CASE REPORT

Recurrent ischaemic stroke unveils polycythaemia vera

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SUMMARY

Polycythaemia vera is a recognised cause of ischaemic stroke. If not treated, this condition may result in recurrent strokes. This is a case of a 61-year-old Caucasian man presenting with the inability to ambulate for 3 days. Brain imaging revealed acute and chronic infarctions in the brain stem and the cerebrum. Polycythaemia vera was diagnosed and treated during the admission. The unique mechanisms and management issues of ischaemic stroke associated with polycythaemia vera are discussed.

BACKGROUND

Thrombotic events are a frequent and significant complication of polycythaemia vera (PV). In up to 49% of patients with PV, thrombosis is the presenting event.¹ A study following the course of patients with polycythaemia over a 20-year period also demonstrated that up to 15% of patients have a thrombotic event within the 2 years prior to diagnosis and up to 40% of patients with PV suffer a thrombotic event during the course of the disease.²

This case presents a patient with recurrent stroke. During his first stroke admission several years prior, he did not meet the criteria for diagnosis of PV. The cause for his elevated blood count was investigated further at the time, when the haemoglobin and haematocrit were unaffected by intravenous fluids.

Increased blood viscosity is a recognised cause of complication in PV. When haematocrit and blood viscosity increase, cerebral blood flow decreases. A second mechanism of cardiac 'micro-emboli' has also been supported by case reports of patients with PV and MRI findings consistent with embolic stroke.³

The unique management issues that must be addressed when a patient with an ischaemic stroke also has PV, as well as support for the microembolic nature of strokes in these patients, are explored in this case report.

CASE PRESENTATION

A 61-year-old Caucasian man presented to the emergency department with a 3-day history of inability to ambulate. The patient had an unstable gait and was having falls at home. He had little to eat or drink during those 3 days. He denied any headache, seizures or loss of consciousness.

The patient had hypertension and a history of two prior ischaemic strokes in the past 3 years with residual expressive aphasia and ataxia. He quit smoking 5 years prior. The patient drank a six-pack of beer daily, but denied any drug abuse. Family history was negative for haematological or neurological disorders.

His prior strokes were attributed to uncontrolled hypertension as investigations for carotid artery stenosis or an embolic source were negative. He related the inability to access his medications for the prior 3 days, but had been previously adherent to therapy including daily doses of aspirin 81 mg, simvastatin 40 mg, amlodipine 10 mg and hydrochlorothiazide 25 mg.

On physical examination, the patient appeared fatigued and dehydrated. His blood pressure was 166/118 and pulse 105 bpm. Cardiac examination was tachycardic but regular. The abdomen was noted to be soft and non-tender with a mildly enlarged spleen. On neurological examination, he was alert and oriented. Expressive aphasia was noted. Cranial nerves II–XII were intact. The patient had difficulty with heel to knee testing bilaterally. Finger to nose testing was intact. Motor testing revealed intact strength without any atrophy or involuntary movement. No sensory abnormalities were observed. Reflexes in four extremities were intact as well.

INVESTIGATIONS

Laboratory investigation revealed haemoglobin of 21.3 g/dL, haematocrit of 60.5%, platelets of 443 thou/cm² and leucocytes of 19.1 thou³/cm² with neutrophils 86.2%. These findings were initially attributed to dehydration.

Brain CT with contrast showed chronic microvascular occlusive disease with infarction in the region of basal ganglia, anterior limb of internal capsule and thalamus, along with subacute infarctions of the left posterior cerebellar hemisphere. Brain MRI without contrast (figure 1) revealed acute infarction in the brain stem and left parietal-occipital region along with chronic cortical and subcortical infarctions involving the left cerebellar hemisphere, brainstem and cerebral hemisphere. CT angiography of the neck was found to be unremarkable.

Transthoracic and transoesophageal echocardiography, carried out to detect an embolic source for the recurrent strokes, were negative.

Despite hydration, the haemoglobin and haematocrit remained elevated. Diagnosis of PV was confirmed by positive JAK2 V617F mutation test, low erythropoietin level and persistent elevation of all cell lines.

TREATMENT

The patient was treated with aspirin 81 mg daily and atorvastatin 40 mg daily in addition to physical, occupational and speech therapy.

