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Grand Rounds—Hammersmith Hospital

Adult moyamoya disease

An unusual cause of stroke

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Moyamoya disease is a cerebrovascular disease of unknown aetiology chiefly reported in the Japanese.[1] It was first described in 1963 and most cases occur in children. Increasing numbers of cases are now being reported in non-Japanese adults, and it is an unusual but important cause of stroke.[2-4] Moyamoya disease commonly manifests with signs and symptoms of cerebral ischaemia or infarction in children, but adults tend to present with intracerebral haemorrhage.[1,5] We report a case of moyamoya in an Indian woman who presented atypically with transient attacks of right sided carpopedal spasm. Subsequently she had a cerebral infarct in the left middle cerebral artery territory—a rare complication of this disease.

Case history

A 43 year old Indian woman presented to the neurological outpatient clinic at Ealing Hospital in February 1992 with a two month history of paroxysmal carpopedal spasm affecting her right hand. The attacks lasted less than five minutes and were sometimes associated with perioral and right hand numbness. Between attacks she had no neurological symptoms. Her symptoms could be induced by hyperventilation and were made worse by hot weather.

Nine days later she developed a severe left sided headache, photophobia, and speech disturbance. She had a severe receptive dysphasia with fluent speech, neologisms, and paraphasic errors. Her right arm had normal power but was severely dyspraxic. She had right visual and somatosensory inattention, dysgraphia, and dyslexia. Funduscopy and cardiovascular examinations gave normal results. Contrast enhanced computed tomography at admission to hospital and seven days later showed a large left temporoparietal infarct in the middle cerebral artery territory. Doppler ultrasonography of the carotids showed dampening of flow in the left internal carotid artery. Echocardiography showed no embolic source. Baseline blood tests, electrocardiography, and chest radiography all gave normal results. A standard screen for young stroke patients including tests for thrombophilia, autoantibodies, and circulating lupus anticoagulant gave negative results.

She partially recovered after speech and occupational therapy and was discharged home 12 days later, having been prescribed 300 mg of soluble aspirin a day. The next day she experienced a transient attack of parasthaesiae and weakness in the right arm and leg. These attacks continued every day. During the attacks she became more dysphasic and afterwards was tired. She did not lose consciousness or have convulsions during the attacks, which could be induced by hyperventilation.

On readmission her neurological status was unchanged except that her right plantar response was now extensor. An electroencephalogram showed increased slow wave activity over the left hemisphere, consistent with the presence of a left sided infarct. Hyperventilation greatly increased the slow wave amplitude, with development of dysphasia and right hemisensory disturbance. Magnetic resonance imaging confirmed the extensive left sided infarct in the middle cerebral artery territory (fig 1), and small foci of high signals were also seen in the left frontal and right peritrigonal areas. High signal lesions were shown on both the T_1 and T_2 weighted images, indicating a combination of haemorrhage and oedema. Non-selective intra-arterial digital subtraction angiography of the extracranial vessels showed a tapering stenosis of the left internal carotid artery with occlusion of the left middle cerebral artery. The appearances were thought to be consistent with a dissection of the left internal carotid artery.

She was given anticoagulating drugs and initially her ischaemic episodes became less frequent. She was discharged with a diagnosis of left frontoparietal infarction due to spontaneous dissection of the left internal carotid artery. However, despite adequate anticoagulation she reported continuing bilateral attacks of carpopedal spasm and numbness at review.

Repeat magnetic resonance imaging showed a more extensive high signal lesion in the left temporal,

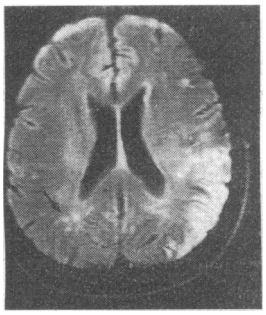

FIG 1—*Magnetic resonance image (T_2 weighted spin-echo sequence) showing extensive high signal areas in left temporal, parietal, and occipital areas. Small high signal foci are present in right peritrigonal region (arrow)*

parietal, and occipital areas with diseased deep white matter. Digital subtraction angiography confirmed diffuse narrowing of the left internal carotid artery with occlusion of the anterior and middle cerebral arteries. Extensive moyamoya vessels were present at the base of the brain and transdural collaterals were seen arising from the occipital branch of the left external carotid artery (fig 2). Although vertebral angiography was not done, the results of magnetic resonance imaging and presence of unusual transdural collateral circulation suggest that the posterior circulation was probably affected. Right carotid digital subtraction angiography showed mild narrowing of the internal carotid artery, occlusion of the middle cerebral artery, and prominent moyamoya vessels (fig 3).

