliotic tissue (6).

The classification system of vascular malformations can be given according to the pathological analysis as arteriovenous malformations (AVM), cavernous malformations, developmental venous anomalies (DVA), telangiectasia, malformations of the vein of Galen and mixed malformations according to the predominant

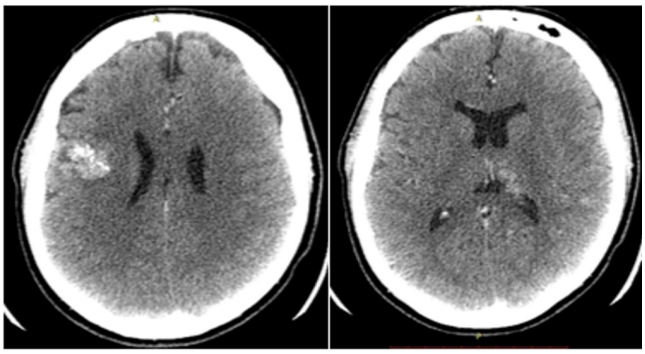

Figure 2: Contrast-enhanced cranial CT: after contrast medium administration there is no enhancement.

anomalous vascular channels (7). Alternatively malformations can be classified as either high-flow (arteriovenous) or low-flow (capillary, cavernous, venous).

Cavernomas are relatively common. A prevalence of 0.5-0.7% is described in the general population by necropsy and MRI studies. They represent 5% to 13% of vascular anomalies in the central nervous system (8). They affect men and women equally, most occur in the supratentorial compartment (80%), followed by the infratentorial compartment (15%) and the remaining 5% occur in the spinal cord (9). They usually present in a multiple and bilateral form, although they can also be solitary (10). Their etiology is related to sporadic or inherited cases. Familial and sporadic cases are particularly evident among Hispanic Americans of Mexican descent (11).

A familial predisposition of up to 55% has been recognized in patients with an affected family member. Genetic studies have mapped a gene that causes cavernous malformation to a segment of the long arm of chromosome 7 (7q). Mutations of three genetic loci are implicated in fCCM: CCM1 (also known as KRIT1), CCM2 and CCM3, all showing autosomal dominant inheritance with incomplete penetrance and variable expression. The biological basis for this clinical variability is unknown (12).

Its clinical course is variable, many patients remain asymptomatic, others manifest seizures (50%), cerebral hemorrhage (25%) (13) these can produce stroke-like symptoms (25%), such as hemiparesis, paresthesia, visual disturbances, vertigo and headaches, depending on their extension and location (14). Most patients present symptoms in their 2nd-4th decade of life (15).

Among the diagnostic detection methods, MRI is considered the most sensitive and specific modality for detecting cavernomas (16). Initially the significantly increased sensitivity of CT provides information about the diagnosis, given that up to 40% of cases were clinically asymptomatic (17). At the tomographic level larger lesions appear as foci of hyperdensity, dystrophic calcifications in up to 30% of

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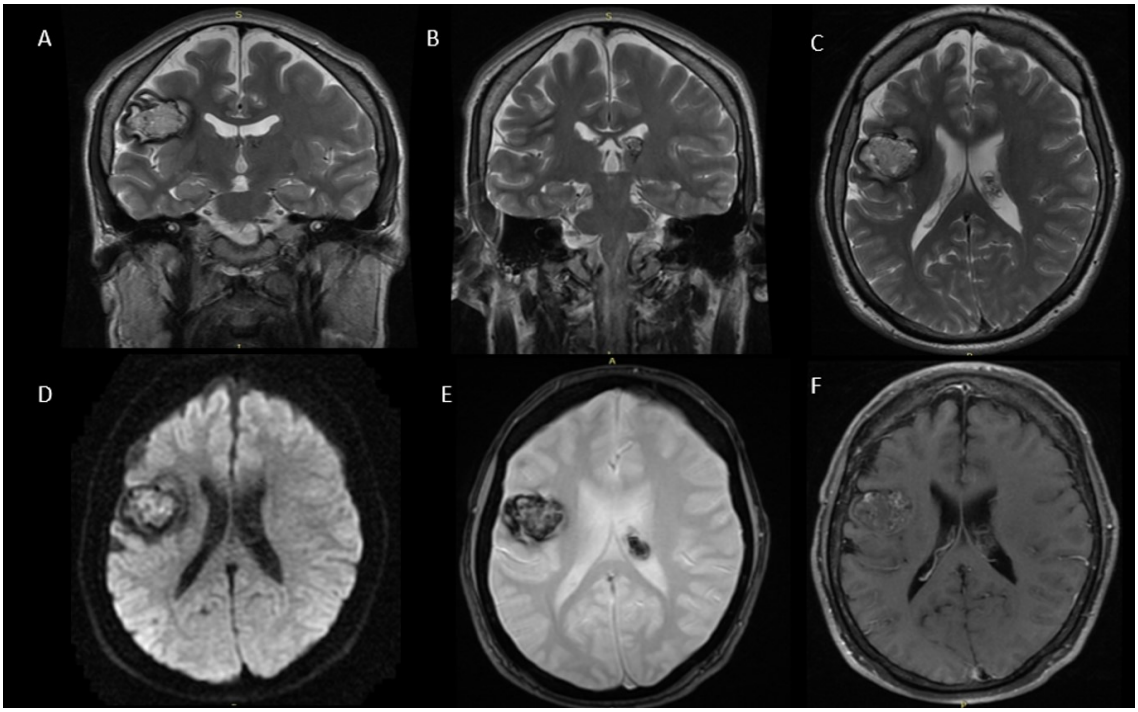

