

Reminder of important clinical lesson

Cerebral cavernous malformation: a diagnostic challenge in a young patient with intracerebral haemorrhage

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Summary

An 18-year-old Caucasian man presented with a sudden onset right hemiparesis. On examination, he had objective evidence of an upper motor neuron lesion affecting the right side of his body. CT scan showed a left thalamic haemorrhage. MRI, gradient echo and cerebral angiogram showed no structural lesion and the cause of the bleeding was ultimately attributed to the use of cocaine. During the subsequent 2 years the patient had two further similar episodes, with an MRI eventually demonstrating a cerebral cavernous malformation. This was excised using frameless stereotactic surgery, following which the patient made an uneventful recovery.

BACKGROUND

Stroke is very common in the elderly population and is usually a complication of atherosclerosis. It is a rare condition in patients under 45 years of age, with this group accounting for only 12% of all strokes.¹ These patients require comprehensive investigations as many causes are treatable. Cerebral cavernous malformation (CCM) is a type of haemangioma which is an important cause of intracerebral haemorrhage, particularly in young patients. They are present in 0.5% of the population and usually present with seizures, focal neurological deficits, stroke and headaches.² We report the case of a CCM in a young teenager, illustrating the diagnostic challenge posed by these vascular malformations.

CASE PRESENTATION

An 18-year-old right-handed Caucasian man presented in 2009 with a sudden onset of weakness in his right arm and leg. He also noted a mild drooping of the right side of his face, which was associated with slurring of his speech. He denied headache, visual disturbance, loss of consciousness or any history of head trauma. His medical history was insignificant. Of note, two of the patient's second-degree relatives died from intracerebral haemorrhages at a young age. He admitted to regular use of illicit drugs including marijuana, ecstasy and cocaine, however not immediately prior to his hospital attendance.

On examination he was afebrile with normal vital signs. Neurological examination revealed a complete right-sided weakness in his arm and leg (Medical Research Council=0) with brisk reflexes and an extensor plantar response on the ipsilateral side. There was reduced sensation on the right with associated hemifacial weakness sparing the forehead. The patient also reported dysphagia and mild dysarthria.

INVESTIGATIONS

Haematological investigations, including a vasculitis screen, were normal. CT of the brain demonstrated a left thalamic

haemorrhage. Subsequent MRI, including T1-weighted and T2-weighted scans, gradient echo (GRE) and MR angiography failed to identify any structural abnormalities.

DIFFERENTIAL DIAGNOSIS

The principle causes of stroke in the young include extracranial arterial dissection, cardioembolism, premature atherosclerosis and haematological disorders. A small proportion of strokes are caused by connective tissue disorders, vasculitides of the central nervous system and rare metabolic conditions. In the presence of normal investigations and strong history of drug abuse, the diagnosis of cocaine-induced stroke was made. Unfortunately, the patient had two further clinically identical strokes in 2010 and 2011, which fuelled the suspicion of a structural brain lesion. Three MRI scans of the brain were performed in 3 years, but only the last scan in January 2012 identified the lesion—a mixed intensity mass with a hypointense rim deep seated in the left insular cortex, highly suggestive of a cerebral cavernous malformation (figure 1). This diagnosis, however, was made 3 years following his first presentation, and two normal MRI scans performed in the acute setting.

TREATMENT

The patient underwent left fronto-temporal craniotomy during which he experienced a generalised tonic-clonic seizure as a consequence of cortical stimulation and the operation had to be discontinued. During the second attempt the CCM was identified deep in the Sylvian fissure with the help of stereotactic guidance. Haemosiderin pigmentation was noted surrounding the lesion. Microscopic dissection was undertaken and the CCM was successfully excised without any intra-operative complications. Histopathological examination confirmed cerebral cavernous malformation.

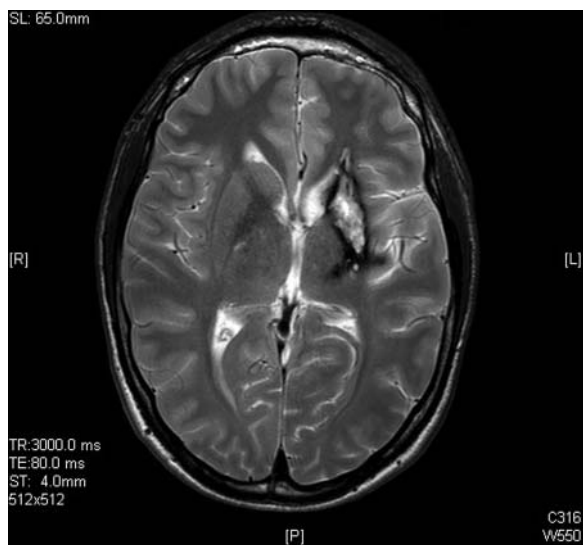


Figure 1 A T2-weighted MRI demonstrates mixed intensity areas adjacent to the left thalamus representing the previous haemorrhage. Posterior to this, a small hyperintense lesion with a hypointense rim is noted in the left insular cortex strongly suggestive of cerebral cavernous malformation.

