CASE REPORT

Blood, brain and binocular vision

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SUMMARY

A man aged 51 years presented with sudden onset, horizontal, binocular, double vision and right facial weakness. Ocular motility examination demonstrated a right horizontal gaze palsy pattern in keeping with a one-and-a-half syndrome. Since this was associated with a concomitant, ipsilateral, lower motor neuron (LMN) facial (VIIth) cranial nerve palsy, he had acquired an eight-and-a-half syndrome. Diffusion-weighted MRI confirmed a small infarcted area in the pons of the brainstem which correlated with anatomical location of the horizontal gaze centre and VIIth cranial nerve fasciculus. As a result of this presentation, further investigations uncovered a hitherto undiagnosed blood dyscrasia—namely polycythaemia vera. Regular venesection was started which resulted in complete resolution of his ocular motility dysfunction and an improvement of his LMN facial nerve palsy.

BACKGROUND

Binocular diplopia can be caused by a wide range of conditions, including ophthalmic disorders, dysfunction of the ocular muscles or neuromuscular junction, cranial nerve III, IV and VI palsies, or disorders of the brain. One-and-a-half syndrome is a rare but important cause of binocular diplopia which occurs when there is a lesion in the paramedian pontine reticular formation or VIth nerve nucleus in conjunction with the ipsilateral medial longitudinal fasciculus located in the pons of the brainstem. Owing to the close proximity of the facial nerve nucleus, this cranial nerve may also be involved resulting in an eight-and-a-half syndrome.

This case illustrates the importance of assimilating clinical signs with its neuroanatomical correlate, particularly when reviewing small defects on neuroimaging that can otherwise be missed. Furthermore, it illustrates the attendant risks of thromboembolic events associated with polycythaemia and the importance of secondary prevention.

CASE PRESENTATION

A man aged 51 years without significant medical history developed sudden onset, horizontal, binocular, double vision while watching television. He also noticed that the right side of his face appeared to droop and he lost the ability to close his right eyelid. He did not experience any headache or any other neurological symptoms. He was a life-long non-smoker and rarely drank alcohol.

Examination performed in A&E revealed a right, lower motor neuron (LMN) facial nerve palsy and an unusual ophthalmoplegia: all of the horizontal eye movements were absent, apart from abduction in the left eye ([figure 1](#)). In addition, an associated

horizontal jerk nystagmus was visible on abduction of the left eye. An ophthalmology opinion was sought which confirmed the pattern of ocular motility dysfunction as a one-and-a-half syndrome.

INVESTIGATIONS

When this patient presented to A&E, a vascular insult was felt to be the most likely cause for the patient's signs and symptoms. Initial investigations were performed to assess neurovascular and cardiovascular risk factors—the results are highlighted below:

BP 157/97, pulse 84 bpm.

Serology

Hb 219 g/L (130–180), Plts $473 \times 10^9/L$ (150–400), PCV 0.616 L/L (0.4–0.500).

WCC: $11.1 \times 10^9/L$ (Neut 8.1, Lymph 2.1, Eos 0.4); MCV 85 fL.

Raised haemoglobin level with haematocrit above 0.6 in a man (PCV=packed cell volume) is diagnostic of erythrocytosis (*NICE Guidelines*).

U&Es: Creat: 84 $\mu\text{mol/L}$; Urea: 4.7 mmol/L; K: 5.5 mmol/L; Na: 137 mmol/L; GFR: 84 mL/min.

LFTs: Bil 23 $\mu\text{mol/L}$; ALT 25 U/L; ALP 111 IU/L; Albumin 44 g/L.

Glucose 4.4 mmol/L; Cholesterol 6.2 mmol/L.

Neuroimaging

CT imaging of his head was unremarkable. MRI and magnetic resonance angiography (MRA) of his head were initially reported as normal. However, a review of the diffusion-weighted images revealed a small area of restriction within the region of the right pons consistent with an infarct (see [figure 2](#)).

Further tests

In view of the raised erythrocyte count in the absence of any known secondary precipitants (eg, smoking), Janus kinase 2 (JAK2) mutation was requested, which was positive. JAK2 mutation positivity is present in ~95% of patients with polycythaemia vera.¹

DIFFERENTIAL DIAGNOSIS

The sudden nature of his symptoms was highly suggestive of a neurovascular event at the outset. The combination of a right-sided one-and-a-half syndrome and an ipsilateral LMN facial nerve palsy localised the lesion to the region of the pons ipsilateral to the weakness. Although the T1 and T2-weighted MRI images of the patient's brain parenchyma appeared normal, the diffusion-weighted modality identified a small area of restriction within the relevant anatomical area consistent with an acute infarct.