FIGURE 3: MRI: a round image with lobulated edges is observed in the right parietal lobe, with heterogeneous signal intensity in the different sequences, inside it presents images of tubular aspect with absence of signal in all sequences, it is associated to perilesional edema, it does not present enhancement after the administration of contrast medium. There are also three images of similar characteristics, located adjacent to the anterior horn of the right lateral ventricle and the left thalamic region with extension to the body of the ipsilateral lateral ventricle. B. Coronal in T2. C. T2 in axial plane. D. Axial, Diffusion with evidence of restriction in DW and ADW. F. T1 + contrast.

cases. Smaller lesions may not be seen in the initial CT scan, they usually measure less than 3 cm, have a similar attenuation to the surrounding parenchyma and experience little or no enhancement after the use of intravenous contrast. Their performance improves when they are slightly hyperdense, associated with calcifications or when there is recent bleeding, in which case edema may be seen around the lesion (18).

Angiography is not a specific detection method for this type of malformations, approximately 20 to 85% of the cases did not show abnormal findings, which suggests the limited effectiveness of angiography in detection and diagnosis, the use of angiography allows to exclude other lesions that are characteristic and specific in angiography such as arteriovenous malformations (AVM) and AVDs (19).

LESION	SIGNAL ON MRI	PATHOLOGICAL FEATURE
Type I: Subacute hemorrhage	T1: hyperintense nucleus	Subacute hemorrhage, surrounded by a ring of hemosiderin, macrophages and gliotic brain.
	T2: Hyper/hypointense nucleus with hypointense ring.	
Type II: Classic "popcorn" lesion	T1: nucleus with reticulated mixed signal.	Loculated areas of hemorrhage and thrombosis of different temporalities, surrounded by brain with gliosis and hemosiderin; areas of calcifications can be seen in large lesions.
	T2: reticulated mixed signal core with hypointense ring.	
Type III: Chronic hemorrhage	T1: Iso/hypointense.	Chronic phase hemorrhage with hemosiderin in and around the lesion.
	T2: hypointense with a hypointense ring that magnifies the size of the lesion.	
Type IV: Multiple punctate microhemorrhages	T1: lesion little or not visible	Lesions in this category correspond to telangectasias.
	T2: lesion little or not visible	
	T2* hypointense punctate lesions	

Table 1: MRI classification of cavernomatous malformations (Zabramski).

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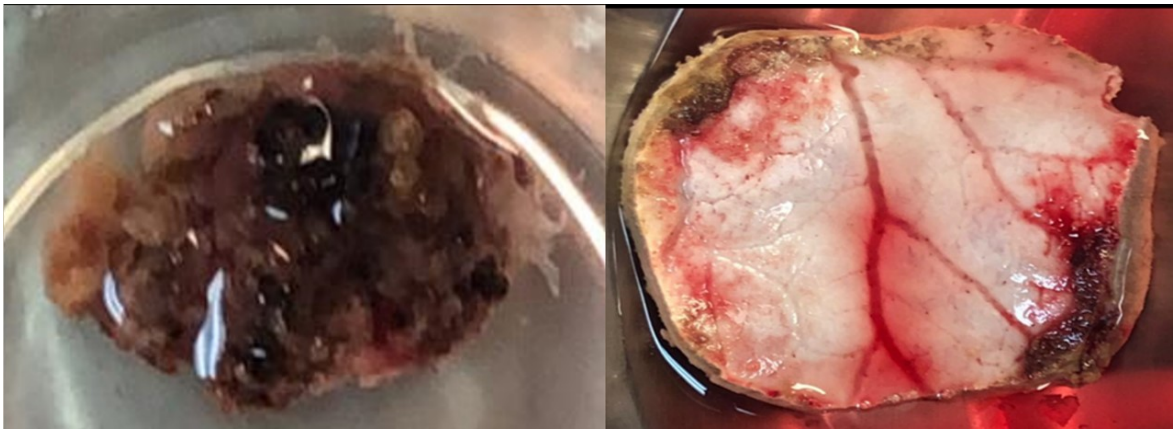

FIGURE 4. Surgical specimens removed

MRI is established as the gold standard for the detection of cavernomas. T2-weighted images reveal the typical blackberry or popcorn-like feature and a dark rim due to deposits of hemoglobin degradation products after hemorrhages. The lesion is typically bordered by this hemosiderin ring, hypointense in T2 sequences, and especially identifiable in T2 or GRE sequences and of later appearance in the susceptibility weighted sequence (SWI) (20).

