EASILY MISSED: POSTERIOR CIRCULATION ISCHAEMIC STROKE

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CASE HISTORY

A 63 year old man with a history of migraine with visual aura (see "Patient Perspective"), hypertension and anxiety, presented to the emergency department with a 5 day history of headache. This headache started similarly to previous migrainous episodes, but became more severe than usual, and was accompanied by intermittent double vision, disturbed balance, speech and swallowing. The patient was treated with intravenous fluids and analgesia, and discharged with a diagnosis of migraine. The following day, his symptoms worsened; clinical examination revealed vertical diplopia, gaze-evoked jerk nystagmus, right sided past-pointing and an ataxic gait. Brain CT and CT angiography demonstrated an acute right superior cerebellar artery territory infarct and thrombus in the V3 and V4 (distal) segments of the right vertebral artery, and subsequent brain MR revealed other posterior circulation infarcts (Figure 1).

WHAT IS POSTERIOR CIRCULATION ISCHAEMIA?

The posterior circulation comprises both vertebral arteries, the basilar artery, and the intracranial vessels that they give rise to[1]. Together, these arteries supply the brainstem, cerebellum, medial and postero-lateral thalamus, occipital lobes, and sometimes parts of the medial temporal and parietal lobes[1] (Figure 2).

[BOX] HOW COMMON IS IT?

Posterior circulation ischaemic stroke are globally recognised and account for approximately 20% of all ischaemic strokes, and affecting more than 20,000 per year in the UK[2 3]. In the New England Medical Center Posterior Circulation Registry (NEMC-PCR)[4] including

patients with posterior circulation ischaemic events (defined using brain imaging); 63% were male, with a mean age of 60.5 years; approximately one quarter (24%; n=98) of the strokes were preceded by a TIA[4].

WHY IS IT MISSED?

More than a third (37%) of posterior circulation strokes are misdiagnosed in the emergency department, more than three times as often as anterior circulation strokes[5] (Table 1). Migraine presents particular diagnostic quandaries: migraineurs are more likely to develop headache secondary to acute ischaemia[6 7]; those with aura have a higher incidence of stroke[8 9]; migraine is associated with higher rates of carotid and vertebral artery dissection[10], and occasionally causes transient neurological deficits without headache (acephalgic migraine or "late-life migraine accompaniments")[11]In this patient's case, the diagnosis was missed because the symptoms of diplopia, dysphagia and dysarthria were either not elicited, or their significance as "red flags" for posterior circulation disease, were not recognised.

Table 1: Why is posterior circulation ischaemia missed?

Reason	**Anterior circulation (carotid artery territory) ischaemia**	**Posterior circulation ischaemia**
Wide range of symptoms	Brain regions supplied by the anterior circulation relatively well defined; tend to present with classical and well-known stroke symptoms (motor, sensory and/or speech or visuospatial disturbance).	The posterior circulation supplies a large number of brain regions with differing functions (Figure 2); this, together with anatomical variability, means that ischaemia can present with a wide range of symptoms and signs, some of which (e.g. vertigo, reduced conscious level, diplopia) are not well-known as stroke symptoms)[1].
Absence of "typical" symptoms	Presentation with "typical" stroke symptoms e.g. speech disturbance and limb weakness mean that "FAST" (Face Arm Speech Test) assessment used by paramedics and promoted as part of the "Act FAST" public health campaign likely to positive.	More likely to be "FAST negative"[3]. Posterior circulation strokes often present with lower scores on the National Institutes of Health Stroke Scale (NIHSS; the most commonly used measure of stroke severity) than anterior circulation strokes[5 12], making them more likely to be misdiagnosed in the emergency department[5].
Presentation with non-specific symptoms	Non-specific symptoms e.g. headache, nausea, vomiting, reduced consciousness less common (usually only in the context of large ischaemic strokes).	Presentation with non-specific symptoms more likely. In particular, headache is more common in posterior circulation strokes[6 7 13], possibly secondary to the denser perivascular innervation in these arterial territories[13].
Absence of cardiovascular risk factors	Usually strongly associated with cardiovascular risk factors (e.g. hypertension, diabetes mellitus, hypercholesterolaemia, smoking, family history of cardiovascular disease)	Arterial dissection (both spontaneous and traumatic) is responsible for a quarter of posterior circulation strokes[14] (compared with 2% of all ischaemic strokes[15]), and so strokes in this territory often occur in younger patients without obvious cardiovascular risk factors[2].

WHY DOES THIS MATTER?

