The “Moya” you look, the “Moya” you find

Jason Scop and Stuart Baker

Clinical record
A 52-year-old woman was the driver of a car struck from the right side at 90 km/h. She was wearing a seatbelt, and attending paramedics believed that the impact led to her striking her head against the window to her right. At the scene, she was conscious but disoriented, with a Glasgow Coma Score (GCS) of 13/15.

During transport to hospital, her condition deteriorated. On arrival in the emergency department, the GCS was 6/15, with decorticate posturing of the right side. The left pupil was 5 mm in diameter, and the right 3 mm.

In the emergency department, she underwent intubation, mechanical ventilation and full trauma evaluation. Urgent cranial computed tomography (CT) showed a 6.3 cm × 4.5 cm acute haematoma in the left temporal lobe, possibly communicating with haematoma in the left sylvian fissure, as well as a small subdural collection (Figure 1A). The haematoma was causing mass effect and midline shift of about 1.1 cm, along with uncal herniation. There was no other intracranial haemorrhage or evidence of contusion, and no sign of extracranial injury or cerebral oedema. Thorough examination revealed no other injury.

In the operating theatre, a left frontoparietal craniotomy was performed with evacuation of the intraparenchymal haematoma. An intracranial pressure monitor was inserted, and the patient was then transferred to the intensive care unit (ICU) for support and ongoing care. She had no intracranial hypertension, and was weaned from ventilation and discharged from the ICU after 5 days. Follow-up CT of the head showed little residual blood and resolution of midline shift.

While in the ICU, some suspicious clinical findings led to further investigation. The patient was presumed to have received the isolated intracranial injury as a result of a blow to the right side of her head, but there was no external bruising or other indication of injury to the right side. On review of the initial cranial CT scan, it was noted that there was no right-sided intracranial or extracranial injury other than the haematoma. It was conceivable that a non-traumatic intracranial event had resulted in her losing control of the vehicle and the ensuing accident.

The haematoma seemed centred around the left sylvian fissure, and follow-up cranial CT was performed with intravenous contrast, seeking vascular abnormalities potentially leading to spontaneous haemorrhage. It was noted that there was no contrast filling of the left middle cerebral artery (Figure 1B).

Three-dimensional reconstructions of the CT angiograms (Figure 2) showed a number of unusual abnormalities. The right internal carotid artery was seen to divide normally at its termination, with normal anatomy of the middle cerebral artery, although some proliferation of local pial vessels was noted. On the left side, the middle cerebral artery had an abrupt stenosis close to its origin from the internal carotid bifurcation and terminated close to this. Collateral flow was seen through the posterior communicating artery, which had a persistent fetal appearance and was surrounded by several small vessels likely to have arisen through vascular proliferation. Formal angiography confirmed occlusion of the origin of the left middle cerebral artery, with distal perfusion provided by development of local collateral vessels, flow from the posterior circulation via the posterior communicating artery, and collateral vessels arising from the ophthalmic artery.

These abnormalities were thought to represent moyamoya abnormalities of the intracranial vessels, which may arise as primary moyamoya disease or secondary to other disorders, as the moyamoya syndrome. The patient recovered neurologically, and was transferred to another centre for investigation and treatment of this condition.

Discussion
We report the case of a woman who presented to hospital with presumed traumatic brain injury after a motor vehicle accident. However, after identification of suspicious features, the intracranial haematoma was found likely to be related to another underlying disorder. Similar cases have been described previously, where intracranial abnormalities have produced or preceded trauma, and changes have been attributed to injury rather than to a primary neurological event.1

ABSTRACT
A middle-aged woman was admitted to hospital after a motor vehicle accident. A large acute intracranial haematoma was initially thought to be traumatic in origin, but its unusual position and the lack of external features of head trauma prompted investigation for other causes of intracerebral haemorrhage. Moyamoya intracranial vascular abnormalities were diagnosed. We discuss the presentation of non-traumatic intracranial haemorrhage in the setting of presumed trauma, and the unusual conditions of moyamoya syndrome and moyamoya disease.
Moyamoya — the condition

In 1969, the descriptive term “moyamoya” was applied by Suzuki and Takaku to intracranial vascular abnormalities which had been described in Japan in 1957. Moyamoya is a Japanese term for “puff of smoke”, describing the angiographic appearance of vascular collateral networks which develop around stenoses. Moyamoya disease refers to the primary form of the condition; similar vascular abnormalities may occur secondarily to a number of disorders, leading to the moyamoya “syndrome” or “phenomenon” (Table 1).

