CASE REPORTS/CLINICAL VIGNETTES

Prolonged Cerebellar Ataxia: An Unusual Complication of Hypoglycemia

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A 51-year-old male with a history of insulin-dependent diabetes and polysubstance abuse presented after overdose on insulin. Soon after resuscitation, he displayed a severe ataxia in all 4 limbs and was unable to walk; all of which persisted for at least 5 days. Laboratory testing was unrevealing, including relatively normal brain magnetic resonance imaging. He had recovered full neurologic function 3 months after the event. This report describes a case of reversible cerebellar ataxia as a rare complication of severe hypoglycemia that may occur in patients with abnormal cerebellar glucose metabolism. Thus, this phenomenon should be included in the differential diagnosis of patients with a history of hypoglycemia who present with ataxia. In this context, the differential diagnosis of cerebellar ataxia is discussed, as is the proposed mechanism for hypoglycemia-induced cerebellar dysfunction.

KEY WORDS: hypoglycemia: ataxia: diabetes mellitus.
J Gen Intern Med 23(1):103–5
DOI: 10.1007/s11606-007-0407-x

INTRODUCTION

The neurologic manifestations of hypoglycemia include behavioral change, confusion, loss of consciousness, and seizures. Rarely, neuroglycopenia can present as ataxia, and prolonged and potentially irreversible deficits may occur with repeated episodes of hypoglycemia.[1,2] This phenomenon is thought to be because of abnormal glucose metabolism in the cerebellum.[3] In this paper, we report the case of a 51-year-old male with diabetes and polysubstance abuse who experienced prolonged but reversible cerebellar ataxia after a severe hypoglycemic episode. His case highlights a seldom-reported cause of ataxia and, in addition to providing an opportunity to review the differential diagnosis of ataxia, serves as a reminder that a history of severe hypoglycemia should be assessed in patients presenting with these findings.

Received February 6, 2007
Revised June 12, 2007
Accepted September 24, 2007
Published online November 14, 2007

CASE PRESENTATION

A 51-year-old African-American male with a history of diabetes presented with gait ataxia and slurred speech 12 hours after being found unconscious with a blood glucose level of 30 mg/dL. He had injected 80 U rather than his usual 8 U of insulin and regained consciousness after receiving glucose from local emergency response personnel. He denied visual disturbances and any previous gait disorder, and admitted to hearing voices telling him to hurt himself. He was initially taken to another hospital where he was found to have a serum screen positive for cocaine, benzodiazepine, and alcohol (his blood alcohol level was not available). His brain CT was reported by the outside hospital as negative.

His medical history included active polysubstance abuse (benzodiazepines, alcohol, cocaine, and tobacco), schizophrenia, hepatitis C, hypertension, and myeloid leukemia in remission. He had a history of multiple hospital admissions for alcohol and illicit drug detoxification, although none documented for a similar presentation. His medications, in addition to his insulin, included felodipine, fosinopril, hydrochlorothiazide, metoprolol, omeprazole, prazosin, risperidone, quetiapine, sertraline, tramadol, and calcium. His glycosylated hemoglobin was 6.4% 1 month before.

On transfer to this hospital, his blood pressure was 163/79, pulse 89, and temperature 97.5°F. In general, he was alert and oriented to person, place, and time, and was acting appropriately. Cardiac and respiratory exam were normal. Abdominal exam revealed no organomegaly. On neurological exam, he was profoundly dysarthric. His pupils were reactive and he had full extra ocular muscle testing with mild endpoint nystagmus bilaterally. Cranial nerves were intact; he had normal strength and sensory testing, and had trace deep tendon reflexes throughout. On coordination testing, he had moderate to severe dysmetria in all 4 limbs (finger to nose and heel to shin), and a wide based unsteady gait that prevented ambulation. His repeat glucose was 106 mg/dL, and additional laboratory studies revealed the following: creatinine 0.9 mg/dL, sodium 137 mmol/L, potassium 4.7 mmol/L, chloride 102 mmol/L, bicarbonate 28mmol/L, white blood cell count 6.6 K/μL, hematocrit 39.8%, and international normalized ratio 1.2. A lumbar puncture was not performed. Magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) of the brain was requested.

