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doi: 10.1136/jnnp.2006.100842

Competing interests : None declared.

References

1 **Frassinetti F**, Nichelli P, di Pellegrino G. Selective horizontal dysmetropsia following prestriate lesion. *Brain* 1999;**122**:339–50.
2 **Ebata S**, Ogawa M, Tanaka Y, *et al*. Apparent reduction in the size of one side of the face associated with a small retrosplenial haemorrhage. *J Neurol Neurosurg Psychiatry* 1991;**54**:68–70.
3 **Cohen L**, Gray F, Meyrignac C, *et al*. Selective deficit of visual size perception: two cases of hemimicropsia. *J Neurol Neurosurg Psychiatry* 1994;**57**:73–8.
4 **Bender MB**, Teuber HL. Spatial organization of visual perception following injury to the brain. *Arch Neurol Psychiatry* 1948;**59**:39–62.
5 **Rizzo M**, Nawrot M, Blake R, *et al*. A human visual disorder resembling area V4 dysfunction in the monkey. *Neurology* 1992;**42**:1175–80.

Improvement in neuroleptic-induced akathisia with intravenous iron treatment in a patient with iron deficiency

Iron deficiency may play a role in the pathogenesis of drug-induced akathisia, but the evidence is conflicting.[1–3] There have been no reports of the effect of iron treatment in this condition. We report the case of a patient with iron deficiency whose akathisia had not responded to standard interventions but did respond dramatically to intravenous iron treatment.

A 68-year-old man with schizophrenia had been well controlled for 10 years on thioridazine 150 mg/day. His treatment was changed to respiridone 1 mg twice daily. Within 2 weeks, he had developed a severe sensation of inner restlessness and anxiety associated with increased leg movements and body rocking. No depressive or psychotic symptoms were noticed, although the patient was greatly distressed. Acute drug-induced akathisia was diagnosed.

No improvement in akathisia symptoms was noticed when the dose of respiridone was reduced or when respiridone was discontinued and thioridazine restarted. Therapeutic trials of alprazolam, benztropine and propranolol failed to alleviate his symptoms and led to side effects.

When seen in our clinic, the patient had had symptoms for >6 months. He reported a ''terrible feeling'' of restlessness and anxiety ''gnawing inside me'' each day. Symptoms were present throughout the day, with no worsening at night, and no limb paraesthesias were noticed. There was no personal or family history suggestive of restless legs syndrome (RLS). Neurological examination was normal apart from reduced facial expressiveness. The Barnes Akathisia Rating Scale (BARS), a well-validated scale of akathisia severity comprising objective and subjective components, was 11/14, which is consistent with severe akathisia.[2]

Electrolytes, serum urea, creatinine and glucose, thyroid function tests, erythrocyte sedimentation rate, C reactive protein, vitamin B_{12}, and folate levels were normal. Haemoglobin was 13.1 g% (abnormal in our laboratory <13 g%), transferrin saturation 12% (abnormal <15%), serum ferritin 36 μg/l (abnormal <12 μg/l), total iron-binding capacity 490 μg/l (abnormal >400 μg/l) and serum iron 520 μg/l (abnormal <600 μg/l). A diagnosis of iron deficiency was made on the basis of the abnormal transferrin saturation combined with a serum ferritin <50 μg/l.[4] Gastrointestinal examination was normal and serial tests for faecal occult blood were negative. He had a distant history of peptic ulcer disease. Dietary history showed inadequate intake of iron-containing foods. His dentition was poor. The patient refused endoscopic investigation of the intestinal tract. Screening tests for coeliac disease were negative.

Oral iron supplements caused unacceptable nausea and epigastric discomfort. The patient was given 400 mg intravenous ferrous sucrose in divided doses (100 mg in 100 ml normal saline on days 1 and 3, and 200 mg on day 5). On day 7, the patient reported that he felt normal for the first time in months. The BARS score was now 3/14 (corresponding to mild or questionable akathisia); haemoglobin was 13.8 g%, ferritin 52 μg/l and transferrin saturation 17%. Dietary advice was given to increase the intake of iron-containing food. Subsequently, he was able to tolerate 300 mg ferrous gluconate (containing 35 mg of elemental iron) every second day. Clinical (BARS score 3/14) and haematological (haemoglobin 13.7 g% and ferritin 68 μg/l) improvement were maintained on review at 5 months.