OUTCOME AND FOLLOW-UP

The patient made an uneventful recovery and remains symptom free after 3 months of follow-up. Follow-up MRI scan confirmed a complete resection of CCM with no evidence of recent haemorrhage. Regular follow-up scans are required to detect any recurrence or de novo formation of CCM.

DISCUSSION

Cerebral cavernous malformations are defined as vascular lesions consisting of multiple dilated sinusoidal capillaries giving a characteristic ‘mulberry’ appearance.^{2–3} They account for 5–13% of all vascular anomalies of the brain and are most commonly located supratentorially (70%) or on the brainstem (20%).⁴ Although initially considered as hamartomatous lesions, de novo formation of CCMs has been reported, particularly following brain irradiation.^{5–6} Currently two forms are recognised: a sporadic form characterised by an isolated lesion and a familial form characterised by multiple CCMs, which shows autosomal-dominant inheritance.⁷ The responsible genes CCM1, CCM2, CCM3, Krev Interaction Trapped Protein (KRIT1) have been identified in 80% of CCMs.⁸ In our case, there is a strong family history of intracranial haemorrhage; however, whether CCMs could have accounted for these was not determined. Most patients present in their early thirties, however the age of presentation ranges from neonates to the very elderly.² CCMs are asymptomatic in 10–40% of patients and are frequently discovered incidentally by neuroimaging. The most common symptoms include seizures (40%), focal neurological deficits (10%), clinically symptomatic haemorrhage (13%) or headaches (6%).² The risk of bleeding is low owing to a low pressure in the dilated capillaries compared to their counterpart, arteriovenous malformations. The annual risk of first significant haemorrhage is 0.25–0.6%, but subsequently increases to as high as 4–23%, which is reflected in our case.⁷



Figure 2 Gradient echo MRI was performed to screen for familial cerebral cavernous malformations, but none were identified.

CCMs are known to fluctuate in size and almost invariably show signs of haemorrhage. Owing to the dynamic nature of the lesion, there is considerable variation in the appearance on neuroimaging. CT scan is helpful in confirming the haemorrhage, however small CCMs are likely to be missed. Cerebral angiogram is not helpful, since most of the CCMs are angiographically occult due to the sluggish blood flow through the dilated sinusoids which fail to enhance.⁸ MRI T1-weighted and T2-weighted modalities are the investigation of choice demonstrating a characteristic ‘popcorn’ appearance with areas of old and recent haemorrhages.⁹ Typically, the core of the CCM shows areas of mixed intensity on T2-weighted images representing the blood and its by-products at various stages of evolution.⁹ The mass is usually surrounded by a hypointense ring, which represents haemosiderin deposits within macrophages.

Our case illustrates that occasionally minute lesions, which can produce considerable complications, might be missed on standard MRI T1-weighted and T2-weighted modalities. In these cases, where a lesion is still suspected, more sensitive techniques such as GRE or pin echo sequences are employed to delineate tiny capillary telangiectasia that can often be multiple in familial cases (figure 2).¹⁰ As in this case however, even these highly sensitive modalities occasionally fail to identify CCMs in the presence of large amounts of acute blood.^{11–12} Although this is rare, there have been previous reports that CCMs are missed in the acute phase and are only subsequently discovered 2–3 years later.¹² This implies that a follow-up MRI scan once the haemorrhage has resolved should be performed in those cases where there is a high index of suspicion for CCM. In this case, diagnosis was delayed due to a very strong history of drug-induced haemorrhage in the presence of normal imaging.

If multiple CCMs are discovered, it is recommended that close relatives should undergo screening for this disease.¹³ Small and clinically silent lesions require no treatment; however, frequent MRI follow-up (every 2 years) is vital.⁷

Medical treatment is indicated in patients suffering from epileptic seizures. Resection is reserved for patients with symptomatic lesions or patients with the large superficial CCMs that are at high risk of bleeding.⁶ Prognosis is excellent and most patients have no further haemorrhages, unless multiple CCMs are present.¹⁴

This case illustrates the diagnostic difficulty of a CCM in a teenager. It is an important cause of intracerebral haemorrhage and thus should always be considered in young patients presenting with symptoms of stroke. Clinicians should be aware that small but significant intracerebral lesions may be present without evidence of radiological abnormality—even the highly sensitive GRE may be normal in the acute setting. In these cases, we would advise a further MRI scan, since small CCMs may be missed in the presence of acute haemorrhage.

Learning points

- ▶ Comprehensive investigations should be carried out in young patients with stroke.
- ▶ Cerebral cavernous malformation should be suspected in recurrent intracerebral haemorrhage.
- ▶ All MRI modalities may fail to recognise small cerebral cavernous malformations (CCMs) in the acute phase, even the sensitive gradient echo or spin echo.
- ▶ Follow-up MRI scan should be performed in these cases as CCMs can be obscured by blood.

Competing interests None.

Patient consent Obtained.

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