Paroxysmal Dyskinesia Associated with Hypoglycemia

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ABSTRACT: The association of movement disorders with hypoglycemia has been rarely noted in the past. We recently observed 2 patients with documented hypoglycemia and paroxysmal dyskinesias. One patient had evidence of an insulin-secreting tumor. The other patient had insulin-dependent diabetes, and also experienced recurrent episodes of hypoglycemic hemiparesis. Classical adrenergic symptoms of hypoglycemia were absent in both patients. Our observations support the concept that the development of neuroglycopenic symptoms cannot be predicted from blood glucose measurements alone, but must depend on other factors controlling the availability or metabolism of glucose in the brain.


In 1937 Golden described the occurrence of a variety of involuntary movements in psychiatric patients undergoing insulin-induced hypoglycemic shock treatment.1 During deeper stages of coma, some patients developed “irregular, thrashing, apparently purposeless movements of the arms and legs” which Golden distinguished clinically from “true epileptic seizures” he had also observed in some patients. He further noted that similar involuntary movements had not been described in association with “accidental hypoglycemia arising as a complication of diabetic treatment nor as a symptom of pancreatic adenoma.”

In more recent decades, since the abandonment of insulin shock therapy, the association of paroxysmal dyskinesias with hypoglycemia has been rarely documented.2,3,4,5

We have recently seen 2 patients who presented with involuntary movements associated with episodic hypoglycemia. The first patient had a pancreatic tumor. The second patient had insulin-dependent diabetes mellitus and, in addition to paroxysmal dyskinesias, suffered episodes of alternating hemiparesis during hypoglycemia.

CASE REPORTS

Patient 1
A 54-year-old man with chronic hypoglycemia of undetermined etiology presented with a 4-year history of episodic uncontrollable limb movements. The attacks usually began with a sudden “restless sensation” in his lower limbs, followed by chaotic thrashing of his legs and sometimes arms. He denied experiencing loss of consciousness, urinary incontinence or tongue biting during the attacks. When the episodes occurred at work, he usually would get out of his chair and lie on the floor to prevent injury. His coworkers would then give him orange juice which reliably aborted the attacks. The episodes lasted from 2 to 15 minutes and occurred approximately 10 to 15 times during the previous 12 months. The movements were not provoked by sensory stimulation nor by attempts to move his limbs.

In addition to the daytime attacks described above, his wife had frequently witnessed 2 types of early morning spells occurring around his usual time of awakening. One type of spell was similar to the daytime episodes of dyskinesia, except in his wife’s opinion, he was also confused during the episode. A second type of early morning event did not include involuntary limb movements; instead it was characterized by passive confusion, staring and automatons, and likely represented complex partial seizures. Either type of early morning attack was more likely to occur if he omitted his 2 a.m. snack, and resolved once his wife was able to get him to drink orange juice.

There was no history of adrenergic symptoms of hypoglycemia, such as diaphoresis, tremor or palpitations, during any of the episodes. Apart from hypoglycemia, he had no other medical illness. The only medication he was taking was diazoxide, which was prescribed to help control his hypoglycemia. There was no family history of movement disorders, seizures or any other form of neurological disease. Except for mild memory impairment for recent events, the rest of his mental status and neurological examination was normal.

The following laboratory investigations were normal: complete blood count; sedimentation rate; electrolytes; renal, liver, and thyroid
Evidence of seizure activity was never witnessed in relation to hemiparesis when measured during an EEG documented seizure. Clinical seizures were musicogenic and her blood glucose level was not impaired of consciousness nor any accompanying adrenergic symptoms of hypoglycemia were absent.

Besides episodes of hemiparesis she also reported separate attacks of choreiform movements, predominantly involving the upper limbs. The attacks were bilateral or unilateral involving either side, and lasted between episodes.

Patient 2

A 24-year-old woman with insulin-dependent diabetes mellitus presented with recurrent episodes of hemiparesis involving either side. Right hemiparetic spells were sometimes associated with aphasia. Several episodes were witnessed in hospital and typically occurred during early morning hours (2 - 6 a.m.) with complete resolution over the course of 6 hours. There were no sensory symptoms and classical adrenergic symptoms of hypoglycemia were absent.

Besides episodes of hemiparesis she also reported separate attacks of choreiform movements, predominantly involving the upper limbs. The attacks were bilateral or unilateral involving either side, and lasted 1 to 2 hours. Similar to the hemiparetic episodes, the attacks of choreiform movements occurred in the early morning hours, and there was no impairment of consciousness nor any accompanying adrenergic symptoms.

She had a history of migraine, but did not experience headaches in association with the neurological symptoms described above. She also had a past history of complex partial seizures lasting 5 to 10 minutes that were well controlled by carbamazepine. Approximately 80% of the seizures were muscigenic and her blood glucose level was not depressed when measured during an EEG documented seizure. Clinical evidence of seizure activity was never witnessed in relation to the hemiparetic spells, nor in association with the attacks of choreiform involuntary movements. There was no family history of neurological symptoms. Her insulin dose was 18/8 units (NPH/Regular) in the morning, 18/4 units in the afternoon. Her neurological examination was normal between episodes.

