July 2001

Neoplastic growth of cerebral cavernous malformation presenting with impending cerebral herniation: a case report and review of the literature on de novo growth of cavernomas.

Arshad Sidiqui
Aga Khan University

Rashid Jooma
Aga Khan University, rashid.jooma@aku.edu

ELSEVIER

Vascular

Neoplastic Growth of Cerebral Cavernous Malformation Presenting With Impending Cerebral Herniation: A Case Report and Review of the Literature on De Novo Growth of Cavernomas

Arshad A. Siddiqui, M.B., B.S., and Rashid Jooma, F.R.C.S.
Department of Surgery (Neurosurgery Division), Aga Khan University Hospital, Karachi, Pakistan

Siddiqui AA, Jooma R. Neoplastic growth of cerebral cavernous malformation presenting with impending cerebral herniation: a case report and review of the literature on de novo growth of cavernomas. Surg Neurol 2001;56:42–5.

BACKGROUND
Cerebral cavernomas are rare vascular anomalies and their expansile growth has been considered to be mainly due to recurrent hemorrhages. They are not generally reported to show aggressive behavior.

CASE DESCRIPTION
A 27-year-old male presented with headache, visual disturbances, and a 17-year history of seizures. He was known to have a temporal lobe lesion on CT scan, consistent with a diagnosis of cavernous malformation but with no relevant family history. Serial clinical and radiological follow-up revealed a progressive increase in the size of the lesion with formation of a growing cyst of 7 cm in diameter, which produced mass effect, resulting in the clinical picture of cerebral herniation. The patient underwent emergency surgical resection with symptomatic relief. There was no evidence of significant hemorrhage at surgery.

CONCLUSION
Cavernous malformations can show expansile growth without any evidence of a presaging hemorrhagic event and, in the manner of a neoplastic lesion, present with raised intracranial pressure and cerebral herniation.

KEY WORDS
Cavernous malformation, de novo formation, cerebral herniation, cystic cavernous angioma, neurosurgical emergency.

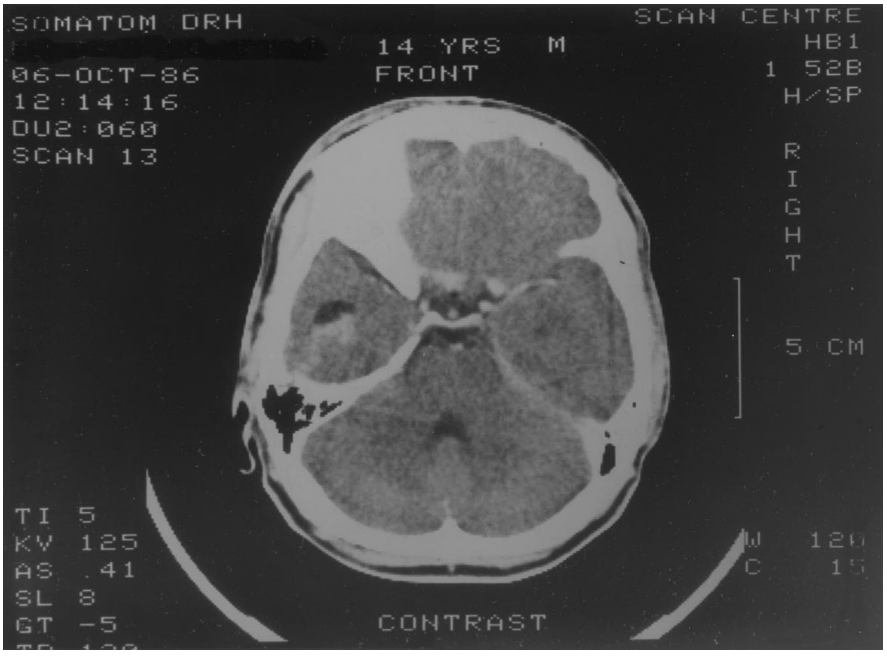
Cerebral cavernous malformation (CCM) is classically considered to be a vascular hamartoma that presents clinically with seizures, hemorrhage, or mass effect [8]. Its natural history has been increasingly clarified in the past two decades with the help of CT and MR scanning and it is clear that although a genetic predisposition to their development is fundamental, their behavior can be dynamic, with change in size and de novo appearance of lesions [3,9]. The expansion of a CCM is usually subsequent to hemorrhage or to growth of the cavernomatous matrix [3]. The progression of a cystic change has been surmised to be secondary to intralesional hemorrhage [11]. We report here the unusual evolution of a small epileptogenic temporal cavernous malformation into a cystic mass large enough to present with impending herniation but without evidence of significant hemorrhage.