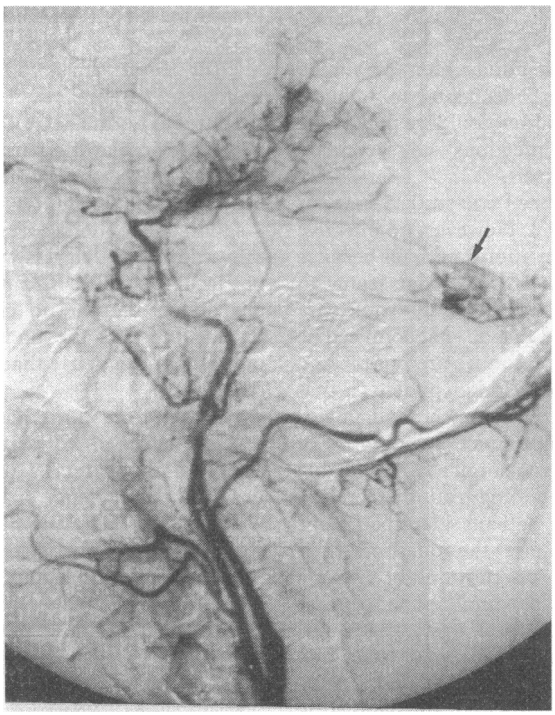

FIG 2—*Selective left carotid digital subtraction angiogram (lateral view) showing diffuse narrowing of internal carotid artery with occlusion of anterior and middle cerebral branches. A leash of moyamoya vessels are seen and transdural collaterals (arrow) arise from the occipital branch of the external carotid artery*

Because of her continuing ischaemic symptoms she had extracranial-intracranial artery bypass surgery. Three months later she reported greatly reduced symptoms.

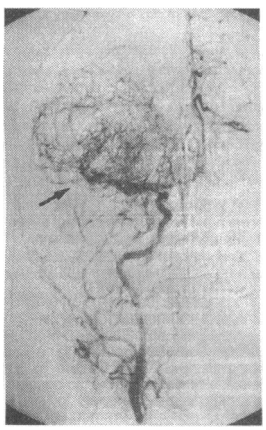

FIG 3—*Selective right carotid digital subtraction angiography (front view) showing middle cerebral arterial occlusion and extensive moyamoya vessels (arrow)*

Comment

Moyamoya disease causes occlusion of the terminal branches of the internal carotid artery and development of a leash of collateral vessels in the base of brain resembling a puff of smoke.[1] This case shows several unusual features of moyamoya disease. Our patient was an adult and was not Japanese. She presented with right sided carpopedal spasms, which were induced by hyperventilation and overheating. This has been reported in children but not in adults with moyamoya disease. Other unusual features in this patient were cerebral infarction rather than primary haemorrhage, abnormal focal slow wave activity on electroencephalography exacerbated by hyperventilation (as were symptoms), dissection of the left internal carotid artery, and moyamoya vessels affecting the posterior cerebral circulation.

Moyamoya disease is most common in childhood with a female to male ratio of 1·5:1. Children may present with alternating hemiparesis, involuntary movements of the limbs, or mental impairment, whereas adults usually present with intracranial haemorrhage.[1]

Moyamoya disease is characterised by vascular stenosis and luminal dilatation of the brain parenchyma.[6] The underlying cause is unknown and there seems to be no relation to risk factors such as hypertension, diabetes, or hyperlipidaemia; there is no evidence of arteritis. Patients have enhanced angiogenesis and the concentration of basic fibroblast growth factor, a potent angiogenic factor, is increased in tissues.[7]

A genetic basis for the disease has been proposed. In Japan, Kitahara *et al* estimated a familial occurrence of 7% in moyamoya disease.[8] Moyamoya disease has been described in identical twins and also complicates several disorders with a genetic origin such as neurofibromatosis, tuberous sclerosis, Down's syndrome, Fanconi's anaemia, and Alagille's syndrome.[9]

Bacterial infections have also been associated with moyamoya disease. Suzuki and Kodama showed that in dogs, injection of foreign protein in the region of the internal carotid bifurcation produces pathological changes similar to those seen in moyamoya disease.[1] They speculated that inflammation of the extensive sympathetic innervation of the internal carotid arteries may be responsible for these localised changes and noted clinical improvement with perivascular sympathectomy in some patients. Pharyngitis or basal meningitis in childhood can lead to cervical sympathetic inflammation with secondary carotid stenosis and moyamoya vessel formation.[1] Several cases of moyamoya disease have been described in association with basal meningitides due to tuberculosis, leptospirosis, and other pyogenic organisms.[1]

In the non-Japanese population adult moyamoya disease is extremely rare. Only around 36 cases of cerebral infarction due to moyamoya disease have been described in non-Japanese adults. The box gives the various presenting features.

