

Case of the month Oct 2013 – EANS website

Lady with a headache – an extreme case of multiple cavernomas

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Introduction

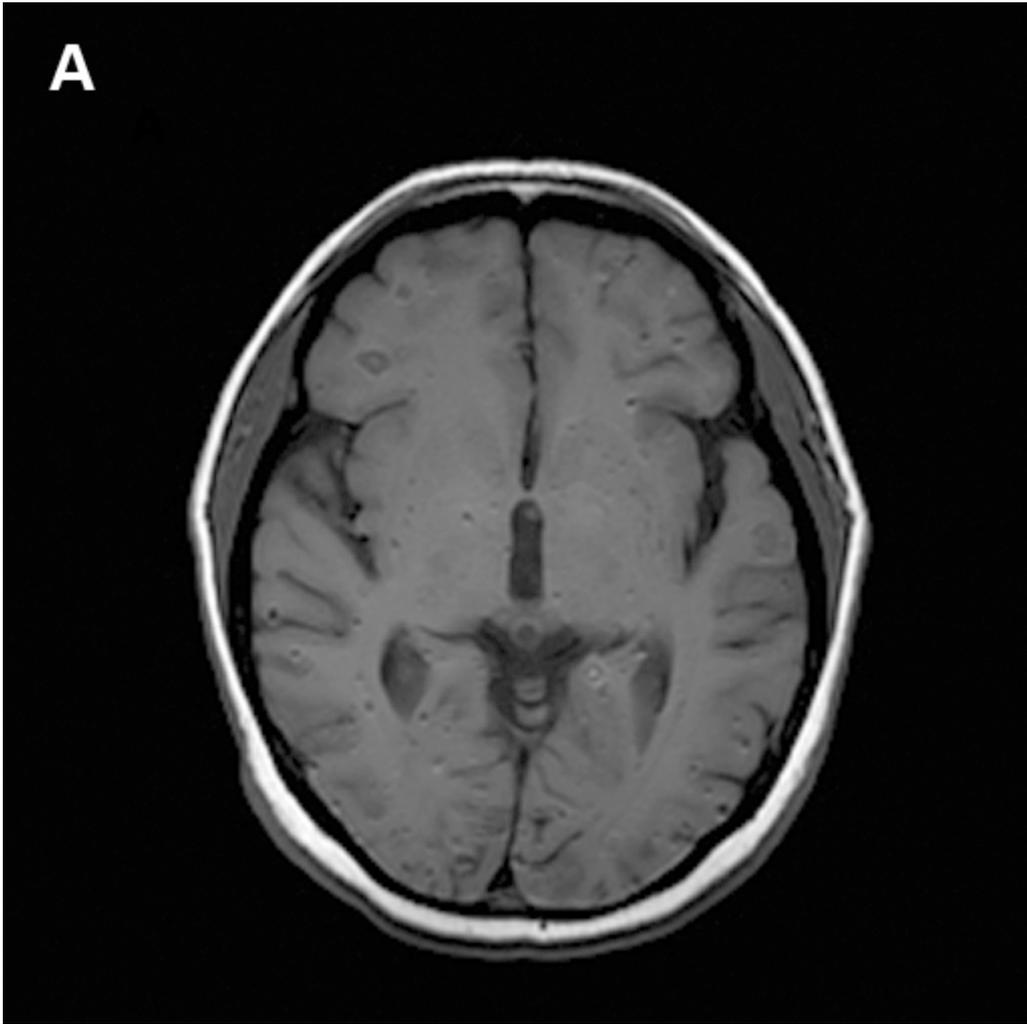
Cavernomas of the brain are rather rare neurovascular lesions, usually diagnosed before the fifth decade of life, if symptomatic. Most patients with symptomatic cavernomas present with seizures, but symptomatic hemorrhages may occur as well, with the approximate risk of 0.5-1.0% per patient-year. The risk of rebleeding from a previously ruptured cavernoma is considerably higher, even 10-60% per patient-year depending on the location. Still, the low flow in these lesions means that hemorrhagic stroke caused by a cavernoma is seldom severe, and most patients with cavernomas have a benign course of the disease. Among patients with cavernomas, probably 10-20% have multiple cavernomas (MCs), with the average of ~10 cavernomas per patient with MCs.

Case Presentation & History

Our female patient was admitted to a neurological emergency room for the first time in 1999 at the age of 32 for headache, vomiting, vertigo and balance problems. Multiple tiny hemorrhagic lesions were visible in MRI. The diagnosis remained open at the time, but she made a full recovery without specific treatment. She was admitted again in 2005 to Helsinki University Central Hospital due to intense headache. No focal deficits were noted, and the level of consciousness was normal. MRI was consistent with cavernomatosis of the brain, with dozens of cavernomas, and signs to suggest recent hemorrhage in several of them. Blood biochemistry did not indicate any coagulopathy, and blood pressure levels were normal. Neurosurgical treatment was clearly not indicated, but she was treated with a p.o. regimen of tranexamic acid 1 g three times daily for a week because of suspicion of recent multiple cerebral hemorrhages.