Case Report

This 27-year-old male was initially evaluated in 1984 for a 2-year history of convulsions. A computed tomography (CT) scan of the brain showed a left temporal lobe lesion, which was thought to be a cavernous malformation (Figure 1). He was placed on anticonvulsant medications and the seizures subsequently remained well controlled. In December 1998, he began to suffer headaches of increasing intensity and a repeat CT scan of the brain showed an increase in the size of the associated cyst. Three

Address reprint requests to: Dr. Arshad A Siddiqui, Department of Surgery (Neurosurgery Division), Aga Khan University Hospital, Karachi-Pakistan.
Received February 16, 2000; accepted February 8, 2001.

0090-3019/01/$–see front matter
PII S0090-3019(01)00505-5

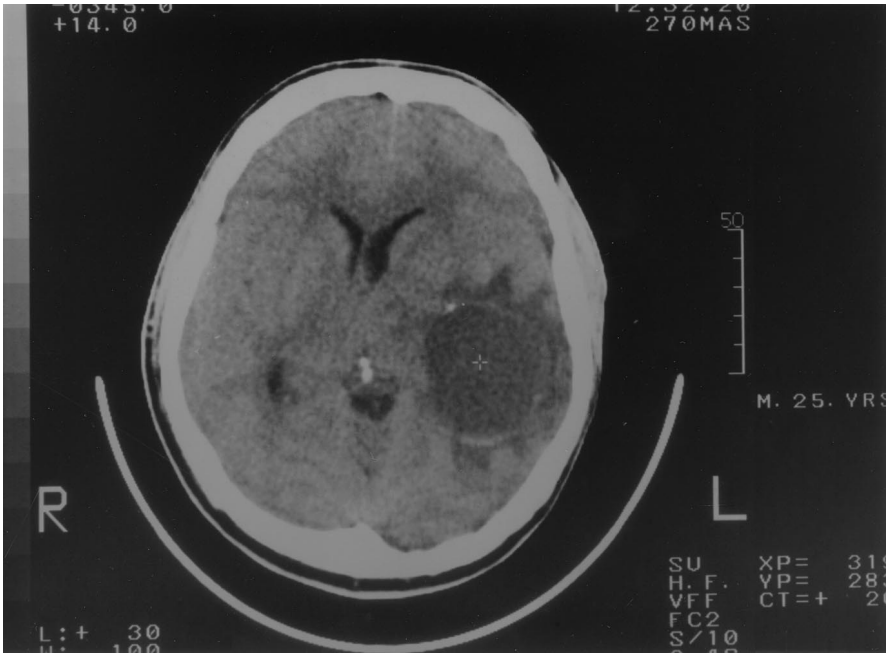


1 Post-contrast CT scan at initial presentation with seizure disorder. A part solid and part cystic lesion is evident in the left temporal lobe.

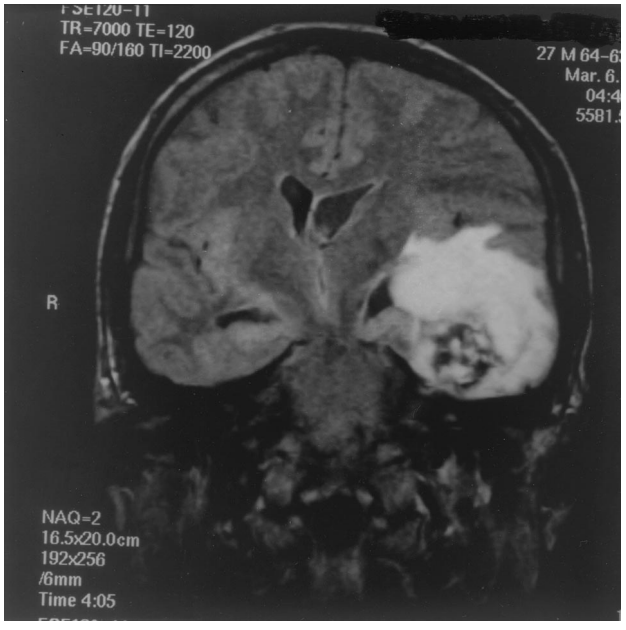
months later, the headaches became constant and severe and were associated with episodes of blurring of vision. The CT scan at this time showed significant enlargement of the cyst (Figure 2).