The differential diagnosis of symmetric cerebellar ataxia can be classified into acute, subacute, and chronic. Acute causes include cerebellar hematoma, viral cerebellitis, drug or alcohol

ingestion, vertebrobasilar ischemic attacks, Wernicke's encephalopathy, and post infectious syndrome, especially after varicella. Subacute presentations may also include chemotherapeutic agents, paraneoplastic syndromes, and nutritional deficiencies including thiamine and vitamin B-12. Inherited causes including ataxia–telangiectasia and spinal cerebellar atrophy are important considerations in progressive ataxia. When this patient initially presented to care, it was evident that his ataxia was acute or subacute as he had a documented normal neurological examination 1 month before. Given his diabetes and hypertension, he was at risk for cerebral ischemic events and intracerebral bleeding. He was also at risk for alcoholic and nutritional causes. Wernicke's was considered, as only one third of patients actually have the classic triad of ataxia, ophthalmoplegia, and confusion. However, the patient was not in a confusional state and 90% of patients with Wernicke's are thought to have disturbances of consciousness and mentation.[4] In addition, he was reported to have been eating regularly thus making it less likely that he had severe thiamine deficiency. MR can be helpful in the diagnosis, and findings may include lesions of the paraventricular regions of the thalamus and hypothalamus, the periaqueductal region of the midbrain, and the mammillary bodies. However, the sensitivity of MR has been shown to be only 53% in 1 case control study.[5] The neurologic manifestations of cocaine use include coma and seizures, and focal neurologic deficits are also possible from subarachnoid hemorrhage or cerebral infarction. We are not aware of prolonged cerebellar ataxia as a manifestation of cocaine toxicity in the absence of infarction. Alcohol can cause acute ataxia, which resolves with resolution of intoxication, and can also cause chronic ataxia as a result of damage to the cerebellum (especially the superior vermis) from chronic alcoholism. There was no history to suggest an infectious etiology and he had no known malignancy to cause a paraneoplastic syndrome. However, ataxia as a result of the latter can be the first presentation of a malignancy.[6] Inherited causes are most often progressive in nature and would have been suspected had his ataxia slowly progressed over time.

Review of his MRI and MRA of the brain was notable for a prolonged T2 signal seen in the white matter consistent with mild microvascular disease and 60% stenosis of the right internal carotid artery (Fig. 1). Hematoma and evidence for vertebrobasilar infarction were not present. Mammillary bodies were not visualized. Mild prominence of the cerebellar folia was noted at the midline. Other laboratory testing revealed anti-Hu and Purkinje cell antibodies to be negative, both of which can be seen in the paraneoplastic syndrome of small cell lung cancer.

During his course, he was monitored on a Clinical Institute Withdrawal Assessment for Alcohol Scale (CIWA) for alcohol withdrawal for which he required minimal benzodiazepines,[7] as he was noted to exhibit little evidence of withdrawal. He also received thiamine and folate in addition to his usual antihypertensive and psychiatric medications. Frequent blood glucose measurements showed a range of 93–271 mg/dL on insulin NPH 12 U/day. Four days into his hospital admission, he continued to display severe ataxia, inability to walk, and slurred speech.

Upon discharge on hospital day 5, he had persistently slurred speech and gait ataxia and was discharged to a nursing facility with the diagnosis of hypoglycemia-induced cerebellar dysfunction. A follow-up MRI was not performed.

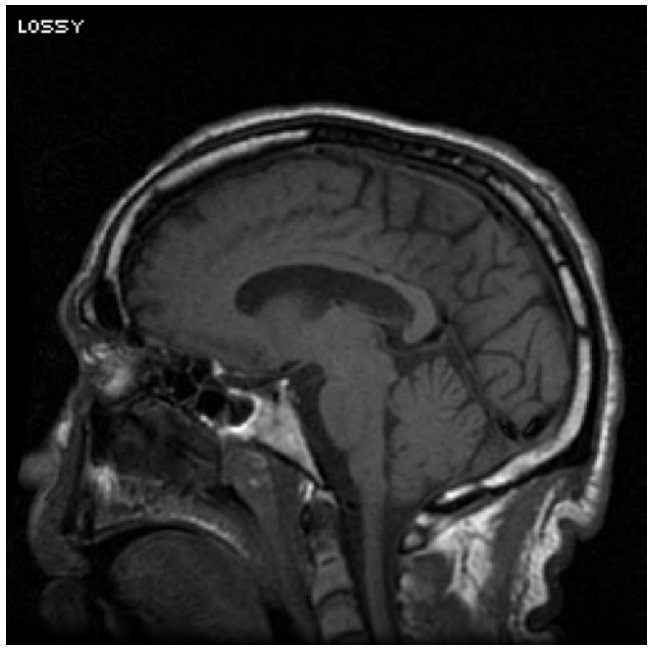

Figure 1. Brain MRI shows prolonged T2 signal consistent with mild microvascular disease. No hematoma or infraction. Mild prominence of the cerebellar folia was noted at the midline. Mammillary bodies were not visualized.