To classify this type of images, Zabramski proposes these lesions in different categories based on MR characteristics (21) (see **Table 1**). Among the differential diagnoses of arteriovenous malformations, other types of vascular malformations such as arteriovenous malformations, venous angiomas and capillary telangiectasias, as well as hemorrhagic tumors with incomplete hemosiderin ring, calcified tumors such as oligodendroglioma, calcified granulomas and hemosiderin foci should be taken into account.

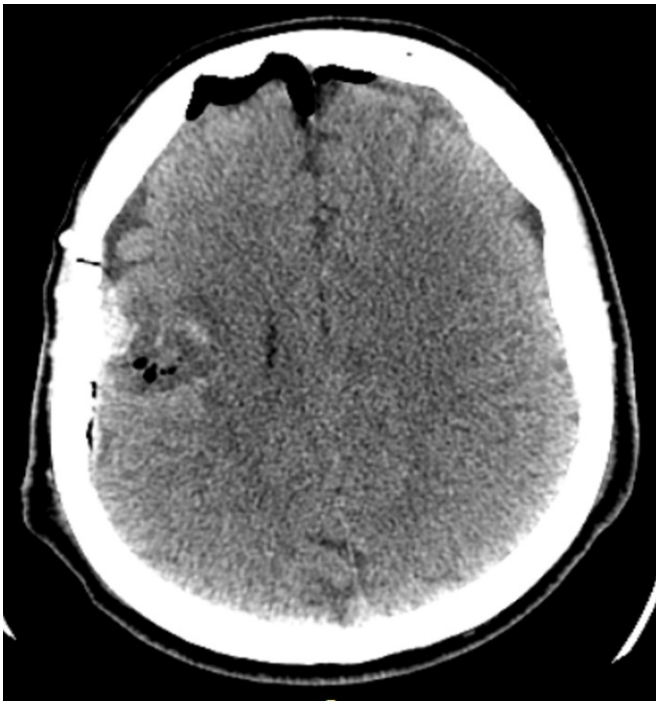

Figure 5. Control single skull CT scan shows post-surgical changes in the right parietal region measuring 33x35x24mm.

Management of patients with cerebral cavernomas can be conservative, but the risk of cerebral hemorrhage, neurological deficit or seizures should be kept in mind, after diagnosis of cerebral cavernous malformation (CCM), the 5-year risks are 2.4% for a first intracranial hemorrhage and 29. 5% for a recurrent hemorrhage, which may be influenced by the sex of the patient and location of the cavernoma (22); alternatively, they can be treated with neurosurgery by excision or stereotactic radiosurgery with the possibility of reducing the previously described risks but also with the risk of treatment complications, which is mainly determined by the location of the lesion. Despite decades of neurosurgical experience in this field, the evidence supporting surgical resection of cavernomas remains conflicting (23).

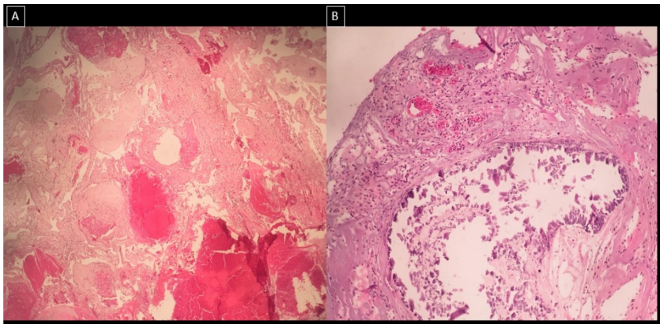

Figure 6. A and B Low magnification vascular lesion with ectatic vascular channels, some small thrombi, lined by endothelium without wall, presence of microcalcifications, no grail tissue between them.

Conclusion

Cerebral cavernomas are a type of vascular malformation of the central nervous system that with the advent of magnetic resonance imaging has been characterized and detected to a greater extent as a differential diagnosis of tumor pathology, being this study the gold standard for its detection, allowing its timely diagnosis and individualized treatment.

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Conflicts of interests

There was no conflict of interest during the study, and it was not funded by any organization.