Both akathisia and RLS are characterised by motor restlessness and sleep disturbances, and RLS can be precipitated by dopamine-blocking drugs. There is convincing evidence that iron status is an important factor in the pathogenesis of RLS, and correction of iron deficiency improves symptoms in RLS.[5] The balance of evidence from previous studies does not suggest that iron deficiency plays a similarly critical role in the development of drug-induced akathisia in most patients. However, many studies either focused on serum iron,[1 2] which is not a good guide to iron status, or used an inappropriately low cut-off for normal serum ferritin.[4] Nevertheless, studies that examined ferritin levels reported that patients with akathisia had lower levels than controls without akathisia.[3]

Studies comparing blood tests with bone marrow examination have shown that serum ferritin at a cut-off of 50 μg/l is the best screening test for iron deficiency in patients with and without anaemia.[4] Furthermore, serum ferritin <50 μg/l has also proved useful for predicting responsiveness to iron supplementation in people with RLS.[5]

The patient in this report had several haematological indices suggestive of iron deficiency and several risk factors for iron deficiency. His serum ferritin of 36 μg/l is also consistent with mild iron deficiency. His haemoglobin level of 13.1 g% was at the low end of normality for a man. As a general rule, 8 mg of storage iron corresponds to 1 μg/l ferritin. Thus, in an iron replete person, 400 mg of intravenous iron would lead to a rise in serum ferritin of about 50 μg/l; the relatively small rise in ferritin levels in our patient suggests that the iron supplement was indeed used to correct a tissue deficiency in iron.

It is unlikely that this patient had an atypical RLS. No night-time worsening of symptoms (a necessary diagnostic feature in RLS) was noticed. The feeling of inner restlessness and body rocking are characteristic of acute drug-induced akathisia. It is not uncommon for akathisia, once provoked, to fail to resolve when the precipitating drug change is reversed.

The close temporal relationship between administration of intravenous iron and resolution of hitherto resistant symptoms in our patient suggests that iron deficiency can contribute to the development or persistence of akathisia in some patients. Iron repletion may be valuable in such cases, although this requires further evaluation. There are, of course, other potential benefits to treating and identifying the cause of iron deficiency. We suggest that haemoglobin, serum ferritin and transferrin saturation should be checked in patients with akathisia, and that patients with iron deficiency should be treated until haemoglobin is normal and serum ferritin is more than 50 μg/l. Although the use of intravenous iron formulations may facilitate examination of the potential effects of iron repletion on akathisia in future studies, biochemical improvement is usually seen within 2–4 weeks of starting oral iron supplements in patients with deficiency and this should remain the initial treatment.

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doi: 10.1136/jnnp.2006.101014

Competing interests: None.

References

1 **Brown KW**, Glen SE, White T. Low serum iron status and akathisia. *Lancet* 1987;**1**:1234–6.
2 **Barnes TR**, Halstead SM, Little PW. Relationship between iron status and chronic akathisia in an in-patient population with chronic schizophrenia. *Br J Psychiatry* 1992;**161**:791–6.
3 **Kuloglu M**, Atmaca M, Ustundag B, *et al*. Serum iron levels in schizophrenic patients with or without akathisia. *Eur Neuropsychopharmacol* 2003;**13**:67–71.
4 **Guyatt GH**, Oxman AD, Ali M, *et al*. Laboratory diagnosis of iron-deficiency anemia: an overview. *J Gen Intern Med* 1992;**7**:145–53.
5 **O'Keeffe S**, Gavin K, Lavan J. Iron status and restless legs syndrome in the elderly. *Age Ageing* 1994;**23**:200–3.

Guillain–Barré syndrome with antibodies to GD1a/GD1b complex

Recently, ganglioside complexes (GSCs) such as GD1a/GD1b, GD1a/GM1, GD1b/GT1b, GM1/GT1b, GQ1b/GM1 and GQ1b/GD1a have been

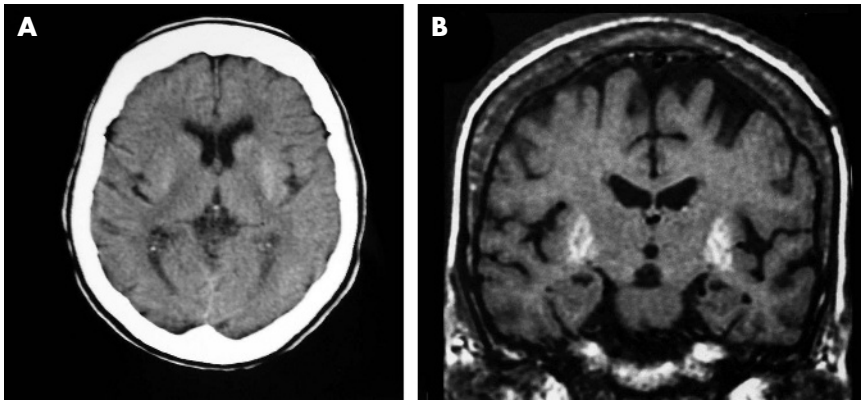

Figure 1 Image findings. (A) CT brain scan on admission—bilateral hyperdense putamen and caudate nuclei. (b) MRI brain scan conducted 2 weeks after admission—bilateral hyperintense putamen on T1W images.