Moyamoya abnormalities are rare, chronically progressive stenoses of the proximal cerebral arteries, associated with relative cerebral ischaemia, along with proliferation of adjacent small vessels and development of a compensatory collateral circulation. These abnormalities may be unilateral or bilateral. Unilateral disease frequently progresses in children to involve contralateral vessels, but this has been observed less often in adults.

Moyamoya disease can present in both children and adults, with two peaks in age distribution: under 10 years and 30–40 years. The childhood form is more common and more usually involves ischaemic events, while intracranial haemorrhage is more common in adults. Moyamoya disease is more common in females, with an incidence 1.8 times that seen in males. Although the disease has been reported worldwide, it is most common among Japanese people.

The aetiology of primary moyamoya disease is unknown, but the high incidence in Japanese patients, along with familial clustering of cases in around 10%, strongly suggests a genetic basis. Familial cases are also more common in Japanese populations than in others, and have been linked to specific chromosomal abnormalities on chromosomes 3, 6 and 17. Increased risk of the moyamoya syndrome has been seen in patients with Down syndrome, Turner syndrome and some congenital cardiac abnormalities.

At autopsy, cause of death in most cases of moyamoya disease is intracerebral haemorrhage, often accompanied by tissue evidence of previous stroke. Haemorrhages are most common in frontal and periventricular areas, with frequent intraventricular haemorrhage. Vascular abnormalities usually involve chronic progressive stenoses of the proximal cerebral arteries, with development of small collateral vessels and persistence of developmental cerebral vessels providing collateral flow to compromised areas.

Stenotic lesions show intimal thickening with multiple elastic and fibrocellular layers, along with development of mural thrombi — changes potentially due to abnormal smooth muscle proliferation and activation. Collateral vessels may be either thin-walled and dilated or, like the primary vascular lesions, thickened and stenotic.

The anterior cerebral circulation is more commonly affected than the posterior, with stenotic lesions of the distal internal carotid artery and proximal anterior and middle cerebral arteries. The posterior circulation is involved in around 30% of cases. Proliferation and aneurysmal dilatation of collateral vessels are almost universal, and there have been a number of reports of an association with development of intracranial aneurysms. These lesions may cause subarachnoid or intraparenchymal haemorrhage on rupture. Intracranial aneurysms are most commonly found associated with stenoses in the anterior cerebral circulation, particularly...
in the anterior cerebral arteries and communicating vessels, but may occur in the posterior circulation and basilar tip in those with bilateral moyamoya.28

Altered concentrations or activity of endogenous angiogenic factors have been described in people with moyamoya abnormalities, including increased vascular tissue and cerebrospinal fluid concentrations of agents promoting neovascularisation, such as fibroblast growth factor29,30 and tissue growth factor (TGF-β).31 Amplified responses of vascular tissues to these factors has also been observed,32 with increased production of elastin and extracellular matrix by smooth muscle cells in response to stimuli potentially leading to intimal thickening and stenoses. It is not known whether these observations represent the cause of the disordered vasculature or an angiogenic response, producing collateral flow past stenoses. Abnormalities of extracranial vessels may also exist, most commonly manifested as renal artery stenoses (5%–6% of patients33), but also potentially involving the extracranial carotid arteries, coronary vessels and pulmonary vasculature. Pathological changes in these extracranial vessels are similar to those in intracranial arteries, with fibrous intimal thickening.33

**Presentation**

Patients most commonly present with cerebral ischaemic or haemorrhagic events. In children, this is most commonly transient ischaemia or stroke,34 and in adults, intracranial haemorrhage, although some adults present with seizure disorders, progressive neurological abnormality or headache. The natural history of the disease is inevitable progression of vascular stenoses and development and dilatation of collateral vessels and aneurysms, increasing the risk of ischaemic and haemorrhagic stroke over time.28 Rate of progression of primary moyamoya disease may be slower in white populations than in Asians.13