Since 2005, we have been following her up regularly. In 2007, she experienced balance problems because of a symptomatic hemorrhage from a cerebellar cavernoma. In 2009, left hemiparesis and right oculomotor palsy resulted from the hemorrhage of a mesencephalic cavernoma. In 2012, hemorrhage from a cavernoma in the right internal capsule resulted in left lower limb paresis. None of the hemorrhages have been life-threatening or resulted in decreased level of consciousness, and no surgical intervention has been necessary nor considered indicated. Focal symptoms have mostly resolved well with time, and she has retained all normal activities of daily living, although she retired because of neurological and neuropsychiatric residual symptoms in 2010 at the age of 43. She has not had any epileptic seizures. The number of her cavernomas has been constantly increasing in serial MRI imaging during the follow-up; in the last estimation the number of cavernomas totalled 532! Figure 1 demonstrates the appearance of her MCs in various MRI sequences. The appearance of individual cavernomas has also changed considerably over time. Despite hundreds of brain cavernomas, both supra- and infratentorial, she has no spinal cavernomas.

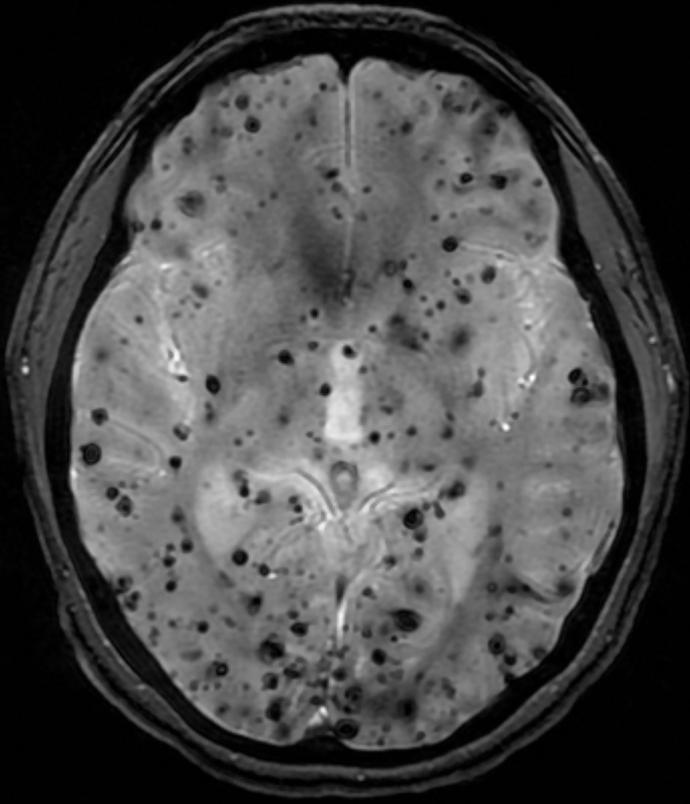
Figure 1. MRI of patient with hundreds of cavernomas. A) T1-weighted image. B) T2-weighted image. C) T2-weighted gradient echo (T2*GRE) image. D) Susceptibility weighted (SW) image.