References

1. Otten P, Pizzolato GP, Rilliet B, cols. 131 cases of cavernous angioma (cavernomas) of the CNS, discovered by retrospective analysis of 24,535 autopsies. Neurochirurgie 1989; 35: 82– 83, 128 –131.
2. Denier C, Labauge P, Brunereau L, cols. Características clínicas de pacientes con malformaciones cavernosas cerebrales con mutaciones KRIT1. Ann Neurol 2004; 55 (2): 213-20.
3. Aliaga A, Palavecino T, Rodrigo E,cols. Malformación cavernomatosa: Revisión de una patología clásica. Revista Chilena de Radiologia 2013; 19 (3): 117-124.
4. Khattar NK, Adams SW, Schaber AS, cols. Cirugía endoscópica endonasal para la resección de un hemangioma cavernoso con extensión sellar. Cureus 2018; 10 (11): 3663.
5. Osborn Anne G, Neurorradiología diagnóstica, capítulo 10. Malformaciones vasculares intracraneales, pag 311-313.
6. Günel M, Awad IA, Finberg K, col, Founder mutation as a cause of cerebral cavernous malformation in hispanic americans. N Engl J Med 1996; 334: 946-951.
7. Vilanova JC, Barcelo J, James, cols: Hemangioma from Head to Toe: MR Imaging with Pathologic Correlation. RadioGraphics 2004; 24: 367–385.
8. Strickland CD, Eberhardt SC, Bartlett MR, cols. Familial Cerebral Cavernous Malformations Are Associated with Adrenal Calcifications on CT Scans: An Imaging Biomarker for a Hereditary Cerebrovascular Condition. Radiology 2017: 284 (2).
9. Liu JK, Lu MY, Raslan AM, cols. Cavernous malformations of the optic pathway and hypothalamus: analysis of 65 cases in the literatura, Neurosurg Focus , 2010; 29 (3):E17.
10. Spiegler S, Rath M, Paperlein C, cols.Cerebral Cavernous Malformations: An Update on Prevalence, Molecular Genetic Analyses Genetic Counselling. Mol Syndromol 2018 febrero; 9 (2): 60-69.
11. Curling O, Kelly DL, Ellster D,cols. An analysis of the natural history of cavernous angiomas. J Neurosurg 1991; 75:702-708.
12. Wang K1, Zhou HJ 1, Wang M 1. CCM3 y enfermedad de malformación cavernosa cerebral. Accidente cerebrovascular Vasc Neurol. 2019 2 de marzo; 4 (2): 67-70
13. Al-Shahi SR, Hall JM, Horne MA,cols. Untreated clinical course of cerebral cavernous malformations: a prospective, population-based cohort study. Lancet Neurol. 2012;11(3):217-224.
14. Robinson JR, Awad IA, Little JR: Natural history of the cavernous angioma. J Neurosurg 75:709–714, 1991
15. Bigner D, McLendon R, Bruner J. Russell & Rubinstein's Pathology of Tumors of the Nervous System. 6th ed. London: Arnold, 1998.
16. Cisneros O, Rehmani R, Garcia KJ, cols. Cerebellar Cavernous Malformation (Cavernoma): A Case Report. Cisneros et al. Cureus 2019; 11(4): e4371.
17. Batra S, Lin D, Recinos PF, cols. Cavernous malformations: natural history, diagnosis and treatment. Nat Rev Neurol 2009; 5 (12): 659-70.
18. Kevin Y. Wang1,2, Oluwatoyin R. Idowu2, and Doris D.M. Handbook of Clinical Neurology, Vol. 143 (3rd series) Arteriovenous and Cavernous MalformationsR.F. Spetzler, K. Moon, and R.O. Almefty, Editors LIN2Chapter 24. Radiology and imaging for cavernous malformations.
19. Wang KY, Oluwatoyin R, Doris DM. Radiology and imaging for cavernous malformations. Handbook of Clinical Neurology,) Arteriovenous and Cavernous Malformations, Chapter 2., 2017 Elsevier B.V. Vol. 143 (3rd series).
20. Cortés J.J, Aramendía LC, Ballenilla M,cols. Malformaciones cavernosas intracraneales: espectro de manifestaciones neurorradiológicas. Radiología. 2012; 54(5):401-409.
21. Rinkel1 LA, Rustam AS, Gabriel JE, cols. Radiosurgical, neurosurgical, or no intervention for cerebral cavernous malformations: A decision analysis, International Journal of Stroke 0(0) 1–7.
22. Moultrie F, Horne MA, Josephson CB, cols. Outcome after surgical or conservative management of cerebral cavernous malformations, Neurology 2014;83:582–589.
23. Akers A, Al-Shahi Salman R, Awad IA, cols. Synopsis of guidelines for the clinical management of cerebral cavernous malformations: consensus recommendations based on systematic literature review by the Angioma Alliance Scientific Advisory Board Clinical Experts Panel.Neurosurgery 2017; 80: 665–6.

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