Chorea-ballismus in acute non-ketotic hyperglycaemia

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Summary

Diabetic patients during hyperglycaemic crises may present a rare syndrome characterised by a typical triad: unilateral involuntary movements (hemichorea-hemiballism), radiological contralateral striatal abnormality, and rapid resolution of symptoms after glycaemic correction.

This study reports a series of patients showing less usual aspects and also discusses the pathophysiology of this clinical-radiological syndrome. We included in this study four patients presenting choreic or ballic involuntary movements and in whom aetiologi
cal assessment revealed frank non-ketotic hyperglycaemia, without other abnormalities that could explain the movement disorder. All the patients underwent CT or MR brain imaging.

Key Words: diabetes, hemichorea-hemiballism, hyperglycaemia, imaging

Introduction

Non-ketotic hyperglycaemia (NKH) has been associated with various neurological disorders, and among these, chorea-ballismus is one of the most frequently observed syndromes (1). A review of the literature shows that in most described cases of this syndrome the clinical presentation, radiological findings and outcome are homogeneus (1-4): patients classically had longstanding, poorly controlled diabetes and presented typically unilateral involuntary movements (hemichorea-hemiballism) associated with a peculiar radiological pattern in the contralateral striatum, consisting of spontaneous hyperinten
tuation on computed tomography (CT) scan and hyperintensity on T1-weighted magnetic resonance imaging (MRI). Movement disorders were often reversible within days of blood glucose normalisation. The pathogenetic mechanisms underlying these clinical and radiological findings are still controversial although many authors are trying to clarify them (1,3,5-7).

Here, we describe four patients who developed NKH-induced chorea-ballismus and discuss some clinical, radiological and outcome peculiarities they presented.

Case reports

Table 1 (over) summarises the main clinical, laboratory, imaging and outcome characteristics of the four patients.

Patient 1

A 76-year-old Caucasian man, with no personal history of neurological illness, was admitted for movement disorders involving the left side of the body which had appeared sub-acutely four weeks previously. Neurological examination revealed choreiform and proximal ballic movements involving the left hemisoma including the face and occurring predominantly in the lower limb. There were no other clinical abnormalities. Laboratory studies demonstrated high glucose values (3900 mg/litre; normal values, 700-1100) with no evidence either of ketosis or of other metabolic abnormalities. A cranial CT scan showed spontaneous high density clearly confined to the right striatum without mass effect (Fig. 1a, over). Achievement of euglycaemia with insulin therapy led to a partial improvement of the symptoms. Haloperidol 6 mg/day provided no additional clinical benefit after two months of treatment. Tetrabenazine 50 mg/day was started, giving considerable benefit but not complete disappearance of the involuntary movements after six months of treatment. A control cranial CT scan one month later showed regression of the striatal hyperdensity (Fig. 1b, over).
Patient 2

A 79-year-old Caucasian man, with a history of type 2 diabetes mellitus and hypertension, complained of the acute appearance, nearly four weeks earlier, of involuntary movements involving his left hemisoma. He presented choreic-ballic movements of both his left arm and left leg with no facial involvement. He presented symmetrically reduced deep tendon reflexes, otherwise his neurological examination was normal. His blood glucose was 4200 mg/litre with a haemoglobin A1c value of 13.3% and no ketone bodies in the urine. He underwent brain MRI, which showed a right striatal hyperintensity on T1-, T2-, and FLAIR-weighted (Fig. 2) images extending to the pallidum with sparing of the internal capsule. Correction of hyperglycaemia with insulin produced only a modest benefit. Pharmacological treatment with haloperidol led, after several weeks, to a progressive and total regression of the involuntary movements. A control CT scan four months later was normal.

Patient 3

A 59-year-old Caucasian woman presented at the emergency department after experiencing uncontrollable and irregular jerking movements of the right side of her body, particularly the right foot, which had begun four days earlier. She had a seven-year history of type 2 diabetes mellitus with poor glycaemic control. A cranial CT scan showed spontaneous hyperdensity of the left striatum (Fig. 3). Peripheral blood investigations revealed frank and isolated hyperglycaemia (4800 mg/litre) with a haemoglobin A1c value of 15% and no ketone bodies in the urine. A diagnosis of NKH-induced hemichorea-hemiballism was made. Insulin therapy was started leading to rapid glycaemic control followed by complete resolution of the abnormal movements within 72 hours. A control CT scan one month later was normal.

