

# Newly diagnosed type-2 diabetes presenting with hemichorea-hemiballismus

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**ABSTRACT** Hemichorea-hemiballismus (HC-HB) is a unilateral, involuntary, random movement disorder that can involve both proximal and distal groups of muscles. It is caused by lesions in the contralateral corpus striatum. The most common aetiology is an acute cerebrovascular event, but infections, drugs, tumours and neurodegenerative disorders can all be implicated. Non-ketotic hyperglycaemia has been identified as a metabolic cause of HC-HB, particularly in elderly female patients with newly diagnosed or poorly controlled diabetes. These patients tend to have a characteristic hyperintense signal in the putamen on T1-weighted MR imaging. Often the movement disorder resolves within days to weeks after correction of the hyperglycaemia, but complete resolution of the radiological signs commonly takes months. An 86-year-old woman with newly diagnosed type-2 diabetes presented with hyperglycaemia-induced right-sided HC-HB and typical contralateral high signal change in the putamen on T1-weighted MR scanning. Her symptoms completely resolved within five days of achieving euglycaemia.

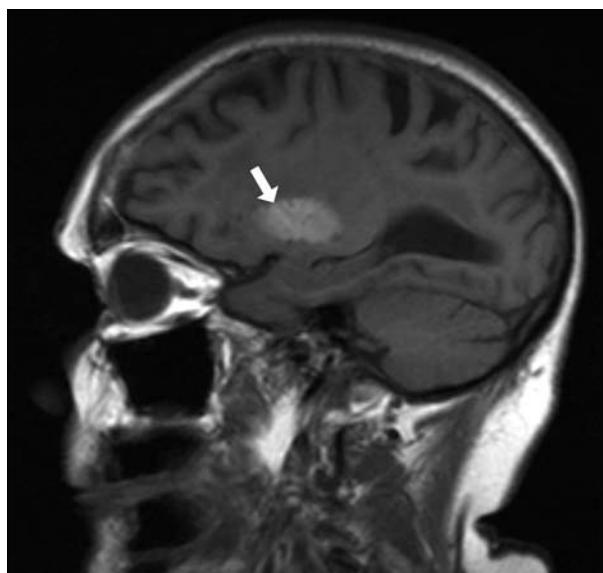
**KEYWORDS** Hemiballismus, hemichorea, hyperintense putamen signal, non-ketotic hyperglycaemia, T1-weighted MRI

**DECLARATION OF INTERESTS** No conflict of interests declared.

## CASE REPORT

An 86-year-old Caucasian woman presented as an emergency with a 24-hour history of confusion and abnormal movement involving the right side of her body. The abnormal movement was jerky, irregular and non-suppressible, but it resolved completely during sleep. She had been diagnosed with type-2 diabetes two weeks prior to admission and started on metformin. She was known to be hypertensive, but otherwise her past medical history was unremarkable. There was no personal or family history of movement disorders and she was not on any medication known to cause abnormal movement.

On examination she was alert as well as fully orientated, and there was no obvious focal motor or sensory deficit. The pertinent abnormality was a right-sided hemichorea-hemiballismus (HC-HB) type movement disorder affecting mainly the upper extremity but also involving the lower extremity. Her random plasma glucose level was significantly elevated, measuring 18 mmol/l with a HbA1c of 15.2%, but there was no evidence of ketoacidosis or hyperosmolar state. A computerised tomography (CT) scan of the brain revealed only small vessel ischaemic changes with no focal lesion, but her magnetic resonance imaging (MRI) scan demonstrated a hyperintense signal in the putamen on T1-weighted images (Figure 1). Her HC-HB resolved completely



**FIGURE 1** An 86-year-old Caucasian woman presented as an emergency with a 24-hour history of confusion and abnormal movement involving the right side of the body. Sagittal view of a T1-weighted MRI scan of the brain showing a high-intensity signal in the putamen (arrow), which is described as a characteristic imaging abnormality in patients with non-ketotic hyperglycaemia associated hemichorea-hemiballismus. The movement disorder completely settles within days to weeks of achieving euglycaemia, but the radiological sign can take months to resolve.

within five days of achieving euglycaemia with insulin infusion. She has since been reviewed as an outpatient, and there was no recurrence of HC-HB five months following her discharge from hospital. We intended to repeat her MRI brain scan to determine whether the high signal putaminal lesion has resolved or not, but the patient declined this because of claustrophobia.

