Primary orthostatic cerebral ischaemia

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SUMMARY Four patients with “primary orthostatic cerebral ischaemia” are described. They complained of dizziness, light-headedness or syncope on standing. None had a significant fall in his systemic blood pressure on assuming the erect posture. Each had bruits over the major neck vessels or absent pulses. Angiography showed widespread narrowing or occlusion of the cervical blood vessels which supply the brain. Carotid endarterectomy relieved the patients’ symptoms and also reduced the fall in retinal artery pressures on standing noted preoperatively. The clinician who is not aware of the poorly documented syndrome of “primary orthostatic cerebral ischaemia” may fail to recognise that a patient’s complaints are due to cerebrovascular disease for they are strikingly different from those of classical transient ischaemic attacks.

Patients who complain of faintness and dizziness on standing are probably suffering from postural hypotension. We report four patients who were seriously inconvenienced by such symptoms but whose complaints could not be explained by a fall in their blood pressure on standing. In fact their disability remained unexplained until they developed the typical focal neurological symptoms of transient cerebral ischaemia. We wish to draw attention to the fact that episodes of cerebral ischaemia may be provoked by changes in posture and may give rise to generalised rather than focal complaints. We believe such attacks indicate that changes in blood flow alone, without emboli, may be the basis for episodes of transient cerebral ishaemia. The recognition of distinct mechanisms for transient ischaemic attacks—cholesterol emboli, platelet emboli and variations in blood flow without emboli—could perhaps lead to more specific and effective treatment. We report four patients with transient ischaemic symptoms due, we believe, to variations in blood flow.

Case reports

Case 1 (AH 446053)
This 57-year-old woman had been diabetic for 25 years and a mild sensory neuropathy had been noted for some months. She had taken thyroxine for hypothyroidism for many years. Her husband reported that for about three weeks before admission she was unable to walk properly; after walking a few yards she would start to drag the right leg, complain of unsteadiness and have to sit down. There was no pain or sensory complaint. The patient had become progressively less intellectually alert over many months but her husband believed that her vagueness was made worse when she adopted a standing position. The patient herself was a less informative historian commenting only that her legs tended to give way. The blood pressure was 170/95 mm Hg with the patient supine and 130/70 mm Hg standing, in both arms. The fundi showed “blot” haemorrhages, microaneurysms and exudates typical of diabetic retinopathy. A soft ejection systolic murmur was heard at the base of the heart. Separate loud systolic bruits were audible over both carotid and both subclavian arteries in the neck. Bruits were heard over both femoral arteries; no pulses below the femoral could be palpated in either leg.

Mental status examination revealed mild dementia. Cranial nerve examination, power, co-ordination and reflexes were normal. Some impairment of vibration and joint position sense was noted in both feet. Gait was unusual, with a tendency to give way at the knees, to fall to the left and at times for the right foot to drag. Examination of mental status during walking was difficult because the patient refused to answer questions while on her feet. Ophthalmodynamometry was not performed in the presence of diabetic retinopathy. Full blood examination, electrocardiograph and serum biochemistry were normal (except for elevated blood glucose). A chest radiograph was normal, while skull radiographs showed some calcification in the internal carotid arteries. Angiography (fig 1) revealed complete occlusion of the right internal carotid at its origin, some stenosis at the origin of the left common carotid, very marked stenosis of the left internal carotid just beyond its origin and some stenosis of the left external carotid artery.
The right vertebral artery was narrowed at its origin. The left subclavian artery contained a plaque proximal to the origin of the left vertebral which was a small vessel and also showed a segment of narrowing. Therefore of the four neck vessels which supply the brain, only three remained patent and each of these was markedly stenosed.

Left carotid endarterectomy was performed. At operation left carotid stump pressure was 48 mm Hg systolic while systolic blood pressure was 170 mm Hg. Routine dissection of the stenosing plaque was performed without complication. When seen two months later the patient and her relatives were delighted by her improvement. She was walking more easily and for longer distances. Her relatives felt that her mental state and concentration had markedly improved. Examination revealed postural hypotension as before. Her gait was now only slightly unsteady, with no tendency to collapse at the knees. Her conversation was more lucid but tests of mental arithmetic were still performed poorly.

