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CLINICAL

Chorea in the older adult: a full blooded answer

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ABSTRACT Chorea is a severe, distressing, movement disorder characterised by excessive, purposeless movements of the limbs, head and orofacial muscles in a generalised and irregularly-timed fashion. In young patients, neurodegenerative (Huntington's disease) and metabolic (Wilson's disease) aetiologies are most common. In the older population, the differential widens to include genetic, structural, metabolic and pharmacological causes. We present a case of an older man who developed progressive choreoathetosis secondary to polycythaemia vera which resolved with serial venesections. The treatment of his underlying condition is discussed.

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CASE PRESENTATION

An 84-year-old man presented to hospital with a two-month history of involuntary body movements. He had a past history of Dukes A sigmoid adenocarcinoma (treated with curative polypectomy) and benign prostatic hypertrophy. He had no significant family history. His regular drug prescriptions included once-daily amlodipine 10 mg and lansoprazole 15 mg. He was an ex-smoker of 40 years and a retired prison guard. Prior to the onset of the symptoms described above, he was mobile and fully independent.

He described jerking movements initially involving his head and orofacial muscles. These progressed to involve all four limbs in the two weeks preceding hospital admission. The movements continued during sleep. Swallowing was affected and, after initially managing a soft diet and normal fluids, he could only tolerate liquids at the time of admission. He had a marked deterioration in physical function, which rendered him bedbound and prompting referral by his general practitioner for inpatient assessment.

On admission he appeared agitated, with gross, involuntary choreoathetoid movements of the limbs, axial and orofaciolingual muscles. He was dysarthric with involuntary coughing and grunting. Reflexes were globally reduced, but neurological examination was otherwise unremarkable. The remainder of clinical examination was normal.

Admission bloods and laboratory investigations are summarised in Table 1. He had a markedly raised haemoglobin, white cell count and haematocrit. Serum erythropoietin level was suppressed. Blood film was reported as a full film with excess red cells but normal morphology. Contrast enhanced computed tomography (CT) of the brain showed patchy deep white matter changes in keeping with small vessel disease. A CT of the chest, abdomen and pelvis was normal. Lumbar puncture was performed with an opening pressure of 13 mmHg. Cerebrospinal fluid analysis was normal. Gene testing for Janus Kinase 2 V617F (*JAK2*) mutation was positive confirming a diagnosis of *JAK2* positive polycythaemia vera (PV).

The patient was initially treated with diazepam, procyclidine and tetrabenazine, although these offered little symptomatic benefit. Following venesection of six units of blood over a two week period, with resultant normalisation of haemoglobin and haematocrit, the patient's choreiform movements improved considerably. On discharge he had a mild degree of lip smacking and dysarthria but was otherwise asymptomatic. He was independently mobile with a Zimmer frame and resumed a normal diet. All sedating medications were stopped with no re-emergence of his symptoms.

He was reviewed at the haematology clinic six weeks later and remained free of symptoms. He required one further venesection at seven months post discharge due to a borderline haematocrit (0.451 L/L). Eighteen months later he remained well with no requirement for further venesection or chemotherapy.

DISCUSSION

Chorea in older adults has a wide differential diagnosis (Table 2). Despite this, the underlying cause of chorea

TABLE 1 Summary of laboratory investigations

Haematology	
Haemoglobin (RR: 13–18 g/L)	**199**
White cell count (RR: 4–11 x10⁹/L)	**21.2**
Neutrophil count (RR: 2.0–7.5 x10⁹/L)	**18.9**
Lymphocyte count (RR: 1.5–4.0 x10⁹/L)	1.2
Monocyte count (RR: 0.2–0.8 x10⁹/L)	**0.9**
Basophil count (RR: 0.0–0.1 x10⁹/L)	**0.2**
Platelet count (RR:150–400 x10⁹/L)	352
Haematocrit (RR 0.4–0.54 L/L	**0.586**
Coagulation screen	Normal
Erythropoietin (RR: 4.3–29 U/L)	**2.4**
ESR (RR: 1–10 mm/hr)	2 mm/hr
Transferrin (RR: 2.00–4.00 g/L)	3.08
Transferrin saturation (RR: 25–55 %)	**19**
B12 and folate	Normal
Biochemistry	
Urea and electrolytes	Normal
Liver function tests	Normal
Thyroid function tests	Normal
Adjusted calcium	Normal
Magnesium	Normal
CSF analysis	
CSF gram stain and culture	Gram stain negative. No growth
CSF Viral PCR	Negative
CSF biochemistry	Normal
Other	
Huntington's disease gene testing	Negative
NMDA receptor, anti-VGK anti-neuronal antibodies	Negative
*JAK2*V617F mutation	**Positive**