## DISCUSSION

Hemichorea-hemiballismus belongs to a spectrum of hyperkinetic movement disorders characterised by purposeless, jerky and involuntary contraction involving proximal and distal muscles of the upper and lower extremities. The movement tends to be more coarse and jerky in hemiballismus because of predominant proximal muscle involvement, whereas hemichorea mainly affects distal groups of muscles. Hemichorea-hemiballismus should not be confused with focal motor seizure, which has a rhythmic, episodic quality and tends to be more localised. The causative lesion is commonly found in the corpus striatum, but it can occur anywhere along the afferent or efferent pathways connecting the striatum to its projection areas. By far the most common cause of HC-HB is a cerebrovascular insult in the region of the striatum and subthalamic nucleus, but a variety of pathologies including tumours, neurodegenerative disorders, encephalitis, drugs, systemic lupus erythematosus (SLE) and metabolic disorders such as hyperthyroidism have all been associated with this condition.

Non-ketotic hyperglycaemia has been described as an unusual metabolic cause of this abnormal movement disorder. Although mostly associated with HC-HB, other rare movement disorders such as oro-buccal-lingual dyskinesia have also been described in hyperglycaemia.<sup>1</sup> These patients tend to have either newly diagnosed or poorly controlled diabetes. In two separate series of six and eight type-2 diabetic patients presenting with HC-HB reported by EJ Lee et al. and BC Lee et al., the mean HbA1c was 10.6% and 12.9% respectively, consistent with poorly controlled diabetes.<sup>2,3</sup> It commonly affects post-menopausal women, possibly related to increased dopamine receptor sensitivity secondary to oestrogen deficiency.<sup>2-4</sup> The mean age for the above two series was 66 years. The majority of reported cases are from Eastern Asia, suggesting a possible underlying genetic predisposition to this movement disorder in the setting of hyperglycaemia.<sup>2-4</sup> Acanthocytosis has also been described as a possible predisposing factor for non-ketotic hyperglycaemia-induced HC-HB in a small case series by Pisani et al.<sup>5</sup>

The pathophysiology of hyperglycaemia-induced HC-HB is not fully elucidated, although several different mechanisms have been proposed. One such mechanism is the prevalence of anaerobic metabolism in a hyperglycaemic state, which forces the brain to use  $\gamma$ -aminobutyrate

(GABA).<sup>2-4</sup> The brain tissue metabolises GABA to succinic acid, thereby inducing metabolic acidosis. Unlike a ketotic state with abundant acetoacetate which can be used to synthesise GABA and acetylcholine, there is a lack of this raw material in non-ketotic hyperglycaemia, causing depletion of both neurotransmitters. The deficiency of these neurotransmitters, along with metabolic acidosis, has therefore been proposed to be the mechanism for hyperglycaemia-induced HC-HB. Other proposed mechanisms include hyperviscosity related to non-ketotic hyperglycaemia and underlying cerebrovascular disease.

The typical radiological feature is the finding of a hyperintense signal on a T1-weighted MRI scan in the putamen and adjacent structures such as the caudate nucleus.<sup>2-6</sup> This characteristic MRI appearance was thought to be due to a haemorrhagic process, but neuropathology studies from the high signal areas only revealed astrocytosis with no haemosiderin deposits.<sup>7</sup> Single-photon emission computed tomography (SPECT) studies have detected disturbed vascular autoregulation, and this, along with impaired glucose metabolism as shown on positron emission tomography (PET) studies, is proposed as a possible mechanism for the high signal lesions on MRI scans.<sup>8</sup>

Hypoglycaemia has also been associated with HC-HB, albeit with different radiological features.<sup>9,10</sup> The clinical manifestations are similar to those seen in hyperglycaemia-induced HC-HB, apart from the accompanying autonomic symptoms of hypoglycaemia. However, unlike hyperglycaemia-related HC-HB, the T1-weighted MRI scans show a low signal in the basal ganglia, whereas the T2 signals are notably of high signal.

The prognosis for non-ketotic hyperglycaemia-related HC-HB is good, with most cases recovering completely within a few days of achieving euglycaemia, as was the case with our patient. Among the six cases reported by EJ Lee et al., the period of recovery ranged from one to six weeks, and in the case series from BC Lee et al. the mean duration to recovery was two weeks. Drugs can be used for symptomatic control, but the response to treatment is variable. GABA mimetic agents such as benzodiazepines and valproate have been used successfully to suppress the abnormal movement, but there are also case reports of a similar response with haloperidol, tetrabenazine and the anticonvulsant topiramate.<sup>11,12</sup>

## CONCLUSION

Abnormal blood glucose levels should be considered as a possible aetiological factor in any patient presenting with hemichorea-hemiballismus. The prompt detection of abnormal blood glucose and treatment that achieves euglycaemia can lead to early recovery from this distressing movement disorder.

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