Hemiballism-hemichorea and non-ketotic hyperglycaemia

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Abstract

Three patients with hemiballism-hemichorea caused by non-ketotic hyperglycaemia are presented, two of whom had hyperosmolar non-ketotic hyperglycaemic syndrome. In two of the three patients, the hyperkinesia was the initial presenting symptom of their diabetes mellitus. The hypersensitivity of the postmenopausal dopamine receptor, decreased \( \gamma \)-aminobutyric acid in the brain in non-ketotic hyperglycaemia, coexisting lacunar infarct in the basal ganglion, and pre-existing metabolic dysfunction in the basal ganglion may all have played a part in the pathogenesis of this movement disorder.

Methods

From January 1986 to December 1992, a total of 20 patients with hemiballism-hemichorea were registered at the special clinic for movement disorders in the neurological department of our hospital; in three of these the disease was caused by non-ketotic hyperglycaemia. Two of the three had HNKS (table 1), based on the fact that patients with HNKS have hyperglycaemia, an absence of ketonaemia, and a plasma osmolality greater than 320 mmol/kg.

Case reports

PATIENT 1

Patient 1 was a 74 year old woman without a history of diabetes mellitus, but with hypertension and cirrhosis of the liver for several years. She suddenly developed continuous, arhythmic, and purposeless choreiform involuntary movements, mainly affecting her left arm. The symptoms were aggravated by talking, or when asked to extend the left arm; were less prominent when relaxed; and nonexistent during sleep. Neurological examination was normal, except for reduced deep tendon reflexes and hemichorea in the left arm. Blood glucose concentration was 30.5 mmol/l and the estimated blood osmolality was 332 mmol/kg. No ketones were detected. She was dehydrated. Insulin was given intravenously and symptoms disappeared within two days. At this time her blood glucose concentration was 13.8 mmol/l and blood osmolality was 290 mmol/kg. A brain CT showed cortical atrophy and calcification of bilateral basal ganglion.

PATIENT 2

Patient 2, a 78 year old man with a history of hypertension but without diabetes mellitus, had polydipsia, polyuria, and weight loss, accompanied for two weeks by involuntary writhing movements over his face and right forearm. Examination revealed uncontrolled...
and purposeless choreiform movements, occasionally accompanied by rapid uncontrolled flinging ballistic movements of his right arm. Involuntary twitching and grimacing of the right side of his face were also seen. Neurological examination was otherwise normal. His blood glucose concentration was 61.4 mmol/l and the osmolality was 367 mmol/kg. No ketonaemia was noted. He was rehydrated and treated with insulin and antibiotics intravenously. The next morning, the involuntary movements had disappeared, but asterixis of both hands was seen later. Treatment with insulin was continued, and the patient’s blood glucose concentration was controlled around 7.2–13.9 mmol/l. Three days later, the asterixis also disappeared. A CT of the brain showed only cortical atrophy.

PATIENT 3
Patient 3 was a 75 year old woman with a history of diabetes mellitus and hypertension. She suddenly developed a right sided weakness with signs of drowsiness. Hemichorea of her right arm was also noted. Neurological examination showed her to be drowsy with a right hemiparesis. The deep tendon reflexes were symmetrically reduced, with flexor plantar responses. Her blood glucose was 36.6 mmol/l and estimated blood osmolality was 390 mmol/kg. She was rehydrated and treated with insulin and antibiotics. The next morning, the hyperkinesia and weakness had resolved. Her blood glucose concentration was 16.4 mmol/l and blood osmolality was 329 mmol/kg. A brain CT revealed an old infarct lesion in the left basal ganglia, with low density in the periventricular region.

Discussion
Hemiballism-hemichorea caused by non-ketotic hyperglycaemia was first reported by Bedwell in 1960. He described a 65 year old woman who developed ballistic movements in all four limbs during three episodes of hyperglycaemia.7 Patients with hyperkinetic movements caused by non-ketotic hyperglycaemia have been reported by Rector et al,8 Tortoritis et al,9 and Sanfield et al,10 but none of the patients had HNKS. In our study, two of the three cases (patients 2 and 3) satisfied the criteria for HNKS.