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Figure 1 The right eye does not adduct or abduct. The left eye cannot adduct, but abduction movement (turning out) is preserved. This is an example of one-and-a-half syndrome ocular motility disorder. It is clear from the picture portrayed that right facial nerve palsy is also present.

Figure 2 MRI diffusion weight imaging revealing a restricted area (bright spot) within the dorsal region of the right pontine area—the neuro-anatomical correlate for the patient's abnormal signs.

Owing to the patient's age and lack of cardiovascular risk factors, serological investigations were performed at presentation to confirm or exclude any hitherto, undiagnosed risk factor/s. A full blood count revealed an isolated erythrocytosis which, as a result of hyperviscosity, is a risk factor for the development of a thromboembolic event. At this stage, one needed to differentiate between polycythaemia vera, secondary erythrocytosis and apparent erythrocytosis.

Apparent erythrocytosis occurs when there is reduction in the plasma volume (eg, patients with a significant smoking or alcohol history or secondary to diuretic use). Absolute erythrocytosis, in contrast, occurs when there is an increase in the total number of red blood cells in the circulation. This is observed in patients with either polycythaemia vera or secondary erythrocytosis.²

Polycythaemia vera is a myeloproliferative condition caused by neoplastic proliferation of erythropoietin cells in the bone marrow.^{3 4} Almost 95% of patients with this disorder will test positive for the JAK2 genetic mutation.¹⁻³ Since primitive cells possess the ability to mature into platelets and white cells, there may be an associated thrombocytosis and leucocytosis.

Secondary erythrocytosis occurs due to increased production of erythropoietin under conditions such as chronic pulmonary obstructive disease, renal artery stenosis or renal tumours.² Secondary causes should be sought in the presence of a relevant medical history and/or the absence of a JAK2 mutation.

TREATMENT

Treatment was divided into management of the underlying myeloproliferative disorder, binocular diplopia and corneal exposure secondary to incomplete eyelid closure from the underlying LMN facial nerve palsy.

Polycythaemia was initially treated with venesection, with subsequent introduction of hydroxycarbamide. The patient was also prescribed clopidogrel and atorvastatin for secondary prevention of subsequent thromboembolic events. Response to treatment was monitored by checking the patient's Hb, PCV and platelet count. Hydroxycarbamide, an antimetabolite, has numerous side effects that include, inter alia, anaemia,

thrombocytopenia, increased infection risk (due to neutropenia), tiredness and infertility. Thus, careful counselling prior to starting treatment is essential.

Corneal exposure is a significant risk following LMN facial nerve palsy. This can lead to desiccation of the outermost layer of the corneal surface (epithelium) which, in turn, may progress to corneal ulceration. Treatment with regular ocular lubricants and taping down the eyelid is a sine qua non of preventing such corneal complications. In this case, covering one eye to protect the cornea automatically eliminated the troublesome, concomitant symptom of binocular diplopia as the second misaligned image is removed.

Long-term management of the patient's anterior segment is dependent on the recovery of the facial nerve and residual presence of lagophthalmos (inability to close the eye). Surgery to the eyelid may be necessary to protect the cornea in the long term. This may be achieved by either inserting a gold weight in the upper eyelid to induce a blepharoptosis or appose the upper and lower lids via a tarsorrhaphy.⁵

Treatment of binocular diplopia includes long-term occlusion/frosting of one eye, prisms incorporated in spectacle lenses or extraocular muscle transposition surgery. The patient regained single vision following treatment with venesection.

OUTCOME AND FOLLOW-UP

Two weeks of venesection (as a part of the initial management of polycythaemia) led to abrogation of his abnormal ocular motility signs and symptoms of binocular diplopia. His facial nerve palsy, in contrast, only partially recovered necessitating eyelid surgery to address the residual lagophthalmos and instillation of topical lubricants on an indefinite basis.

DISCUSSION

There have been no previous cases in the literature where an eight-and-a-half syndrome was linked to a new diagnosis of polycythaemia. Notwithstanding, Sampath Kumar *et al*⁶ described a case of an eight-and-a-half syndrome in a person aged 65 years secondary to lacunar pontine infarction and two of the three cases described by Eggenberger were secondary to infarction.⁷ Additionally, it is important to note that lesions in the ipsilateral abducens nucleus can cause the same signs.⁸

Learning points

- ▶ Binocular, double vision, frequently described and referred to as an ophthalmological symptom, can frequently be a manifestation of brain pathology.
- ▶ Knowledge of neuroanatomy is essential when trying to localise the potential lesion based on clinical presentation.
- ▶ To the best of our knowledge, this is the first reported case of an eight-and-a-half syndrome as the first presenting feature of polycythaemia vera.

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