Patient 4

A 68-year-old Caucasian woman with no personal history of illness, particularly diabetes, was admitted to hospital because of involuntary movements which had begun suddenly three days earlier. Clinical examination revealed typical generalised chorea of the four limbs, trunk and face without ballic components. She was not taking neuroleptic medication and there was no family history of chorea. Brain imaging including CT scan and MRI did not reveal any lesion in the basal ganglia. The aetiological diagnostic workup confirmed the presence of severe hyperglycaemia (5100 mg/litre) without further abnormalities (especially in thyroid function tests, antistreptolysin O, antinuclear, antiDNA and antiphospholipid antibodies). Regular, subcutaneous insulin therapy induced a progressive correction of the metabolic disequilibrium as well as a parallel reduction of the abnormal involuntary movements, which had disappeared totally 48 hours after the start of treatment.
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Discussion

Several authors have offered pathophysiological explanations for the movement disorders and abnormal radiological features observed in severe hyperglycaemia, but these studies remain inconclusive (3,5,6). A striatal lesion may, via disinhibition of the subthalamic nucleus, be responsible for the hyperkinetic involuntary movements, but a role for the metabolic disorder must also be considered, given the possible occurrence of clinical symptoms without radiological abnormalities (8,9) and the rapid regression usually seen following only correction of the glycaemia (1,3,4). Most authors (3,7) attribute the radiological findings (striatal hyperdensity on CT scan and hyperintensity on T1 MRI) to a petechial haemorrhage secondary to erythrocyte diapedesis caused by hyperglycaemia-induced blood-brain barrier dysfunction (7). Other possible explanations are also advanced, in particular a reversible calcium deposit (10) or local cytotoxic oedema and gemistocyte accumulation induced by a mild ischaemia (5,6). Anatomopathological study of biopsy specimens (6) and necropsy reports (7) have not put an end to this debate.

The clinical-radiological presentation and outcome profile of the NKH-induced chorea-ballismus syndrome are relatively homogeneous (see above). This study describes some less usual aspects:

i) In patients 1 and 4, there was no known history of diabetes. Classically, patients with this syndrome have longstanding, poorly controlled diabetes responsible for a vasculopathy thought to predispose to striatal damage in hyperglycaemic crises (2,7). The present observation and others (1,11) show that abnormal movements may be the first manifestation of undiagnosed diabetes mellitus.

ii) Patient 4 developed, within hours, choreic movements not confined to a single hemisoma. Generalised chorea, with or without a ballistic component (biballismus), occurring in association with NKH is rarely reported (2,7-9). This suggests that acute hyperglycaemia should be suspected as a possible aetiology of generalised chorea such as that seen in degenerative, infectious, autoimmune and other metabolic (e.g. thyroid) diseases or in drug abuse (12).

iii) Case 4 illustrates the point that the morphological imaging can be strictly normal. In 53 cases studied by Oh and al. (2), of which 49 were drawn from the literature, radiological abnormalities were consistently found. Observations showing no radiological lesion (as in the present case) have rarely been published (8,9) and these reports argue that hyperglycaemia, causing striatal neuronal dysfunction, may play a direct role in the pathogenesis of the clinical symptoms. On the other hand, striatal hyperintensity has been detected in patients with NKH but no abnormal movements (13).

iv) Normalisation of the glycaemia is not always sufficient to get rid of the involuntary movements (10,14), and indeed two of our patients required symptomatic treatments in order to achieve a satisfactory improvement. In patient 2, haloperidol had a marked clinical effect, while it was not effective in patient 1, in whom tetrabenazine was needed to improve the clinical symptoms. In patient 1, the abnormal movements did not disappear completely, still being present after six months of treatment. Although tetrabenazine, a presynaptic dopamine depletor, is very effective in a variety of hyperkinetic movement disorders, its use in the chorea-ballismus associated with NKH has been reported in only one publication (15), in which the therapy was successful. Unlike patients 3 and 4 who showed a rapid recovery after simple correction of the glycaemia, patients 1 and 2 had a relatively long delay before coming to our attention and receiving treatment, which suggests that a delay in diagnosis (and consequently in treatment) could be a factor contributing to a poor outcome prognosis.

In conclusion, patients reporting sudden onset of involuntary movements, choreic or ballistic, should undergo glycaemia measurement, even in the absence of a known diabetes history. Radiological abnormalities are classically found in the striate area, but their absence re-
mains compatible with diagnosis. Prompt insulin therapy of the underlying hyperglycaemia usually leads to complete resolution of the abnormal movements, although these may persist despite symptomatic treatments.

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References

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