The following laboratory investigations were normal: complete blood count; sedimentation rate; electrolytes; renal, liver, and thyroid function tests; CT scan of brain; and a routine EEG. The glycated hemoglobin A1c was 9.5%. Her blood glucose levels varied between 7 and 18 mmol/l and were generally lowest between 2 and 4 a.m. During 2 of the early morning hemiplegic episodes her glucose levels were 2.3 and 4.1 mmol/l respectively.

Video-EEG Recorded Event

An attack of bilateral upper limb choreoathetotic movements was recorded during a trial of insulin-induced hypoglycemia. She also displayed mild confusion during the episode. Her blood glucose level was 6.0 mmol/l before the event and 2.0 mmol/l during the episode which was subsequently aborted by administration of intravenous glucose. No evidence of epileptiform activity was recorded on the EEG during the hypoglycemic period.

DISCUSSION

Dyskinesias occur in a variety of hereditary, structural, infectious, metabolic, and toxic conditions. However, there are few disorders in which involuntary movements occur primarily as paroxysmal events and these can be broadly grouped into familial forms and those presumed to be secondary to an identifiable abnormality. The three main familial varieties are paroxysmal dystonic choreoathetosis, paroxysmal kinesigenic, and an intermediate type. Secondary forms of paroxysmal dyskinesia have been attributed to multiple sclerosis, head trauma, thalamic infarction, birth asphyxia, hypernatremia, thyrotoxicosis, and hypoparathyroidism.

It is well known that besides diffuse cerebral manifestations such as coma, both hyperglycemia and hypoglycemia can induce either negative (e.g., hemiparesis, hemianopsia) or positive (e.g., seizures) focal neurological symptoms. Paroxysmal dyskinesia is another form of positive neurological symptom that has been reported in several patients with hyperglycemia.

Our second patient illustrates that hypoglycemia may cause recurrent hemiplegia mimicking transient ischemic attacks. In their review of the literature, Foster and Hart noted that 86% of 29 patients with hypoglycemia-induced hemiplegia had diabetes mellitus and were receiving insulin or oral hypoglycemic drugs, and the attacks alternately involved the left or right side in 39%.

We are aware of only 4 patients described in the recent literature with paroxysmal involuntary movements associated with hypoglycemia. Newman and Kinkel observed a 45-year-old woman with diabetes mellitus who had recurrent episodes of choreoathetosis and altered sensorium during insulin-induced hypoglycemic episodes. Haan et al. reported an 80-year-old woman who initially presented with hyperglycemia, seizures and hemiparesis, but following treatment developed fluctuating choreoathetotic movements whenever the blood glucose level decreased below 5 mmol/l. Prajua et al. documented the occurrence of paroxysmal choreoathetosis in a 55-year-old male with alcohol-induced hypoglycemia. Sudhakar et al. described a 49-year-old male with a 10-year history of episodic involuntary movements associated with hypoglycemia of undetermined etiology.

Our first patient was found to have a pancreatic tumor that was presumably the source of the inappropriately elevated insulin levels. To our knowledge however, the occurrence of paroxysmal dyskinesias has not previously been noted in patients with insulinomas. Despite a high incidence of neurological symptoms in patients with insulinomas, Daggett and Nabarro did not identify any patients with involuntary movements among the 30 patients in their series nor among 220 patients reported in the literature.

Except for the patient described by Sudhakar, adrenergic symptoms have been conspicuously absent in previously described cases of hypoglycemia-induced dyskinesias, as is true for our 2 patients. Similarly, in a review of 125 visits to an emergency room by patients with hypoglycemia and neurological symptoms, Malouf and Brust also noted adrenergic symptoms to be rare. It is well recognized that hypoglycemia may fail to induce an epinephrine response in patients on beta-blocker medication or in diabetic patients because of underlying autonomic neuropathy. It also appears that non-diabetic
subjects, with presumably normal autonomic function, may fail
to manifest classical warning signs of hypoglycemia during the
development of neuroglycopenia.

It is apparent that blood glucose levels should be determined
in any patient with paroxysmal dyskinesias, especially diabetics
since they may develop glucopenia or hyperglycemia, both of
which can cause involuntary movements. However, neurological
symptoms do not necessarily correlate well with single blood
value determinations during an attack. For instance, although
those with a normal range (4.1 mmol/l). Whether variation in
threshold is due to different rates of decline in blood glucose
levels, different rates of glucose transport into the nervous system,
or some other mechanism, remains to be determined.17

It is not known why some patients develop focal neurological
symptoms in response to perturbations of blood glucose concen-
trations while most individuals do not; however, the presence of
pre-existing asymptomatic brain lesions has been suggested.5,12
Indeed, at autopsy Sudhakar’s patient was found to have
changes in the basal ganglia “compatible with subinfracture Por-
tional insults”;3 Vincent’s patient with hyperglycemia-induced
choreoathetosis had a vascular malformation in the lentico-
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