Case 2 (AH 470169)
This 79-year-old woman had been treated for hypertension for more than 40 years. Four weeks before admission she complained of some episodes of dizziness, general malaise and blurred vision while erect (but never while sitting or supine). Her blood pressure was 250/120 mm Hg, and her hypotensive medication was adjusted. Her blood pressure remained at around 180/90 mm Hg thereafter. However three weeks before admission the patient began to complain of attacks of dizziness and malaise lasting for five minutes and accompanied by numbness and weakness of the left side of the face and limbs. All the attacks occurred soon after the patient stood up and forced her to sit again. She experienced such episodes about three times daily although more frequently an attempt to rise was greeted with light-headedness. Examination revealed an alert old lady. Bruits were heard over both carotids and both subclavian arteries in the neck. Mental abilities were quite normal except for some difficulty with arithmetic. Neurological examination and gait were also normal although the patient took a moment to become steady on her feet. Ophthalmodynamometry showed pressure of 36/10 g (systolic/diastolic) in both eyes while the patient was lying and only 12/5 g (both eyes) while the patient was sitting. At the same time, blood pressure was 170/100 mm Hg in both arms with the patient supine, falling only to 160/90 mm Hg when the patient stood up. Arch aortography revealed marked narrowing at the commencement of both internal carotid arteries (fig 2) as well as stenosis at the origin of the left vertebral artery and some atheroma.
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near the origin of both subclavian arteries. Dynamic isotope brain scan showed reduced flow to the right cerebral hemisphere. Supra-orbital artery Doppler flow studies revealed no predominant direction of flow on the left but definitely abnormal flow on the right into the skull.

Bilateral carotid endarterectomy was performed. First the left carotid artery was exposed in the neck; while systemic blood pressure was 236 mm Hg (systolic) (155 mm Hg (mean)), stump pressure in the left carotid was 34 mm Hg (systolic) (29 mm Hg (mean)). Endarterectomy was performed without a shunt. The right carotid artery was then explored; while systemic blood pressure was 228 mm Hg (systolic) (147 mm Hg (mean)), stump pressure was 84 mm Hg (systolic) (68 mm Hg (mean)). Again endarterectomy was performed without a shunt. Post-operatively the patient was markedly improved. She could stand and walk without any dizziness and when reviewed a month later had no recurrence of focal ischaemic episodes. Ophthalmodynamometry post-operatively showed diastolic pressures while the patient was seated of 35 g in the right eye and 20 g in the left, which were considerably higher than those measured pre-operatively.

Case 3 (AH 457907)
This 71-year-old retired male school teacher had been treated for hypertension and mild diabetes for several years. He presented because of two episodes, each resolving completely after 20 minutes, of blindness of the left eye. However, his family reported, and he agreed, that his intellectual function had been deteriorating over the past two or three years. For several months he had suffered from intermittent distressing episodes which occurred only when he was standing; during these he would feel "vague" and his legs would "go funny" so that he felt he must sit down. He had not collapsed during such an attack. Examination revealed a loquacious elderly man with marked corneal arcus. Blood pressure was 130/70 mm Hg lying and standing in both arms. The vascular system was extremely diseased; a soft systolic ejection murmur in the heart radiated to the right carotid and subclavian arteries but much

Fig 2  Angiogram (a) and line drawing (b) of case 2.
louder, more prolonged, separate bruits were audible over the left carotid and subclavian arteries. All of these vessels were easily palpable. Pulses could not be felt in the right popliteal fossa or below and bruits were audible over both femoral arteries. The right superficial temporal and occipital arteries were strikingly prominent, pulsatile and not tender. Neurological examination was quite normal. Skull and chest radiographs, full blood and bio-chemical examinations were normal. Electro-cardiogram showed first degree atrio-ventricular block and right bundle branch block. Arch aortogram (fig 3) revealed complete occlusion of the right internal carotid artery at its origin and failure of the left common carotid to fill higher than 10 cm from its origin; the left internal and external carotid filled, apparently retrogradely by collaterals, so that the left carotid bifurcation was patent while the common carotid just proximal to this region was not. Additionally there were stenoses at the origin of both vertebral arteries and a flat atheromatous plaque on the left subclavian artery.