At the time of admission (in March 1999), the patient was drowsy and had florid papilloedema along with bilateral sixth nerve palsies. There were no motor or sensory deficits but the deep tendon reflexes were hyperactive in both lower extremities with an extensor plantar response. Magnetic resonance (MR) imaging revealed a large heterogeneous lesion in the left temporal lobe, composed of a solid calcified intramural part and a large cystic component (7.5 × 6 × 5 cm) associated with perifocal edema. Midline shift was evident (Figure 3).

Emergency surgical treatment was undertaken and a low temporal exposure fashioned. As the cyst was entered through the inferior temporal gyrus, there was little evidence of recent hemorrhage and the fluid within the cyst was a pale yellow-green.



2 CT scan 8 years later when patient returned with mass effect. There is considerable enlargement of the cyst with enhancement of its wall and surrounding edema. There was no hematoma.



3 Coronal MRI section before emergency surgery. The variegated intensity typical of a cavernoma is noted, with perifocal edema and brain shift.

The cyst wall was vascularized. As the solid vascular tumor component was excised, hemosiderin staining in the left parahippocampal gyrus was evident. Histopathological examination revealed the closely packed tissue of a cavernous malformation with large vascular spaces, lined by a single layer of endothelium in both the solid and cystic parts of the lesion. The darkly stained patches of fine calcification were also visible inside the tumor. At the time of discharge a week after surgery, the patient's clinical evaluation demonstrated improvement of his symptoms and the sixth nerve palsy had resolved. At a 6-month follow-up visit, he was functionally normal and had not had a seizure.

Discussion

The incidence of cavernomous malformation is 0.5% of all brain tumors in large prospective series [3]. Although clinical onset is observed at all ages with equal incidence in both sexes, 25% of cases are diagnosed under the age of 18 years; most of these occur in males, the incidence of overt hemorrhages is significantly high in females [3,10]. They usually present with epilepsy, intraparenchymal hemorrhages, progressive neurological deficits, and only rarely with raised intracranial pressure [11]. Zabramski et al recently suggested that the familial form of CCM is a dynamic disease, in view of the de novo formation of vascular malformations [14]. It is certainly unusual for a case of CCM to present with impending cerebral herniation.

Radiologically, two forms of CCM may now be identified, the typical "solid" form and a rare cystic form [9]. On CT scan, the former type appears as a discrete, hyperdense calcified lesion with minimal surrounding edema and mass effect; whereas the latter type appears as a ring-shaped cystic growth with mass effect and perifocal edema [9]. Both types enhance minimally after injection of contrast [9]. Calcification is seen in 11% to 40% of the cases [9]. The typical MR image of a cavernous malformation consists of a reticulated or honeycomb core of mixed density and the cystic form shows a well-defined capsule [12]. Recently, clinical and MRI features of de novo lesions in familial cases of CCM have been evaluated in terms of lesions/patient-year, concluding that occurrence of de novo lesions is independent of age, sex, and total number of pre-existing lesions [1]. With the ease of diagnosis provided by CT and MR scanning, a wealth of information has been accumulated in the past two decades about the behavior and natural history of cavernous malformations [6,8,9,12,13]. As they are generally considered to be hamartomatous lesions, of particular interest in recent reports has been documentation of the dynamic nature of CCMs in some patients, with the appearance of new lesions or changes in the MR characteristics and size of demonstrated cavernomous malformations [3]. Interestingly, Notelet et al have attempted to explain the evolutionary potential of cerebral cavernomas by immunostaining of proliferative cell nuclear antigen (PCNA) in the endothelium of the lesions [7].

The de novo formation of CCM is well known in patients affected by the familial form of the disease and has been reported at a rate of 0.4 lesions per patient per year [2]. New lesions have been described after both whole brain radiation and stereotactic irradiation [5]. Detwiler et al described a patient without any family history of this disease or a history of treatment with cranial radiation, which invalidates the assumption that CCMs are congenital lesions [2]. The pathophysiology of lesion expansion has been ascribed to growth of the cavernous matrix when the mass is solid, and organization and encapsulation of a perilesional hemorrhage where cyst formation occurs [3,10,11,12]. In the latter instance, an osmotic effect of the blood breakdown products in the cyst has been assumed to contribute to its enlargement [4]. Neither of these mechanisms seems to have operated in our case, as there was little evidence of a hemorrhagic event on clinical and radiological examination or at surgery. Unlike the reactive glial wall of a cyst associated

with resorbing hematomas, the histological appearances of the tumorous (solid) and cystic parts of the lesion in our patient were similar, suggesting that the enormous growth was due to a proliferative mechanism in the lesion itself.