RR, reference range

TABLE 2 Causes of chorea in the older adult

Vascular
Ischaemic stroke
Intracerebral haemorrhage
Subarachnoid haemorrhage
Post cardiac bypass
Drugs
Dopamine receptor blocking medications (e.g. haloperidol)
Levodopa
Dopamine agonists
Anticonvulsants
Calcium channel blockers
Selective serotonin reuptake inhibitors
Lithium
Benzodiazepines
Antihistamines (H1 and H2 blockers)
Anti-cholinergics
Autoimmune or inflammatory
Coeliac disease
Systemic lupus erythematosus
Vasculitis
Neoplasia
Paraneoplastic syndrome
Basal ganglia involvement
Metabolic/endocrine disturbance
Hepatic failure
Hypo/hypernatraemia
Hypo/hypercalcaemia
Hypomagnesaemia
Hypoparathyroidism
Polycythaemia vera
Hyperthyroidism (Hashimoto's thyroiditis)
Infection
Meningitis
Encephalitis
Lyme disease
Prion disease (especially variant CJD)
HIV
Late onset neurodegenerative
Huntington's disease
Neuroacanthocytosis

can be found in the majority of patients.[1] Work up should begin with a comprehensive medical and psychiatric history including detailed medication history. Family history should include an enquiry into 'missing relatives' and early or unexpected deaths. Laboratory investigations, neuroimaging and genetic testing (where appropriate) can help to confirm the underlying diagnosis or exclude important differentials. Although more common in the younger population, Huntington's disease remains an important cause with a third of cases presenting in patients aged over 50.[2] Our case addresses polycythaemia vera; a simply treated, potentially reversible cause of this distressing symptom.

Polycythaemia vera is a myeloproliferative disorder with an incidence of 2–10 per million, usually presenting in the older population (50–70 years).[3] The major diagnostic criteria include a raised haemoglobin of > 18.5 g/dL in men or > 16.5 g/dL in women, and the presence of a *JAK2* mutation.[4] The *JAK2* gene promotes the production of blood cells from haemopoeitic stem cells. A gain of function mutation in this gene (most commonly *JAK2*V617F) is seen in 95–100% of patients with PV resulting in increased production and survival of red blood cells.[5,6] Symptoms develop secondary to hyperviscosity of the blood and include pruritus, eyrthromelalgia and thrombotic events.[7] Neurological complications occur frequently (50–80%) and include headache, dizziness and paraesthesia.[8] Chorea is an unusual neurological complication, affecting 0.5–5% of those with the condition.[9] It is even less frequently reported in secondary polycythaemia (i.e. due to chronic lung disease).[10] Interestingly, while PV has a slight predominance in males (2:1),[9] polycythaemia vera-related chorea occurs predominantly in females (4:1).[11]

The pathophysiology resulting in polycythaemia vera-related chorea remains unclear. The main hypothesised

abnormality is cerebral hypoperfusion (particularly in the basal ganglia) secondary to the increased red cell count.[9] An inverse relationship between cerebral blood flow and packed cell count has been demonstrated, showing improvement with venesection.[12] However, the wide spectrum of neurological symptoms in polycythaemia vera and the absence of chorea in other hyperviscosity syndromes such as multiple myeloma and Waldenstrom's macroglobulinaemia implies additional causative mechanisms.[13] Dopamine is likely to play a role. Platelet congestion within cerebral vessels may cause excess dopamine accumulation within the basal ganglia.[14] Oestrogen deficiency may also cause dopamine receptor hypersensitivity hence the increased incidence of polycythaemia chorea in females.[14]

Recognition of polycythaemia vera-related chorea is important as it is potentially reversible and should prompt treatment to prevent the sequelae of polycythaemia vera itself, including stroke and venous thromboembolism.[15] Management involves regular venesection to reduce haemoglobin and haematocrit to within the normal ranges.[15] Cytoreduction with chemotherapeutic agents such as hydroxycarbamide may be required to maintain remission in severe or persistent cases with or without chorea.[13,15] The use of low dose aspirin has been shown to be a safe method of reducing thrombotic events.[16] In patients with polycythaemia vera-related chorea, haloperidol and tetrabenazine (a presynaptic dopamine depleter) are typically given first line for symptomatic relief and can be withdrawn as symptoms improve.[8,10,17] Regular venesections are usually effective in controlling the symptoms of chorea, with the majority of cases resolving. Aggressive therapy is essential as the severity of chorea appears to be inversely related to the haemoglobin and haematocrit.[18] There are, however, some reported cases in which treatment does not improve symptoms, implying a degree of permanent cerebral damage.[19]

CONCLUSION

Polycythaemia vera should be considered as a reversible cause of chorea in older adults. The mainstay of treatment involves serial venesections to reduce haemoglobin and haematocrit to within normal ranges. Adjunctive chemotherapy may be required. The majority of patients achieve symptomatic improvement or resolution with treatment, although in some patients chorea persists indefinitely.

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