Delayed or incorrect diagnosis results in inadequate acute care and poorer outcome. Posterior circulation strokes have longer door-to-needle times for intravenous thrombolysis than anterior circulation strokes[16 17], and are more likely to arrive in hospital after the 4.5 hour thrombolysis "time window"[18]. Prompt diagnosis is important to detect and treat two life-threatening presentations. Cerebellar infarction can become "malignant"[1] (10 - 20% of cases), when oedema associated with the infarct results in obstructive hydrocephalus and brainstem compression, necessitating urgent neurosurgical intervention[19]. Basilar artery occlusion, whilst rare (1% of all strokes), infarcts brain-stem, thalamic or posterior cerebral hemispheres, which can cause severe syndromes including complete limb and facial paresis with preserved consciousness (the "locked-in" syndrome), reduced conscious level and eye oculomotor abnormalities (e.g. from midbrain and bilateral thalamic damage, as part of the "top of the basilar" syndrome), coma, and cardio-respiratory disturbances, depending on the site of occlusion[20]. It has an extremely poor prognosis, but can benefit from intra-arterial thrombolysis or mechanical thrombectomy (clot retrieval) even 24 hours after symptom onset[1].

HOW IS THIS DIAGNOSED?

Clinical

All patients with suspected posterior circulation ischaemia should be immediately referred to a hyperacute stroke service. As in all strokes, the symptoms and signs of posterior circulation stroke typically start suddenly; the most frequent are shown in Figure 3[1 21]. Double vision

(15% of cases)[21], visual field loss, disorientation, confusion and memory loss are less common[2]. Presentation with isolated "dizziness" (vertigo or disequlibrium) or headache is the most common reason for misdiagnosis[5]; a detailed "posterior circulation" history should thus be taken from every patient presenting with these symptoms. This includes characterising "dizziness" as vertigo (a feeling of rotation or motion), disequilibrium (an unsteady feeling on walking), presyncope (a feeling of an impending loss of consciousness), or light headedness[22]; vertigo and disequilibrium are most suggestive of posterior circulation ischaemia. However, in practice, dizziness often does not fall clearly into any of these categories. The history should focus on the exact onset and nature of symptoms (whilst sudden onset is typical, onset can be staggered with severe atheromatous disease or small vessel occlusions[1]) and identifying any cardiovascular risk factors (including atrial fibrillation) or features suggesting arterial dissection (e.g. new unilateral, posterior neck pain, a history of repetitive or sustained neck movements, or trauma). The presence of "Red flags" (BOX) should prompt further investigation.

[BOX] "Red flags" for posterior circulation stroke: our specialist opinion

The presence of any of the following should prompt discussion or referral to a hyperacute stroke unit:

- Sudden onset vertigo or disequilibrium WITH one or more additional posterior circulation symptoms (headache, gait or limb ataxia, visual change (i.e. diplopia or partial visual field loss), dysarthria, dysphagia, limb weakness)

- Sudden onset vertigo or disequilibrium with a HINTS examination (see below) suggesting a central cause
- In those with known migraine, presentation with any new posterior circulation symptoms, even with headache, should be referred. In those with only a reported change in their usual headache pattern (e.g. changes in duration or severity), a posterior circulation stroke history and examination should be completed, with a low threshold for discussion with an acute stroke team
- Presence of any two new acute onset posterior circulation symptoms (especially if there are risk factors for stroke)
- Presence of any new focal posterior circulation neurological signs

Patients must have a full neurological examination, focussing on eye movements, limb power and co-ordination (Figure 3). In isolated acute vestibular dysfunction (rapid onset vertigo, nausea, vomiting, and unsteady gait, with or without nystagmus) presenting to hospital, the three-step "HINTS" (Head-Impulse-Nystagmus-Test-of-Skew) examination (Figure 4; videos at https://collections.lib.utah.edu/details?id=177180) is reported to have high sensitivity (100%) and specificity (96%) for identifying central lesions[23].

Investigations

CT is the first line investigation for suspected acute posterior circulation stroke, but lacks sensitivity, particularly in the brainstem[2]. MRI, specifically high signal on diffusion weighted imaging (DWI), is nearly always seen in acute infarction. However, a recent meta-analysis[24] found that whilst only 6.8% (95% CI 4.9% to 9.3%) of patients with acute

ischaemic stroke have negative DWI, this is five times more common in posterior circulation stroke (OR 5.1, 95% CI 2.3–11.6, p<0.001). Clinical assessment and concurrent vascular imaging (CT or MR angiography to identify relevant occlusion or stenosis) can also be important to help clinch the diagnosis.

HOW IS IT MANAGED?