Illustrating the predominant ischaemic presentation in children, Scott et al described presenting features in 143 paediatric patients: stroke (68%), transient ischaemic events (43%), seizures (6%), headache (6%), abnormal movements (4%), incidental finding (4%), and intracerebral or intraventricular haemorrhage (3%).6

Although moyamoya deformities are relatively rare, they form part of the differential diagnosis of ischaemic or haemorrhagic stroke in children and young adults, being associated with 6% of cases.15 In young patients with stroke, a number of aetiologies are possible and should be investigated, with particular consideration given to possible anatomic abnormality, trauma or vascular dissection, hypercoagulable states and vasculitides.

Up to 90% of patients diagnosed in adulthood present with intracranial haemorrhage,35 caused by the failure of dilated thin-walled collateral vessels or rupture of associated intracranial aneurysms, commonly around the age of 40 years. Intracranial aneurysms are found in 14% of adult patients with
moyamoya and are of three forms:24 berry aneurysms (60%), aneurysmal dilatation of collateral vessels (40%), and dissection of intracranial vessels (rare).36 In one case series, 56% of aneurysms were found in the anterior cerebral circulation, 27% in the posterior circulation, and 18% around the basal ganglia associated with smaller vessels.35

Diagnosis
The diagnosis of moyamoya has traditionally been via invasive cerebral angiography, demonstrating stenosis or occlusion at the terminal portion of the internal carotid artery or proximal anterior or middle cerebral arteries, along with abnormally prolific adjacent vascular networks and collateral circulation. These abnormalities may also be apparent on CT angiography and magnetic resonance (MR) angiography, which are sensitive4,37-39 and less invasive alternatives to angiography in suspected cases of moyamoya and relatives of patients. After diagnosis by MR angiography, invasive angiography is still required in planning surgical treatment.

Management
Treatment is initially directed at the presenting cerebral ischaemia or haemorrhage and then at preventing subsequent ischaemia or haemorrhage. Medical therapies have been largely disappointing, failing to reverse the underlying disorder. If intracerebral haemorrhage has occurred, then management of hypertension (if present) is imperative, and surgical intervention and intensive care admission to control intracranial hypertension may be necessary.

In ischaemic stroke, anticoagulation or antiplatelet agents may be considered to prevent further stroke, especially where vascular stenoses are found, as these may predispose to extension of ischaemic areas. The decision to systemically anticoagulate patients or to administer antiplatelet agents depends on the balance of relative risk and benefit to the patient. This may be guided by the severity or partial versus complete nature of the stroke, angiography findings, and the judgement of clinicians experienced in stroke management. Particularly given the usually young age of these patients, consultation with an experienced neurologist may help guide appropriate therapy.

The only other medical therapy thought to have a potential role in ongoing treatment is the administration of vasodilators, particularly calcium channel blockers. In small series and case reports, long-term therapy has reduced the incidence of refractory headache, seizures and transient ischaemia in children,5,40 and has also had an effect in some patients with persistent symptoms after surgical revascularisation.41

Surgical intervention may be necessary to evacuate acute intracranial haemorrhage and secure intracranial aneurysms, with re-bleeding occurring in 40%-60% of untreated cases.42-44 Risk of re-bleeding increases with age and hypertension. Initial haemorrhage carries a mortality risk of 10%-20%, while recurrent haemorrhage significantly increases risk of death and markedly reduces the likelihood of good functional recovery.44 Aneurysm surgery in patients with moyamoya is technically difficult because of abnormal vascular anatomy, the high frequency of posterior circulation aneurysms, presence of existing ischaemic injuries and scarring which impede dissection and retraction, and the poor tolerance of brain tissue to retraction and manipulation given its already tenuous perfusion. Intravascular treatment of aneurysms by coiling is an alternative, especially for aneurysms in the posterior cerebral circulation, with successful outcomes seen in the short term.45-47 Long-term follow-up of treated patients is still required to confirm these benefits.