The patient was commenced on Warfarin for his two attacks of amaurosis fugax. The cause of his attacks of vagueness and leg weakness was not defined. Some eight months later the patient returned for review. There had been no more attacks of transient blindness. However, his postural symptoms had become more troublesome; when standing (particularly after rising quickly) he frequently became unstable and had to sit. On a few occasions he had actually collapsed to the floor, perhaps with momentary loss of consciousness. Examination was unchanged. Ophthalmodynamometry showed pressures of 42/24 g (systolic/diastolic) in the right eye and 30/12 g in the left eye while lying which fell to 24/18 g and 18/8 g respectively when the patient stood up. The systemic blood pressure was 130/70 mm Hg without a postural change.

Because of the increasing postural symptoms it was agreed that surgery should be reconsidered. Aortic arch angiogram was unchanged. A selective injection into the left common carotid stump revealed that the vessel was in fact patent at a point just below the bifurcation (fig 4). Doppler studies of supraorbital vessels revealed reverse flow in the right orbit (with prominent flow into the orbit from the face) and equivocal results on the left.

It was felt that surgery on the right carotid system was not feasible but that left common carotid endarterectomy might be possible and could lead to improved cerebral perfusion. At operation, endarterectomy of common, internal
and external carotid arteries in the region of the bifurcation was performed. Stump pressure was 68 mm Hg (systolic) and 51 mm Hg (mean) while systemic blood pressure was 150 mm Hg systolic. Postoperatively the patient's course was complicated. He awoke alert but with mild left arm weakness and remained stable for the next three days. He then became less mentally alert and his left arm became weaker. The next day focal fitting involving the right arm and leg occurred and was controlled with anti-convulsants. Treatment with heparin was commenced. Two days later he gradually became less alert and passed into coma. His only response was some facial grimacing on painful stimulation. He was generally hypertonic with bilateral Babinski signs. His blood pressure was 140/80 mm Hg but his temperature was 38°C. Cultures of blood and urine were negative. Cerebrospinal fluid analysis was normal. Computed tomography of the brain showed no abnormality. Isotope brain scan showed no flow of isotope up the right internal carotid artery while the left internal carotid artery flow appeared quite normal. Static scans were normal. The patient's dramatic decline was therefore not readily explained. Antibiotics and dexamethasone were given. After being comatose and apparently moribund for three days the patient improved over a day or two in an equally inexplicable fashion. He was as alert as before the operation and had no focal neurological signs. When reviewed two months postoperatively he was alert and declared the operation a "great success" as his postural symptoms had now completely disappeared. Ophthalmodynamometry now showed remarkable improvement with systolic pressure of 125 g (supine) and 115 g (standing) recorded in both eyes by the indirect method.