The patient signed himself out of the nursing facility 11 weeks later against medical advice as he felt he no longer required a wheelchair to ambulate safely. Two weeks later, a normal abbreviated neurological exam performed by a physician assistant is documented in the record.

DISCUSSION

Hypoglycemia-induced cerebellar dysfunction is a rare complication of severe hypoglycemia. The neurological findings of hypoglycemia include behavioral change, confusion, loss of consciousness, and seizures.[6] The cerebellum is normally protected from hypoglycemia, and several studies in rat and in man have shown differences in glucose metabolism in the cerebellum compared to the cerebrum, providing a physiologic explanation for such protection.[3,8,9]

Few other cases have been reported on hypoglycemia-induced cerebellar dysfunction. In those cases, myelinolysis appears to be associated with continued neurologic dysfunction. By contrast, in the single case reported in which the patient did not have myelinolysis, the neurologic dysfunction was transient, as was the case in our patient. Rajbhandari et al. describe a 24-year-old female type I difficult-to-control diabetic with HBA1c as high as 21.7% who presented to a diabetes clinic with slurred speech and mild cerebellar ataxia of the limbs.[1] Shortly before, she had had an episode of hypoglycemia where she was found unconscious and resuscitated by an emergency physician with glucagon. MRI findings revealed changes typical for central pontine myelinolysis. This patient had gradual improvement in her symptoms at 6 months with normal speech although she had residual impairment of heel/toe walking.

Schwaninger et al. report on a 41-year-old male who presented with a 2-year history of recurrent severe hypoglyce-

mia and was found to have cognitive impairment, motor neuropathy, and cerebellar gait ataxia.[2] On workup, he was found to have an insulinoma. MRI showed prolongation of T2 relaxation time in the middle cerebellar peduncle and the anterior limb of the internal capsule, consistent with extrapontine myelinolysis. Four months after removal of the insulinoma, the gait ataxia had partially improved although the MRI lesions were still apparent.

Kim et al. report on a 52-year-old female diabetic who presented with hypoglycemia and was found to have transient cerebellar ataxia that resolved after 12 hours.[3] Workup was otherwise unrevealing including a normal brain MRI. Using insulin and glucose administration along with PET scan evaluation of the brain, this patient was then studied to compare the glucose uptake and metabolism kinetics of her cerebrum and cerebellum compared to that of normal controls. In normal controls, glucose uptake was higher in the cerebellum relative to the cerebrum, but the rate of glucose metabolism was lower in the cerebellum. In the case patient, by contrast, the rate of glucose uptake was lower in the cerebellum and metabolism was similar to that of her cerebrum. This metabolic difference would seem to make their case patient more susceptible to hypoglycemic cerebellar injury, whereas in the controls, the cerebrum is more likely to be adversely affected by prolonged and severe hypoglycemia.

In summary, glucose uptake and utilization in the cerebellum appear to be protective with regard to hypoglycemia. Hence, cerebellar dysfunction is a rare complication of hypoglycemia. This disorder may occur in patients with altered cerebellar glucose kinetics. In the case reported above, we present a diabetic with prolonged and severe cerebellar ataxia after an episode of severe hypoglycemia. These abnormalities persisted after a 5-day hospitalization but had normalized by 3 months. In contrast to the other reported cases of prolonged ataxia from hypoglycemia where MR imaging of the brain showed pontine myelinolysis, our patient had no abnormalities of the brainstem or cerebellum seen on brain MRI. The only other patient in the literature with normal MRI findings in the setting of hypoglycemia-induced cerebellar dysfunction had normalization of her ataxia within 12 hours of onset.[3] It appears that the neuronal damage in our patient was severe enough to cause prolonged ataxia, however, the damage was reversible as evidenced by the normalization of his ataxia. A question that remains unanswered is whether the relatively normal MRI findings in the setting of hypoglycemia-induced cerebellar dysfunction predict complete recovery as occurred in our patient.

This case highlights a seldom-reported cause of ataxia and reviews the likely mechanism for hypoglycemia-induced cerebellar dysfunction and why most patients do not manifest neuroglycopenia in this manner. In addition, the differential diagnosis of ataxia is reviewed and serves as a reminder that a history of hypoglycemia should be assessed in patients presenting with ataxia.

Acknowledgements: *We would like to thank Dr. Carlos S. Kase, Department of Neurology, Boston Medical Center, for his review of the manuscript.*

Conflict of Interest: *None disclosed.*

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