Apart from acute management of intracranial haemorrhage, surgical intervention in moyamoya aims to restore cerebral perfusion in areas affected by vascular stenoses, reducing the risk of ischaemic stroke, in the absence of proven medical therapies. Surgery largely utilises diversion of extracranial to intracranial arterial flow in the hope of developing collateral perfusion. Procedures can be divided into those involving direct extracranial to intracranial anastomoses, indirect revascularisation, or a combination of the two (Table 2). Slowed dilatation of collateral vessels and aneurysms may also reduce the risk of haemorrhagic stroke, although this has not been conclusively shown. Surgery is indicated for those with recurrent or progressive ischaemic symptoms, or reduced cerebral perfusion reserve. This may be quantified by inducing transient hypocapnia through administration of acetazolamide, and observing clinical changes or alteration in cerebral perfusion studies.4,48 Reduced perfusion reserve may lead to cerebral ischaemia with minimal stimulation, producing symptoms in children with hyperventilation or anxiety, and has been correlated with risk of stroke.49 Patients who present for treatment while symptoms are evolving have a better prognosis than those who present with static symptoms indicating com-

### Table 1. Conditions associated with moyamoya vascular abnormalities

- Idiopathic (moyamoya disease) (44%-9)
- Neurofibromatosis type I (10%-9)
- Chromosomal abnormality (Down syndrome, Turner syndrome)
- Congenital cardiac defects
- Cranial radiotherapy
- Infectious vasculopathy (tuberculous meningitis, some viral and bacterial infections)
- Fibromuscular dysplasia/renal artery stenosis
- Severe vasospasm after subarachnoid haemorrhage
- Hyperthyroidism
- Atherosclerosis
- Cocaine abuse
- Spontaneous middle cerebral artery occlusion9

Critical Care and Resuscitation • Volume 8 Number 2 • June 2006
Table 2. Surgical revascularisation procedures to treat moyamoya abnormalities

Direct external to internal carotid anastomoses
- Superficial temporal artery (STA) to middle cerebral artery bypass

Indirect external to internal carotid anastomoses
- Encephaloduroarteriosynangiosis (EDAS): STA sutured to open dura via burrhole
- Encephalomyosynangiosis (EMS): temporalis muscle flap applied to brain surface
- Dural splitting, placing external surface on brain surface
- Pial synangiosis: various branches of external carotid artery directed through craniotomy onto brain surface with arachnoid opened

Combined direct and indirect anastomoses

Other procedures
- Cervical sympathectomy
- Placement of free omental grafts

Prognosis in moyamoya depends on the progression of disease, development of collateral circulation, and severity of the disease at presentation.5,57 Severity of neurological damage at presentation seems to be the strongest predictor of poor outcome, judged either clinically6,57 or on MRI or CT scanning.58 While lesions are known to progress frequently in patients diagnosed during childhood, progression of moyamoya lesions diagnosed in adults has previously been considered rare and described only in case reports.59-65 Increasing use of CT and MR angiography has revealed a higher incidence of adult moyamoya than previously believed, and more frequent progression. Kuroda et al described the course in 120 adult patients diagnosed with moyamoya abnormalities, with progression of lesions seen at follow-up in a quarter of those who survived initial haemorrhage (more marked in females than males).66

Conclusion
The reported case illustrates the need for an “open mind” in assessment of patients — the ultimate diagnosis may not obviously relate to the presentation. Our patient was assessed and managed as if intracranial haemorrhage were purely traumatic, but further investigation led to the diagnosis of a rare condition. In her case, this may prevent further episodes associated with neurological damage.

References
CASE REPORTS


53 Imazumi T, Hayashi K, Saito K, Osawa M, Fukuyama Y. Long-term...

Corrections
Re: “Book review: Clinical anaesthesiology”, by A Gardner in the March 2006 issue of the Journal (Crit Care Resusc 2006; 8: 77) Dr Gardner’s affiliation is incorrectly given as Royal Perth Hospital. He is in fact a consultant anaesthetist at Sir Charles Gairdner Hospital, Perth.
Re: “Unexplained anaemia after massive transfusion for haematemesis”, by D Law and M Lennon in the March 2006 issue of the Journal (Crit Care Resusc 2006; 8: 52-55) Dr Lennon’s affiliation is Sir Charles Gairdner Hospital, Perth. His surname is misspelt on the contents page.