**Case 4 (AH 474729)**

A 58-year-old man had a 16 year history of insulin dependent diabetes and a six month history of hypertension. He had a nine month history of frequent episodes during which his "legs went to jelly", his vision became blurred, he complained of "dizziness" and he became mentally dulled. He described these attacks as a "semi-blackout", but could recall falling to the ground only twice. On the other occasions the attacks settled, usually within two or three minutes, when he lay down or put his head down. The attacks were almost invariably caused by standing up from a chair, although a rare episode occurred while he was seated in front of the television after a heavy meal. On two occasions he actually fainted while standing and remained unconscious for about 5 minutes. After the second such episode he was noted to have an ataxic gait and slurred speech and complained of pins and needles in both feet. These findings, which persisted for two hours, led to his referral for investigation of his cerebro-vascular status. The patient was confident that these attacks differed from the occasional hypoglycaemic attacks he had suffered over the years. He could not recall any attacks related to using his right arm. Examination showed a weak delayed fight radial pulse. Blood pressures were measured with the patient supine as 100/85 mm Hg in the right arm and 140/85 mm Hg in the left arm and did not change when the patient sat or stood. Bruits were audible over both carotid arteries and the right subclavian and both femoral arteries. Apart from a moderate degree of ataxia present bilaterally, neurological examination was normal. Routine blood tests were normal. Subraorbital artery flow studies using Doppler technique showed flow from the forehead into the orbit on the left (the reverse of the normal pattern) but normal direction of flow on the right. Arch aortography (fig 5) showed very severe stenosis of the left internal carotid artery, marked atheroma at the bifurcation of the right common carotid artery with moderate stenosis at the origin of the right internal carotid artery. In addition the right subclavian artery was almost completely occluded over its proximal 3 cm and late filling from above the right vertebral artery (which arose distal to the stenosis) was demonstrated. The left vertebral artery was a large calibre vessel which showed some kinking by a vertebral osteophyte; this varied in severity but in some films appeared quite marked.

The left carotid artery was explored and severe stenosis confirmed. Systolic stump pressure was 80 mm Hg while the systemic systolic blood pressure was 190 mm Hg. Routine internal carotid endarterectomy was completed.
without mishap. The patient returned home and over the next six months found that the attacks of postural faintness were rather less frequent but were certainly not completely abolished. They were similar in nature to those before his operation. He now admitted to some impairment in memory and concentration, which he felt was not altered by the endarterectomy. He was seen during an attack at this stage. He became vague shortly after standing and was unable to answer sensibly. He clumsily leaned back onto his bed and after two minutes lying semi recumbent was back to normal. Pulse rhythm, blood pressure and blood glucose were all normal during the attack. Brachial blood pressures were similar to those during his earlier admission and again did not alter when he stood. Vascular and neurological examinations were also unchanged. Ophthalmodynamometry by the indirect method yielded systolic pressures in the left eye of 125 g falling to 110 g and in the right eye of 100 g falling to 35 g with the patient lying and sitting respectively; he could not stand long enough to be examined.

Angiography showed that the left internal carotid was patent although the lumen diameter was only 50% of normal. This was a considerable improvement on the initial situation. Otherwise there had been no change from the previous study.

Six months after the left carotid endarterectomy the right carotid artery was explored. A moderate stenosis was found. Systolic stump pressure was 96 mm Hg while systemic blood pressure was 204 mm Hg (systolic). A routine endarterectomy was performed. Postoperatively the patient was markedly improved. He was able to walk about and even stand up suddenly without faintness. Ophthalmodynamometry confirmed an improved right retinal artery pressure; systolic pressures measured indirectly were 125 g, 105 g, and 90 g in the right eye with the patient supine, sitting and standing respectively. Pressures in the left eye were unchanged. The patient was reviewed two months after right carotid endarterectomy and no longer experienced any symptoms on standing.
**Discussion**

We have become accustomed to thinking of transient ischaemic attacks as occurring in the carotid and vertebrobasilar territories. The four patients reported here were referred only when they developed focal neurological symptoms attributable to one or other of these vascular territories. Yet, at the time the focal attacks commenced, the patients were already suffering from a condition which warranted treatment in its own right. In each case, it passed unrecognised. We therefore wish to draw attention to the syndrome of “primary orthostatic cerebral ischaemia”.

Each patient's symptoms occurred shortly after standing. They were characteristically and frustratingly vague, but this vagueness is a part of the syndrome. In two instances the relatives noticed that the patients were less coherent when standing. We found that one patient refused to answer questions whilst on her feet. The behavioural changes, and the associated symptoms, were, we believe, due to a drop in cerebral blood flow on standing that was severe enough to impair performance. The other complaints were reminiscent of syncope; a sensation of dizziness and unsteadiness, a feeling of faintness and a compulsion to sit down. In addition, some patients also developed numbness or weakness in their limbs. Walking rapidly became difficult, or even impossible, but the patients recovered almost immediately on sitting.