He was also given two phlebotomies in the hospital, which reduced his haemoglobin from 21.3 to 17.5 g/dL and his haematocrit from 60% to 51%. He was scheduled for regular phlebotomies with a

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Figure 1 MRI demonstrates a hyper-intense signal in the area of the brainstem consistent with acute infarction.

goal haematocrit below 45%. Hydroxyurea 500 mg twice daily was started as a cytoreductive drug.

OUTCOME AND FOLLOW-UP

The patient was discharged to a skilled nursing facility for physical and occupational therapy, with neurology and haematology outpatient follow-up.

DISCUSSION

PV is a primary myeloproliferative stem cell disorder causing elevations of leucocytes, haemoglobin, haematocrit and platelets.¹ This patient met both of the major WHO criteria for diagnosis of PV, including having a positive JAK2 V617F mutation test and haemoglobin above 18.5 g/dL. The JAK2 mutation is present in 95% of patients with PV. JAK2 is a tyrosine kinase that regulates cell proliferation via signalling of erythropoietin, and the mutation causes inappropriate stimulation of the hematopoiesis.⁴

Patients with PV can present with a variety of neurological manifestations including headache, dizziness and weakness. PV leads to increased haematocrit, which increases blood viscosity. This results in decreased cerebral blood flow, precipitating thrombus formation and ischaemic stroke.¹

Recent case reports have also documented embolic lesions in patients with PV with two of those reports demonstrating microemboli in the left atrium by transoesophageal echocardiography.² It is hypothesised that in patients with PV and a distribution of ischaemic events suggestive of embolism on imaging, microemboli may not be visible on echocardiogram.² Our patient received intravenous hydration prior to his echocardiograms, making it less likely that microemboli would be visible. MRI images in our case demonstrate multiple, small ischaemic strokes involving several areas of the brain.

Recurrent strokes are not uncommon in patients with polycythaemia. In one large prospective study, the recurrent thrombosis risk was 5% among individuals under 65 years and 10.9% among those over 65 years of age.³ Advanced age and a history of thrombosis are among the two important risk factors for vascular complications in patients with polycythaemia. Hypercholesterolaemia, hypertension, smoking and diabetes mellitus are also predictors

for thrombosis occurrence. Leucocytosis has been reported as an independent risk factor for thrombosis in PV.⁵

This patient was considered high risk for future thrombosis due to being aged above 60 years and stroke history. For this reason, hydroxyurea was added to his treatment plan of phlebotomy and aspirin. During his prior stroke admissions, the haemoglobin was 16 g/dL, which is well below the major WHO diagnostic criteria of 18.5 g/dL.

While management of acute stroke due to PV follows ischaemic stroke guidelines, it is the only condition where the American Heart Association stroke guidelines recommend haemodilution as a treatment.⁶ This is an important consideration for physicians as intravenous fluid in the initial phase of a cerebral vascular event can improve outcomes for patients with PV.

In addition to phlebotomy, antiplatelet agents such as aspirin have been very effective in the treatment of patients with polycythaemia, with 67% reduction in the rate of stroke recurrence.⁵ Hydroxyurea was associated with 30% reduction in the rate of recurrence in those patients.⁵

Hydration, phlebotomy, antiplatelet and cytoreductive drugs are very effective in managing patients with PV and reducing rates of recurrent strokes.

Patients with PV also require education about the need to be adherent with haematology follow-up. Patients need to be aware of their increased risk for recurrent stroke, portal vein thrombosis and leukaemic transformation and to understand the importance of compliance. Haematology visits and treatment are very effective in reducing the risks in these patients.

Learning points

- Hydration is recommended for acute management of polycythaemia vera (PV) induced strokes. PV associated strokes are the only cerebral vascular event for which the American Heart Association recommends intravenous fluids in initial management.
- Elevated blood viscosity has been proposed as the mechanism for stroke in patients with PV. Recent studies suggest that microemboli may also contribute to cerebral vascular events in these patients.
- Hydroxyurea, antiplatelet agents and phlebotomy to keep haematocrit under 45% are essential to prevent recurrence of strokes in patients with PV.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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