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Familial cavernous angiomas masquerading as multiple sclerosis

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Summary

We report here two cases of cavernous angioma, in the proband and her father, with quite different clinical presentations. The proband presented with a brainstem syndrome, mimicking multiple sclerosis, while the father had a history of mild epilepsy. Both patients were managed conservatively. The cases also demonstrate the utility of magnetic resonance imaging in the diagnosis of cavernous angioma.

Keywords: cavernous angiomas; multiple sclerosis; magnetic resonance imaging

Cavernous angiomas (also known as cavernomas and cavernous haemangiomas) are a form of intracranial vascular malformation that are reported to affect 0.5% of the population.¹ In up to 75% of patients the lesions are multiple. They are characterised by collections of large, abnormal vascular spaces without intervening brain parenchyma.² Up to 50% of patients with cavernous angiomas have a familial form of the disorder which is inherited in an autosomal dominant mode, with incomplete clinical penetrance.¹ The familial form may be more frequent in the Hispanic population.³ Recent genetic studies have identified linkage of this trait to chromosome 7q11.2-q21 in some families.^{1,2} Although cavernous angiomas are rarely life-threatening, they may cause significant morbidity related to their size and location.

Case reports

Case 1

A 19-year-old, right-handed woman was admitted in 1988 with a 5-day history of progressive neurological dysfunction. At the onset she had awoken with numbness of the left side of her tongue, which spread over 24 hours to affect the whole left side of her face. She sub-

sequently developed horizontal diplopia, worse on right lateral gaze, and incoordination, with a tendency to fall to the left. On the day prior to admission she had developed patchy sensory disturbance in her left arm and leg. Her medical history was unremarkable. She was taking the oral contraceptive pill. She was one of four siblings and her father had epilepsy.

On general medical examination the only findings of note were haemangiomas on the dorsum of her left hand, left calf and right thigh. Neurologically, her gait was ataxic. Fundoscopy was normal, but there were bilateral partial sixth nerve palsies, and upbeat nystagmus on upgaze. There was a left sensory trigeminal neuropathy and mild subjective blunting of hearing on the left side. In the limbs there was a mild left-sided pyramidal weakness, with subjective reduction of light touch and pin-prick distally in the left arm and leg. A diagnosis of demyelination was suspected. Visual evoked potentials were normal. A computed tomography (CT) scan of the cranium revealed two small high-density lesions in the right side of the brainstem and left putamen, thought to represent areas of haemorrhage. Cerebrospinal fluid (CSF) examination was entirely normal, with absent oligoclonal bands. The patient's condition spontaneously improved, and follow-up CT brain scan 2 weeks later showed considerable resolution of the high density lesions.

Eight months later she was re-admitted with a relapse comprising similar brainstem symptoms and signs, following a minor acute neck sprain. Cranial magnetic resonance imaging (MRI) scan revealed three separate lesions typical of cavernous angiomas, including a large lesion in the tegmentum of the midbrain, eccentrically located to the right (figure).

The patient has been managed conservatively to date. She has suffered a number of relapses referable to the brainstem cavernous angioma but has recovered to normal

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Figure (A) Axial T2-weighted image at the level of the midbrain, showing large cavernous angioma with very hyperintense central signal and peripheral hypointensity; (B) sagittal T1-weighted image from same patient showing separate lesion adjacent to the posterior horn of the lateral ventricle. Both the central signal hyperintensity and the peripheral hypointensity are typically less marked than on T2-weighted images

neurological function after each of these. Repeat MRI scans have shown increase in size of the lesions, with signal changes in keeping with haemosiderin deposition, due to recurrent haemorrhage.

Case 2

This 54-year-old man, the father of Case 1, subsequently presented in 1996 with a history suggestive of right-sided transient ischaemic attacks. He had a history of extensive peripheral vascular reconstructive surgery and was an ex-smoker. He also reported two generalised seizures, the last of which was in 1985. He was still taking sodium valproate at the time of presentation.

Learning/summary points

- intracranial cavernous angiomas may be asymptomatic or present with seizures, focal neurological disturbance, headaches or haemorrhage
- up to 50% of cases are familial and inherited as an autosomal dominant trait
- varied presentation and often indolent clinical course may lead to diagnostic delay or misdiagnosis
- MRI scanning is the diagnostic method of choice

On examination, he was normotensive, but peripheral pulses were weak in the legs. General medical and neurological examinations were otherwise normal.

A CT brain scan showed areas of increased density in the right temporal lobe and another in the right fronto-parietal region with no evident mass effect. An MRI brain scan subsequently showed five separate lesions all having the typical signal characteristics of cavernous angiomas. The patient has been managed conservatively to date.

Discussion

These cases illustrate the different ways in which cavernous angiomas may present. Symptomatic patients typically present between the ages of 20 and 40, although symptoms can begin at any age. Focal neurological deficits may occur in 10–35% of cases and when angiomas are located in the brainstem, a mixed diagnosis of multiple sclerosis has been reported in up to 10% of patients.⁴ Vrethem *et al* reported the case of a 35-year-old man with symptoms mimicking multiple sclerosis who went 15 years before MRI scanning revealed a brainstem cavernous angioma.⁴ This case was exceptional, however, because the patient had oligoclonal bands in the cerebrospinal fluid; such a finding would normally be supportive of multiple sclerosis and has not been reported in any other case of cavernous angioma (including our Case 1).

Epilepsy is the more common clinical presentation of cavernous angiomas, occurring in between 30% and 50% of patients.¹ Seizures can be focal, generalised, or both.⁵ Other clinical presentations include headaches (20–30%), and recurrent haemorrhages, more often occult.^{1,5} In several cases the lesions may be asymptomatic and only detected incidentally.^{2,3} CT brain scanning has a 10% false negative rate, while angiography may be normal in about one-third of reported cases with cavernous malformations.^{6,7} The investigation of choice is MRI scanning, which has good sensitivity and specificity. Cavernous angiomas have typical appearances on MRI which are considered diagnostic. These include central signal hyperintensity and prominent peripheral signal hypointensity on T1- and T2-weighted sequences corresponding to subacute haemorrhage and haemosiderin, respectively. There is usually no mass effect or oedema, no feeding

arteries or draining veins and no enhancement after intravenous contrast agent.⁸ MRI is also safe for monitoring patients with cavernous angiomas, and is able to demonstrate the dynamic state of the lesions, with new lesions appearing in nearly 30% of patients at 2.2 years follow-up in one study.³

The management of cavernous angiomas ranges from observation, with treatment of seizures along conventional lines where necessary, to surgical extirpation for accessible lesions that produce repetitive or progressive symptoms. Prophylactic resection of asymptomatic lesions is not indicated.

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