Physical examination suggested the presence of widespread arterial disease. There were invariably bruits over the carotid arteries and, sometimes, over the femoral arteries as well. Most of the remaining lower limb pulses were impalpable. One patient had a diabetic retinopathy and in another, prominent branches of the external carotid artery coursed over the face and scalp to bypass an occluded internal carotid artery. All of the patients were hypertensive; three were diabetic.

Although the symptoms were reminiscent of a faint, we were unable to attribute them to a fall in the patient's blood pressure on standing. In only one instance was there an appreciable fall in the blood pressure and this remained even when the patient's symptoms were relieved. However ophthalmodynamometry suggested that the pressure in the cerebral circulation dropped markedly on standing. When the patients had lost their symptoms after arterial surgery the retinal artery pressures were higher at rest and fell less when the patient stood.

Cerebral angiography demonstrated the widespread arterial disease that had been suspected clinically and showed that it was haemodynamically disruptive. Every carotid artery was either occluded or very severely stenosed and atheromatous changes were also present in the vertebral and subclavian arteries. The severity of the carotid stenoses was confirmed by intraarterial pressure measurements during surgery.

We believe this syndrome differs significantly from the transient ischaemic attacks described in standard texts. Our patients' symptoms were constantly related to standing, which would be most unusual in orthodox transient ischaemic attacks. The faintness, unsteadiness and vagueness they experienced were more suggestive of syncope than the focal neurological disturbances typically seen in transient ischaemic attacks. The attacks were not only clinically distinct from orthodox transient ischaemic attacks but probably also resulted from a different mechanism and this has clear implications for their treatment. There is good reason to believe that the majority of transient ischaemic attacks are due to emboli. Conglomerations of platelets or fragments of cholesterol have been seen during attacks and demonstrated histologically. Alterations to the systemic circulation usually do not produce the characteristically focal symptoms of transient ischaemic attacks, so it seems reasonable to attribute them to a temporary disruption of a portion of the brain's circulation by emboli. It is this belief which provides the rationale for prescribing anticoagulants and antiplatelet drugs in the hope of preventing further transient ischaemic attacks and the strokes which they may precede.

The syndrome we are describing is, we suggest, due to an overall, though transient, reduction in cerebral bloodflow and does not result from emboli. Consequently anti-coagulants and anti-platelet drugs could not be expected to prevent such symptoms and, indeed, failed to do so in the third patient whose symptoms became more troublesome whilst he was treated with Warfarin for attacks of monocural blindness. Since the attacks are due to an abnormality in bloodflow they can only be abolished by surgery which improves the cerebral circulation. It is therefore no accident that the largest number of patients with this condition reported in the literature is to be found in a series of papers from the Mayo Clinic describing surgical ways of improving cerebral bloodflow. Almost a third of the 74 patients operated on had what the authors termed “primary orthostatic cerebral ischaemia”, (the remainder had orthodox transient ischaemic attacks). From their brief description it is clear this is the condition we are describing. The Mayo Clinic patients had “a major postural fall in their retinal artery pressures without a proportionate fall in peripheral blood pressure, and frequent episodes of fainting or deficits of cerebration or memory”. These patients...
They observed each one of four patients had patients between their infarct. (We encountered four examples in 18 months.) None of the published accounts adequately describe the condition.

Ford and his colleagues reported on their experiences of carotid endarterectomies on patients with dizziness, drop attacks and confusion. A member of his audience described a patient with severe bilateral carotid stenoses "who was bedridden; if he raised his head from the pillow he got dizzy and if he stood up he fainted." Caplan and Sergays fully described four patients of particular interest. All had severe occlusive cerebrovascular disease and each one developed posturally related symptoms without a marked fall in his systemic blood pressure. They observed these phenomena whilst their patients were in hospital recovering from a cerebral infarct. But there were two interesting differences between their patients and ours and these would suggest that the syndrome of "primary orthostatic cerebral ischaemia" may be more variable than we have described. First, Caplan and Sergays reported clear focal symptoms whereas our patients experienced rather vague and generalised ones. In two instances their complaints could be attributed to left hemisphere dysfunction and in the remaining two, to brain stem disturbance. Second, these posturally related symptoms subsided spontaneously in a week or two whereas our patients seemed to become increasingly disabled by their attacks.