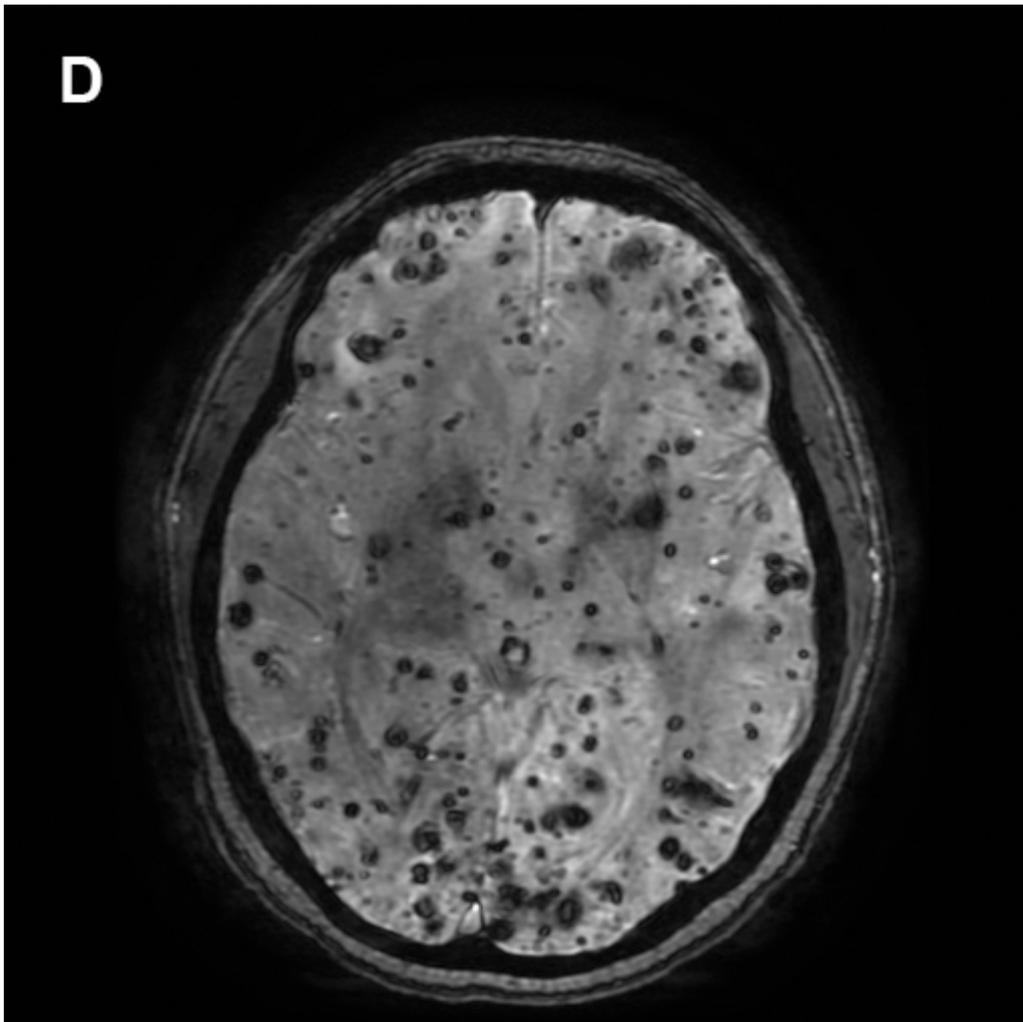


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Question 1. What is known about genetics of cavernomas?

Question 2. What is the Zabramski classification of cavernomas?

Question 3. What MRI sequences are most sensitive for cavernomas?

Question 4. What are the indications for microsurgical treatment for patients with MCs?

Answer 1. Cavernomas occur in both sporadic and familial forms. In Caucasian patients, familial forms affect approximately 10-20% of the patients, whereas in Hispanic-Americans familial form of the disease accounts for up to 50% of the cases. Patients with the familial form are more likely to harbor multiple cavernomas. Three genes responsible for the familial form have been identified, CCM1, CCM2 and CCM3 (Bacigaluppi et al., 2013).

Answer 2. Zabramski classification is based on the appearance of cavernomas on various MRI sequences (Zabramski et al., 1994). *Type I* represents cavernomas with subacute hemorrhage, and they are often visible in CT as well. They are hyperintense in both T1- and T2-weighted imaging in the initial state, but degradation of hemoglobin affects the appearance over time. *Type II* is the most typical appearance of a cavernoma, with a classical reticulate core of mixed signal surrounded by a hypointense ring seen in T1- and T2-weighted images. *Type III* cavernomas are hypointense on both T1- and T2-images and represent chronic hemorrhage. *Type IV* lesions are seen mainly in gradient echo sequences and are invisible in conventional T1- and T2-images (see below).

Answer 3. Hemosiderin-sensitive T2-weighted gradient echo (T2*GRE) sequences are much more sensitive than conventional T1- and T2-weighted images. A more recent application of GRE sequence, susceptibility weighted imaging (SWI) is even more sensitive than T2*GRE, and is

capable of showing cavernomas without surrounding hemosiderin which are invisible even in T2*GRE images (Campbell et al., 2010).

Answer 4. The rationale behind microsurgical treatment of cavernomas is elimination of hemorrhage risk and amelioration of epilepsy, if present. While the indication for surgery may sometimes be unclear and difficult to justify even in cases with a single cavernoma, depending on e.g. location of the cavernoma, symptomatology and age of the patient, the presence of MCs makes decision-making even harder. If clinically the most active and symptomatic cavernoma can be identified – often it is the largest one, with signs of recent bleeding – the surgical outcome of its removal may be rather favorable even in patients with MCs. In our own case series with the mean follow-up of almost 8 years, removal of the symptomatic cavernoma seemed to clearly decrease the hemorrhage risk in patients with MCs, and 70% of epileptic patients achieved Engel class I (although with continuing use of antiepileptic drugs) outcome despite remaining “silent” MCs (Kivelev et al., 2009).

Conclusions

Surprisingly, our patient has no familial history of cavernomas, and genetic testing for known CCM mutations has been negative. Most of the hundreds of cavernomas in our patient are Zabramski Type IV cavernomas, but still numerous Type I-III cavernomas have been visible in all of her MRI scans. Typically for patients with MCs, the pattern of Type I-III cavernomas has changed over years, with various lesions becoming either more or less visible in conventional sequences. Contrary to our experience with “normal” patients with a “reasonable” amount of MCs, the patient of this case report has received symptoms from a different cavernoma in every occasion, and the decision to continue conservative follow-up so far seems to have been the wisest one.

References

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