Intravenous thrombolysis is effective treatment for acute ischaemic posterior circulation stroke, [25-27], if given within 4.5 hours of symptom onset[28]. There is substantial evidence for mechanical thrombectomy for large vessel occlusions in anterior circulation stroke[29], but less data for the posterior circulation, with the exception of proven basilar artery occlusion[1 2]. All patients with suspected posterior circulation ischaemia should be referred to a hyperacute stroke unit. Those with large cerebellar infarcts require monitoring on a neurocritical care unit (or equivalent) to facilitate prompt referral for possible neurosurgical intervention. As with all strokes, the underlying causes and risk factors, including atrial fibrillation, require investigation and treatment.

[BOX] WHAT YOU NEED TO KNOW

- Posterior circulation ischaemia is easy to miss because of the wide range and non-specific nature of presenting symptoms
- All patients with new “dizziness” (vertigo or disequilibrium) or “headache” (including a change in migraine symptoms) need a posterior circulation history and urgent discussion with a stroke unit if there are “red flags” for posterior circulation stroke (see Box)

- Use the HINTS examination to identify peripheral causes of acute vestibular dysfunction; a clear-cut result in a patient with isolated vertigo can help rule out posterior circulation ischaemia

[BOX] EDUCATION INTO PRACTICE

- Do you feel confident performing the HINTS assessment? What about your colleagues? How might you improve this?
- Think about the last time you referred a patient to the acute stroke team with suspected posterior circulation ischaemia – how did it go, and what would you do differently now?
- Diagnosing posterior circulation ischaemia can be challenging, even for stroke specialists – why do you think this is the case, and what aspects of the history and examination could you use to help?

PATIENT PERSPECTIVE

"I am 63 years old, not obese, and relatively fit, apart from borderline hypertension. I am generally healthy, although did start getting the kind of migraine headaches presaged by visual disturbance (a "colourless kaleidoscope") approximately 7 years ago; these were generally cleared up by over the counter medication straight away. However, more recently I experienced a particularly intense, painful migraine that unusually lasted for the best part of a week, with occasional loss of balance and intermittent double vision. I thought these symptoms were all related to migraine, but after five days my symptoms continued to worsen, and I felt very unwell, so I visited my local A&E. Whilst in the waiting room I experienced severe difficulty swallowing and speech was difficult; the doctor on duty referred me to a nurse, who in turn referred me to a second doctor. My daughter had to push me between the nurse and second doctor in a wheelchair, as I had lost my balance. I was monitored for two to

three hours, given aspirin, oxygen and a drip before being discharged, despite having high blood pressure and having lost my balance completely. I went home, went to bed and my wife called an ambulance in the small hours of the morning, when I awoke choking and unable to breathe. The ambulance staff were exceptional and took me to another hospital, as it has a dedicated, acute stoke unit, which they felt that I needed immediately. I had had a stroke in my right hand, rear brain and lost all balance and had hugely compromised eyesight. I was released within 48 hours and continue my rehabilitation at home."

[BOX] HOW WERE PATIENTS INVOLVED IN THE CREATION OF THIS ARTICLE?

The case description is based on a real patient, who also wrote the "patient perspective" section describing his experiences.

CONFLICTS OF INTEREST/DISCLOSURES

We have read and understood the BMJ Group policy on declaration of interests and declare the following interests: none.

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CONTRIBUTORSHIP STATEMENT

DJW and GB had the idea for the article and developed the article outline. GB wrote the first draft which was revised by DJW and SS.

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FIGURE LEGENDS

Figure 1: MR brain imaging from the patient described in our case history

Axial T2 (A, B) and axial diffusion weighted (C,D) MRI sequences showing acute infarcts in the right occipital lobe (A, C) and right cerebellum (B, D). Contrast enhanced magnetic resonance angiography (E) shows an abrupt occlusion of the right vertebral artery (thick arrow). The left vertebral artery (thin arrow) takes continues via a tortuous route, before terminating in the posterior inferior cerebellar artery (interrupted arrow). The basilar artery (arrowhead) receives no flow from either vertebral artery, and instead shows retrograde filling from the Circle of Willis.

Figure 2: Brain regions supplied by the posterior circulation

Figure 3: Presenting signs and symptoms in 407 patients with posterior circulation strokes, taken from the New England Medical Centre Posterior Circulation Registry[1 21]

Figure 4: The Head-Impulse-Nystagmus-Test-of-Skew (HINTS) examination

Adapted from references[1 23]. A video of the examination can be found at https://collections.lib.utah.edu/details?id=177180 .