Case report

Bilateral paramedian pontine infarcts: a rare cause of bilateral horizontal gaze palsy

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SUMMARY

A 73-year-old man presented to accident and emergency with headache and diplopia. Examination of the eye movements revealed a bilateral complete horizontal gaze palsy. On admission, a CT scan of the brain was performed, which was unremarkable. An MRI of the brain was then performed, which confirmed tiny acute infarcts involving the pons and the right cerebellum. This man was promptly treated with aspirin 300 mg one time per day, as per the stroke pathway. Further diagnostic workup later revealed atrial flutter. This man was therefore commenced on apixaban. The differential diagnoses for bilateral gaze palsy include the following: multiple sclerosis, infarction, haemorrhage and space occupying lesion. Bilateral gaze palsy is often associated with other neurological symptoms.

BACKGROUND

In this case, small infarcts have simultaneously affected the paramedian pontine reticular formation (PPRF) bilaterally. In this patient, the infarcts have caused bilateral gaze palsy with minimal other neurological signs. The authors are not aware of previous reports of acute ischaemic stroke presenting with isolated bilateral horizontal gaze palsy.[1] Because this presentation of stroke is extremely rare, it can easily be overlooked.[2]

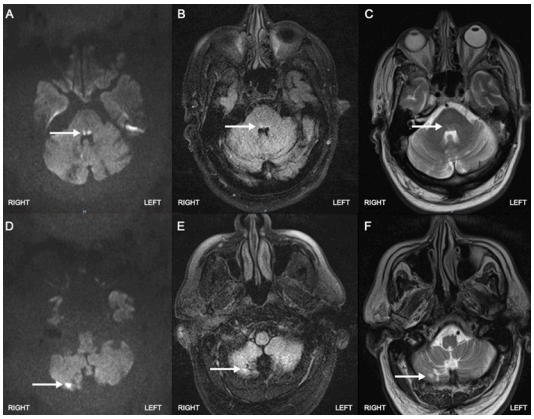

Figure 1 MRI head (lesions indicated with arrows): (A) diffusion-weighted images (DWI) demonstrating increased signal in the mid-brain affecting the paramedian pontine reticular formation bilaterally. (B) Fluid-attenuated inversion recovery (FLAIR) imaging demonstrating high signal in the mid-brain ischaemic lesions. (C) High T2 signal within both mid-brain paramedian pontine reticular formation regions. (D) DWI demonstrating increased signal in the right cerebellar hemisphere. (E) FLAIR imaging demonstrating high signal in the right cerebellar hemisphere. (F) High T2 signal within the right cerebellar hemisphere.

CASE PRESENTATION

A 73-year-old man presented to hospital with a 1-day history of headache and diplopia. He also described a sudden onset of unsteadiness when walking. On examination of the cranial nerves, he had bilateral complete horizontal gaze palsy, minimal left facial droop, no visual neglect, normal visual fields and convergence. The rest of the examination revealed only upgoing plantars on the right. His speech and swallow assessment was unremarkable. He had normal power in all muscle groups, and sensation was fully intact. Cerebellar examination did not reveal ataxia or incoordination. His medical history included hypertension, a previous coronary artery bypass graft, type II diabetes mellitus and hyperlipidaemia.

INVESTIGATIONS

This man had a CT head which demonstrated age-related generalised atrophic changes and leucoaraiosis. There was no evidence of mass lesion, infarct or intracranial haemorrhage. In view of the patient's vascular risk factors, and the acute presentation with focal neurological deficit, the patient was promptly started on 300 mg aspirin for suspected stroke. He went on to have an MRI head, which revealed two small acute infarcts involving the paramedian pons bilaterally, with another small infarct involving the right cerebellum on diffusion-weighted sequences (figure 1).

To investigate possible causes for stroke, an echocardiogram was performed which demonstrated a subtle patent foramen ovale shunt of little clinical significance. This man then had carotid Dopplers, which revealed patent carotid and vertebral arteries with normal flow. A 24-hour ECG showed atrial flutter.

TREATMENT

This patient was promptly commenced on apixaban.