Cavernous malformations are considered to be histologically benign hamartomas and usually any growth of this vascular anomaly has been assumed to be the result of hemorrhage. However, CCMs are not always clinically dormant lesions with an indolent progression; they can have an acute presentation requiring an immediate neurosurgical intervention.

Conclusion

We have documented expansion of a cystic cavernoma in the manner of a vascular neoplastic lesion with aggressive clinicopathological behavior. This has implications for management, as in our patient. Although anticonvulsant therapy successfully controlled the seizures after his initial presentation with a small lesion, the progression of the mass ultimately required an emergency craniotomy.

REFERENCES

1. Brunereau L, Levy C, Laberge S, Houtteville J, Labauge P. De novo lesion in familial form of cerebral cavernous malformation: clinical and MR features in 29 non-Hispanic families. Surg Neurol 2000;53:475–82.
2. Detwiler PW, Porter RW, Zabramski JM, Spetzler RF. De novo formation of a central nervous system cavernous malformation: implications for predicting risk of hemorrhage: Case report and review of the literature. J Neurosurg 1997;87:629–32.
3. Houtteville J-P. Brain cavernoma: a dynamic lesion. Surg Neurol 1997;48:610–4.
4. Ito H, Komai T, Yamamoto S. Fibrinolytic enzyme activity in the lining wall of chronic subdural hematomas. J Neurosurg 1978;48:197–200.
5. Larson JJ, Ball WS, Bove KE, Crone KR, Tew JM. Formation of intracerebral cavernous malformation after radiation treatment for central nervous system neoplasia in children. J Neurosurg 1998;88:51–6.
6. Maraire JN, Awad IA. Intracranial cavernous malformations: lesion behavior and management strategies. Neurosurgery 1995;37:591–605.
7. Notelet L, Houtteville JP, Khoury S, Lechevalier B, Chapon F. Proliferating cell nuclear antigen (PCNA) in cerebral cavernomas: an immunocytochemical study of 42 cases. Surg Neurol 1997;47:364–70.
8. Pozzati E, Acciarri N, Tognetti F, Marliani F, Giangaspero F. Neurosurgery 1996;38:662–9.
9. Rigamonti D, Drayer BP, Johnson PC, Hadley MN, Zabramski J, Spetzler RF. The MRI appearance of cavernous malformations. J Neurosurg 1987;67:518–24.
10. Robinson JR, Awad IA, Little JR. Natural history of the cavernous angioma. J Neurosurg 1991;75:709–14.
11. Steiger HJ, Markwalder TM, Ruelen HJ. Clinicopathological relations of cerebral cavernous angiomas. Neurosurgery 1989;21:879–84.
12. Simard JM, Garcia-Bengochea F, Ballinger WE, Mickle JP, Quisling RG. Cavernous angioma: a review of 126 collected cases and 12 new clinical cases. Neurosurgery 1986;18:162–72.
13. Tekkok IH, Ventureyra EC. De novo familial cavernous malformation presenting with hemorrhage 12.5 years after the initial hemorrhagic ictus: natural history of an infantile form. Pediatr Neurosurg 1996;25:151–5.
14. Zabramski JM, Wascher TM, Spetzler RF, Jhonson B, Golfinos J, Drayer BP, Brown B, Rigamonti D, Brown G. The natural history of familial cavernous malformation: results of an ongoing study. J Neurosurg 1994;80:422–32.

COMMENTARY

The case reported by Siddiqui and Jooma demonstrates the fact that some cerebral cavernomas present as tumors and not—as is commonly believed—as vascular malformations.

This patient had a very large lesion, with no sign of bleeding except some perilesional deposits of hemodsiderin, corresponding to an oozing phenomenon. This report confirms our own experience [1,2], which led us to surmise that cavernomas are in reality benign vascular tumors with a hemorrhagic risk, rather than vascular malformations. It is important to be aware of this feature both from a nosological and a practical point of view. When a neurosurgeon makes the decision to operate on a cavernoma, it is mandatory that the entire lesion be removed to prevent regrowth and hemorrhage.

Prof. Jean-Pierre Houtteville
Service de Neurochirurgie
Universitaire de Caen
Caen, France

REFERENCES

1. Houtteville JP. Brain cavernoma: a dynamic lesion. Surg Neurol 1997;48:610–4.
2. Notelet L, Houtteville JP, Khouri S, Lechevalier B, Chapon F. Proliferating cell nuclear antigen (PCNA) in cerebral cavernomas: an immunocytochemical study of 42 cases. Surg Neurol 1997;47:364–70.