support an autoimmune aetiology in the form of a secondary antiphospholipid syndrome caused by infection. However, no prothrombotic state was documented in the clinical and laboratory data and the neuropathological data provided no evidence of disseminated intravascular coagulation. In addition, patient age did not favour a primary autoimmune aetiology.

Regarding the signal changes observed on imaging studies, a critical appraisal of the published case reports with neuropathological results[3–5] emphasises the heterogeneity of the available data in terms of the time delay in neuropathological specimen collection, neuropathological findings, timing of imaging studies, characteristics of basal ganglia findings and the presence of concurrent relevant lesions. In two reported cases,[4 5] an association was postulated between the presence of reactive astrocytes and MRI changes. However, in the former case no significant hyperglycaemia was documented and an additional area of temporoparietal infarction was identified which could be associated with chorea onset. In the latter case, the findings were not observed in other regions with an identical signal alternation, namely the pallidum. In a third report,[3] calcium deposits and focal microhaemorrhages were found in the lesioned putamen and caudate where a confluent area of infarction was also observed. Although calcium was observed only on non-recent infarction areas, an association with the signal changes on CT and MRI was postulated. In addition, signal changes on MRI were localised to the anterior putamen only and did not involve the putamen more extensively, as usually observed in this syndrome.

Studies focusing on CT and MRI findings have also been inconclusive. Chu *et al*[1] conducted a gradient echo and diffusion weighted MRI study and suggested that signal changes corresponded to cytotoxic oedema. Conversely, another study[2] involving similar imaging procedures drew the same conclusions as our report. Nevertheless, both studies did not have access to neuropathology data which would confirm the accuracy of the imaging interpretation.

In our case, neuropathological findings were consistent with small previous haemorrhages in the striatum. This favours the hypothesis of petechial haemorrhages as the cause of this syndrome, suggested to be secondary to erythrocyte diapedesis due to hyperglycaemia induced blood–brain barrier dysfunction.[6] The observed vessel wall changes were consistent with a diabetes vasculopathy, which also provides an explanation for brain barrier dysfunction. Thus the initial CT changes correspond to blood and the later MRI findings to the presence of hemosiderin. Because of the transitory nature of this syndrome, a careful analysis of the reported cases, namely the timing for image and neuropathological data collection, is essential to fully understand its aetiology. Using other MRI sequences such as gradient echo or diffusion weighted imaging will further help in characterising image–neuropathology correlations.

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doi: 10.1136/jnnp.2006.105387

Competing interests : None declared.

References

1 **Chu K**, Kang DW, Kim DE, *et al*. Diffusion-weighted and gradient echo magnetic resonance findings of hemichorea–hemiballismus associated with diabetic hyperglycemia: a hyperviscosity syndrome? *Arch Neurol* 2002;**59**:448–52.
2 **Lai SL**, Tseng YL, Hsu MC, *et al*. Magnetic resonance imaging and single-photon emission computed tomography changes in hypoglycemia-induced chorea. *Mov Disord* 2004;**19**:475–8.
3 **Nath J**, Jambhekar K, Rao C, *et al*. Radiological and pathological changes in hemiballism–hemichorea with striatal hyperintensity. *J Magn Reson Imaging* 2006;**23**:564–8.
4 **Ohara S**, Nakagawa S, Tabata K, *et al*. Hemiballism with hyperglycemia and striatal T1-MRI hyperintensity: an autopsy report. *Mov Disord* 2001;**16**:521–5.
5 **Shan DE**, Ho DM, Chang C, *et al*. Hemichorea–hemiballism: an explanation for MR signal changes. *AJNR Am J Neuroradiol* 1998;**19**:863–70.
6 **Iwata A**, Koike F, Arasaki K, *et al*. Blood brain barrier destruction in hyperglycemic chorea in a patient with poorly controlled diatetes. *J Neurol Sci* 1999;**163**:90–3.