OUTCOME AND FOLLOW-UP

Over the following weeks, ophthalmic assessments confirmed bilateral gaze palsy with variable difficulty in abduction and adduction of the eyes, as well as significant diplopia on near and distant gaze. This patient also exhibited increased neck

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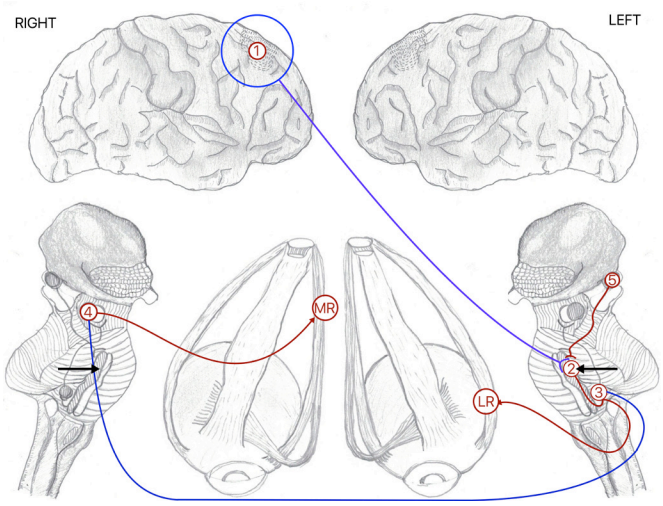

Figure 2 Hand-drawn diagram summarising the key pathways involved in the generation of left horizontal saccadic eye movements (paramedian pontine reticular formation (PPRF) lesions indicated with arrows). Right frontal eye field (1) sends a signal to the contralateral left PPRF (2), which then increases activity of contralateral left sixth nucleus (3). This in turn innervates the lateral rectus (LR) muscle of the left eye. The left sixth nucleus (3) also communicates with the right third nucleus (4) via internuclear neurones which run in the medial longitudinal fasciculus. The right third nucleus (4) then stimulates the medial rectus of the right eye (MR). This results in an overall left-sided saccade. Blue colour denotes neural pathways which cross to the contralateral side.[3–5]

movements on visual tracking, to compensate for his restricted horizontal gaze. There was also impairment of his vestibulo-ocular reflex and horizontal smooth pursuit. However, there was no evidence of manifest strabismus, and there were normal convergence and colour perception. There was no evidence of vertical or gaze-evoked nystagmus. There was no slowing of vertical gaze saccades or limitation of upgaze. His vertical pursuit was preserved, and there was no relative afferent pupillary defect. No intra-ocular pathology was identified. The above findings were then replicated at 1 month post-discharge, on repeat orthoptic assessment. This patient had minimal recovery.

DISCUSSION

In order to understand the pathology of this rare presentation, it is important to consider the neuro-anatomy underlying the control of eye movements (figure 2).

The PPRF is a collection of cells in the pons anterior and medial to the medial longitudinal fasciculus (MLF). It is involved in the control of horizontal gaze. The fibres from the PPRF project to the ipsilateral sixth nerve nucleus and to the contralateral third nerve nucleus through the MLF, which stimulates both eyes to move horizontally.[3]

To produce a left horizontal saccade, the right frontal eye field sends a signal to the premotor neurons in the contralateral left PPRF. This increases activity of the lower motor neuron in the left abducens nucleus, which innervates the lateral rectus muscle in the left eye.[4] The left PPRF also receives input from the superior colliculus via the predorsal bundle. There is also an increased activity of internuclear neurons in the ipsilateral left abducens nucleus which run along the MLF and innervate the lower motor neurons in the right third nerve. The right third nerve innervates the medial rectus on the right eye, to produce conjugate eye movements to look towards the left.[5]

Pathology involving any part of the above neuroanatomical pathway can result in gaze palsy. Causes are broadly divided into peripheral and central.