We note that three of our four patients had diabetes mellitus. We do not, however, believe that diabetic autonomic neuropathy played a significant role in the patient's symptoms. Two of the diabetic patients did not experience any fall in their systemic blood pressures on standing. The blood pressure did drop in the third patient but this drop persisted after operation even though the symptoms were relieved. Evidently, the attacks were not dependent on posturally related falls in systemic blood pressure resulting from impaired autonomic control. Could the attacks have been due to an effect on the autonomic regulation of cerebral blood flow? We believe not though we lack the data to prove this assertion. The fall in retinal artery pressures we recorded, on standing, were so great that, it seemed to us, unnecessary to postulate an additional, autonomically induced failure or arteriolar dilation to account for the presumed drop in cerebral perfusion. The occurrence of similar symptoms in Takayasu's disease further supports our view for autonomic neuropathy is not a feature of this condition.

Patients with Takayasu's disease developed widespread arterial narrowings and occlusions. The angiographic abnormalities may be extensive as in the patients we have described, though the arterial lesions are due to an arteritis rather than atherosclerosis. In two series the majority of patients experienced posturally related dizziness or syncope. One patient had a major seizure whenever his head was elevated, presumably as a result of cerebral ischaemia.

Ross Russell has attributed the sensitivity to postural changes seen in patients with severe and widespread arterial narrowings to an exhaustion of the compensatory reserves of the cerebral circulation. Normally when one major extracranial vessel is occluded, the Circle of Willis and the other extracranial vessels will help maintain the cerebral circulation. But if these arteries are also diseased then cerebral blood flow can only be maintained by the dilatation of intracerebral resistance vessels. It is these vessels which normally dilate to compensate for a fall in cerebral perfusion pressure. Once they are maximally dilated the brain can no longer make further adjustments for any reduction in arterial pressure. It will become exquisitely sensitive to seemingly minor changes in cerebral arterial pressure. On standing, the pressure in the carotid arteries will inevitably be diminished by the 15 to 20 cm column of blood from the heart to the neck. In the presence of widespread cerebrovascular disease patients may actually require a rise in their brachial blood pressures on standing in order to maintain adequate cerebral perfusion and could well prove intolerant of even the mild postural hypotensive effects of drugs such as antidepressants and tranquilisers.

The remedy for such an unhappy situation is surgery, and its effectiveness is readily apparent. Carotid surgery in conventional transient ischaemic attacks is often performed in the hope of preventing a cerebral infarct which such transient ischaemic attacks may portend. Patients with orthostatic cerebral symptoms and severe cerebrovascular disease may also face a considerable risk of cerebral infarction but their immediate problem is the symptoms they develop whenever they try to get up from their bed. These symptoms can be abolished by vascular surgery. We were able to offer our patients surgery to their carotid arteries but in the presence of widespread arterial occlusions this may not always be
feasible. Indeed the Mayo Clinic patients already referred to required an anastomosis between their extra-cranial and intra-cranial arteries. The results of this more demanding procedure were equally gratifying: 17 of the 21 patients with “primary orthostatic cerebral ischaemia” were improved by surgery.\(^\text{10,11}\)

Surgery however is not without its hazards. We have described the turbulent post-operative course of our third patient, a course remarkably similar to the confusion and fluctuating focal signs one of the Mayo Clinic patients developed.\(^\text{10}\) Beyond stating that the graft was functioning no explanation was offered. In our case the disobliteration of an occluded carotid was followed by a profound and global disturbance of cerebral function which we too found hard to explain. It would be helpful to follow such a patient in a centre which had the facilities to measure cerebral blood flow. Fortunately both patients made a satisfactory recovery and we continue to believe that “primary orthostatic cerebral ischaemia” is a condition worthy of diagnosis and treatment.

References