Our patient presented with paroxysmal attacks of carpopedal spasms affecting her right hand, occasionally associated with bilateral sensory symptoms. The spasms and sensory symptoms could be induced by hyperventilation and exposure to heat. Infarctions in moyamoya disease tend to occur in the watershed regions between anterior, middle, and posterior cerebral arteries.[5] Hyperventilation induced hypocapnia causes cerebral vasoconstriction and the resultant "low flow" in watershed or distal vascular territories may lead to ischaemic symptoms in vascular territories where the circulatory reserve is already compromised.[10,11] In our patient, precipitation of symptoms by hyperventilation or heat could thus represent critical perfusion in an area near her infarction.

Presenting features of adult moyamoya disease

Motor transient ischaemic attack
Hemiparesis or monoparesis
Dysphasia
Hemianopia
Visual and sensory inattention
Headache
Paraparesis
Dyspraxia

Rarely reported:

Personality change
Epilepsy
Paraesthesiae
Chorea
Scintillating scotoma
Balint's syndrome

The diagnosis of moyamoya disease is based on intracerebral angiography. Computed tomography may be useful, showing multiple, often bilateral, areas of infarction with a predilection for watershed zones. Treatment remains unsatisfactory as the pathophysiology is still not clearly understood. Vasodilators, steroids, anticoagulants, and antibiotics are all ineffective. In our patient ischaemic symptoms continued despite satisfactory anticoagulation.

Surgical treatment has concentrated on procedures aimed at revascularising the ischaemic areas. These include synangiosis, where a muscle flap with its own established network of vessels is applied to the dural surface, and extracranial-intracranial bypass operations, where isolated vessels are used.

Discussion

JS: I have seen strokes in adults after presumed tonsillitis and carotid stenosis occurring in infancy, and it strikes me that the disorder could be partly due to oropharyngeal or tonsillar infections with secondary carotid inflammation and stenosis.

DJB: Certainly there have been two studies suggesting a role for bacterial infection. However, no infective aetiology has been identified in adults, perhaps because the condition is much rarer. This disorder seems to have a strong environmental component, being very much a Japanese disorder, and that is what confused us in this woman. I suspect the reason we are not picking up moyamoya disease in white or Indian patients is that few young people with strokes have cerebral angiography. Most have a digital subtraction angiography of the carotids to check if there is a surgically remediable lesion. An American group doing routine cerebral angiography in young stroke patients identified eight cases of moyamoya.[5] I suppose the question then arises, so what if you pick up moyamoya disease? There is a lot of strong anecdotal evidence that superficial temporal-middle cerebral artery anastomosis greatly reduces the frequency of transient ischaemic attacks. But these reports are retrospective and uncontrolled. The prognosis of untreated moyamoya is difficult to ascertain. There are few follow up studies and the suspicion is that untreated the condition may "burn out."

JS: At what stage is the cerebral vasculature plastic enough to proliferate extensively as seen in this disorder? It is something that happens early in life or can it happen in adulthood?

DJB: We just do not know. This woman in her early 40s may have had the disorder for decades.

JS: One hypothesis is that this condition relates to peritonsillar lymphadenitis and secondary cervical inflammation leading to carotid stenosis. At an early age such stenosis could lead to new vessels forming in the brain. It seems that this is what is seen.

DJB: What is clear is that if you get a stenosis or occlusion due to other causes later in life you do not get this sort of collateral circulation developing. However, in animal models you can induce new vessel formation by injecting foreign albumin or bacteria such as *Streptococcus sanguis* into carotid vessels.[12] So I think your hypothesis is a reasonable one. This may be a neonatal or congenital phenomenon.

AR: I do not get a clear picture of what moyamoya disease is. What is the natural course of these collaterals?

JS: The established feature is very abnormal blood vessels, and the essential part of the disorder is the carotid stenosis.

DJB: Medial atrophy is seen in both dilated and stenosed vessels. The degree of intimal thickening determines stenosis or dilatation.

PROGNOSIS

AR: What happens to the dilated vessels with time?

DJB: In patients who are serially followed they tend to disappear. As the middle meningeal and ophthalmic artery collaterals develop the blood is channelled through those and the internal anastomosis tends to resolve. In some patients who have had serial angiography these collaterals have completely disappeared.

JS: That is what happens after surgery presumably?

DJB: After anastomosis there is a generalised increase in cerebral circulation which over a year tends to return to normal level.

KRC: Most of the patients that have been followed up have had bypass surgery. So the natural course is little known in adults.

CDP: I wondered if an alternative aetiology for moyamoya was that this was perhaps a childhood form of vasculitis such as Kawasaki's disease that preferentially affects the carotid circulation. By the time the disease presents the underlying vasculitis has burnt out. Is there evidence that steroids have worked in this condition?

KRC: Steroids have been tried in Japanese patients without success. Ultrastructural studies in cerebral arteries and collateral vessels in moyamoya disease do not show any evidence of arteritis.

RE: I appreciate the reluctance of doctors to refer stroke patients for selective cerebral angiography. However, recently a paper from Japan showed magnetic resonance angiography to be an effective method in investigating these patients. This is non-invasive and may replace angiography in future.

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