Peripheral causes directly affect the intra-orbital muscles or the fascicles of the axons of the cranial nerves three, four or six and tend to present unilaterally. Examples include the following: nerve compression syndromes, vascular causes, central nervous system infections, trauma or metabolic causes. An example is Duane syndrome, a congenital syndrome affecting the sixth nerve.[6]

Central causes include pathologies of the brainstem, cerebellum or higher level centres. Central disturbances can result from fascicular, nuclear or supranuclear lesions as a result of ischaemia or demyelination.[7]

Important differential diagnoses of bilateral gaze palsy include ischaemia and multiple sclerosis. Ischaemic damage to the PPRF will cause an inability of either eye to move horizontally towards the side of the lesion. Hence, bilateral lesions to both left and right PPRF will cause bilateral complete horizontal gaze palsy. In extremely rare cases, bilateral complete horizontal gaze palsy results from a midline pontine infarct affecting both left and right PPRF.[8] In contrast to this, demyelinating lesions involving bilateral MLF are characterised by bilateral adduction impairment with preserved abduction, associated with a compensatory nystagmus of the abducting eye. In addition, some patients with bilateral MLF lesions may exhibit bilateral exotropia and present with a syndrome referred to as wall-eyed bilateral internuclear ophthalmoplegia.[9] Vertical nystagmus may be present due to bilateral MLF lesions involving cell groups of paramedian tracts.[10] Therefore, ischaemic stroke is the most likely diagnosis in this patient.

In this patient, bilateral PPRF infarcts alone may not be sufficient to explain the diplopia. Diplopia may have resulted from asymmetrical ischaemic lesions with possible unilateral involvement of the abducens nucleus or its axonal fascicles which are in close proximity to the PPRF. Involvement of either abducens fascicle would result in unopposed oculomotor tone to the contralateral medial rectus muscle, with subtle disturbances in vergence on near and distant gaze. This would result in perceived horizontal diplopia. Possible involvement of the abducens nucleus would also explain the impaired vestibulo-ocular reflex and smooth pursuit, with preserved convergence. These signs are not classically seen in isolated PPRF lesions.[11–13] Unilateral abducens nucleus involvement is also supported by the patient's left facial droop, as sixth and seventh nuclei are commonly affected together due to their close anatomical relationship.

Headache is a common symptom of ischaemic stroke with an estimated prevalence between 7% and 65%.[14–16] The exact mechanism is unclear but studies indicate a likely vascular origin through involvement of the sensory fibres and vasoactive neuropeptides which become released in response to ischaemic injury, stimulation of arterial vasodilation and activation of platelets.[17–19] Diplopia itself can also cause a headache.

Bilateral PPRF ischaemia is therefore first a clinical diagnosis in the absence of CT findings. However, MRI can be used to support the diagnosis due to high specificity and sensitivity.

In conclusion, bilateral horizontal gaze palsy can present in patients with stroke. In this particular case, the most likely mechanism is ischaemic infarction affecting bilateral PPRF and the left abducens nucleus.

Stroke is associated with a high morbidity and mortality thus early detection and secondary prevention are crucial. MRI should be considered in patients with this presentation if CT head shows no cause. In our patient, since multiple infarcts

Learning points

- Horizontal gaze palsy can result from either peripheral or central causes, most commonly ischaemia or demyelination.
- Bilateral horizontal gaze palsy likely results from a central cause affecting the mid-pons.
- Stroke is an important differential and should be considered early.
- MRI head should be sought if CT head shows no acute pathologies.
- Multidisciplinary approach is always needed in stroke patients, with ophthalmology and orthoptic involvement for ophthalmolplegia.
- Horizontal gaze palsy may be the only manifestation of a pontine infarct.

were seen on MRI, a rapid 24-hour Holter assessment was done which confirmed atrial flutter. Since infarct sizes were small, he was treated with early anticoagulation to prevent further ischaemic embolic events and consequent morbidity and mortality.

Contributors DC: collected information on patient's case, designed layout, collaborated with stroke consultant in charge of patient care; contributed to Pathophysiology section and the Case summary; edited final draft of report; he is a sole contributor to design and creation of Figure 2; and obtained consent from patient's relatives. MEK: responsible for Case Report Presentation and Outcome and Follow-Up sections of the report. FH: responsible for Discussion section of the report. MB: clinical supervisor; consultant stroke physician; identified the case and diagnosed the patient; and refined and edited the case report.

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