Patients with diabetes mellitus often initially present with symptoms including polyphagia, polydipsia, weight loss, generalised weakness, and fatigue.11 In our study, two of the three cases (patients 1 and 2) also had hemiballism-hemichorea as an initial presenting symptom. Movement disorders as the initial presenting symptoms of diabetes mellitus are rare; only Hahn et al12 and Sanfield et al13 have reported cases of generalised chorea and hemichorea.

A total of nine cases of hemiballism-hemichorea caused by non-ketotic hyperglycaemia have been reported, mostly in older women (table 2). Oestrogen can decrease the dopamine (DA) function of the nigrostriatal system and subsequently increase the density of the DA receptors.13 16 Concentrations of oestrogen decrease in women after the menopause, which contributes to the development of supersensitivity in the striatal DA receptor. Studies have also shown the concentration of DA in the striatum and substantia nigra to be normal or slightly increased in patients with Huntington’s chorea,17 and that hemichorea can be suppressed by neuroleptic drugs.4 18 We postulate that DA hypersensitivity in postmenopausal women is the reason for their predisposition for developing this type of hyperkinesia with non-ketotic hyperglycaemia.

In hyperglycaemia, cellular energy demand shifts towards anaerobic metabolism, which inhibits the function of the tricarboxylic acid cycle and causes the brain to metabolise γ-aminobutyric acid as an alternative energy source.19 Patients with ketosis would have an abundant source of acetocacetate from which γ-aminobutyric acid might be resynthesised, but non-ketotic patients would be rapidly depleted. In animal studies, γ-aminobutyric acid antagonists can cause a lesion in the subthalamic nucleus, inducing contralateral hemichorea.20 We therefore propose that the depletion of γ-aminobutyric acid in the brain may play an important part in the pathogenesis of the non-ketotic hyperglycaemia, and HNKS induced hemiballism-hemichorea.

Most cases of hemiballism-hemichorea associated with non-ketotic hyperglycaemia have occurred in elderly patients with hypertension or diabetes mellitus. Hypertension and diabetes mellitus greatly increase the risk of stroke, as well as increase the incidence of lacunar infarction of the brain.21 Deep lacunar infarctions may not be visible on CT, so that coexisting lacunar infarction in the contralateral basal ganglion might be the cause of this type of hyperkinesia in patients with non-ketotic hyperglycaemia. Two of our three patients showed calcification in the basal ganglia and multiple infarcts on CT. The acute metabolic effect of non-ketotic hyperglycaemia on this background, produces the movement disorder.

Most patients with hemiballism-hemichorea show partial or complete resolution after treatment with neuroleptic drugs, but it is usually necessary to continue the drugs for a long period.4 18 Some patients on the other hand do not respond to any medication.4 In our study, all three patients dramatically recovered from their hyperkinesia after control of the hyperglycaemia was achieved, showing that hemiballism-hemichorea caused by hyperglycaemia is a treatable disorder with a good prognosis.

Table 2 Multiple series of hemiballism-hemichorea caused by non-ketotic hyperglycaemia

<table>
<thead>
<tr>
<th>Source Year</th>
<th>No of patients</th>
<th>Age (y)</th>
<th>sex</th>
<th>No of patients</th>
<th>Age (y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bedwell’ 1960</td>
<td>1</td>
<td>65/F</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rector et al1982</td>
<td>3</td>
<td>80/F, 62/M, and 46/F</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tortoritis et al1982</td>
<td>1</td>
<td>77/F</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sanfield et al10 1986</td>
<td>1</td>
<td>76/F</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>This study 1994</td>
<td>3</td>
<td>64/F, 78/M and 75/F</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>9</td>
<td>46–80/M:F = 2:7</td>
<td></td>
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</tr>
</tbody>
</table>
In conclusion, although hemiballism-hemichorea is rarely caused by a dysfunction of glucose metabolism, we advise checking blood glucose whenever patients with this type of hyperkinesia are encountered, particularly in older women, as the condition may rapidly resolve with hydration and resolution of the hyperglycaemia. It is also advisable to keep in mind that this movement disorder may be the initial presenting symptom of diabetes mellitus.

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1 Martin TP, Alcock NS. Hemichorea associated with a lesion of the corpus luyius. Brain 1934;57:504-5.