Chorea in the Setting of Hyperglycemia – A Case Report and Review of the Literature

The precise mechanism for chorea–ballism secondary to hyperglycemia is unknown, but evidence shows that glycemic control can help alleviate motor symptoms.

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A 57-year-old woman with a 10-year history of type 2 diabetes mellitus and pulmonary sarcoidosis was admitted to the neurology service with a six week history of involuntary movements of her arms and legs. These movements were sudden in onset, were not suppressible, and were interfering with sleep and activity. At the time of admission, her movements were creating so much difficulty with ambulation that she required a wheelchair. She could not identify any alleviating or exacerbating factors and she had no associated symptoms. Her diabetes was well managed with oral hypoglycemic agents until eight to 10 weeks ago, when she began to have frequent hyperglycemia (i.e., blood sugars 300-500). At that time glargine insulin 20 units daily was added to her oral diabetes regimen. On admission, she was also taking hydrochlorothiazide 25mg for a history of hypertension. She was a former smoker, did not drink alcohol, and had no family history of neurologic diseases. Her physical exam was notable for bilateral upper and lower extremity ballistic and choreiform movements, which she could only suppress for 30 seconds.

Chemistries included the following: serum sodium 137 mmol/l, BUN 15 mg/dL, calcium mg/dL, glucose 384 mg/dL with no evidence of DKA, and HbA1c 10.3%. Estimated serum osmolarity was 301mOsm/L. Additionally, her WBC count was 9.3 B/L with no left shift, hemoglobin 13.0 g/dL, TSH 2.03 uIU/mL, and hepatic function panel was normal. CSF studies, serum ACE level, ceruloplasmin, ANA, and paraneoplastic studies were unremarkable. MRI revealed a diffusely abnormal hyperintense signal in the bilateral putamen on T1 and T2 flair images (see Figure 1).

Expert neurological opinion found no evidence of a neurodegenerative disorder, structural lesion, vascular event, paraneoplastic syndrome, infection, or medication responsible for this patient's chorea. In the absence of other metabolic abnormalities and systemic processes, such as lupus, hyperthyroidism, and uremia, coupled with resolution of her movement disorder by control of hyperglycemia and addition of Risperdal (risperidone), it was concluded that this patient's chorea was likely the result of her hyperglycemia.

Chorea and Glucose Abnormalities
Although rare, glucose derangements have been reported to cause cases of chorea and ballism. For example, chorea-ballism has been described in nonketotic hyperglycemia, as the initial presenting symptom of diabetes, and with hypoglycemia.[1] In brief, nonketotic hyperglycemia (NKH) is defined as elevated blood glucose levels in the absence of

Fig. 1. The patient's MRI demonstrated abnormal diffuse hyperintense signal in the bilateral Putamen on pre-contrast T1 (left) and FLAIR (right) images.
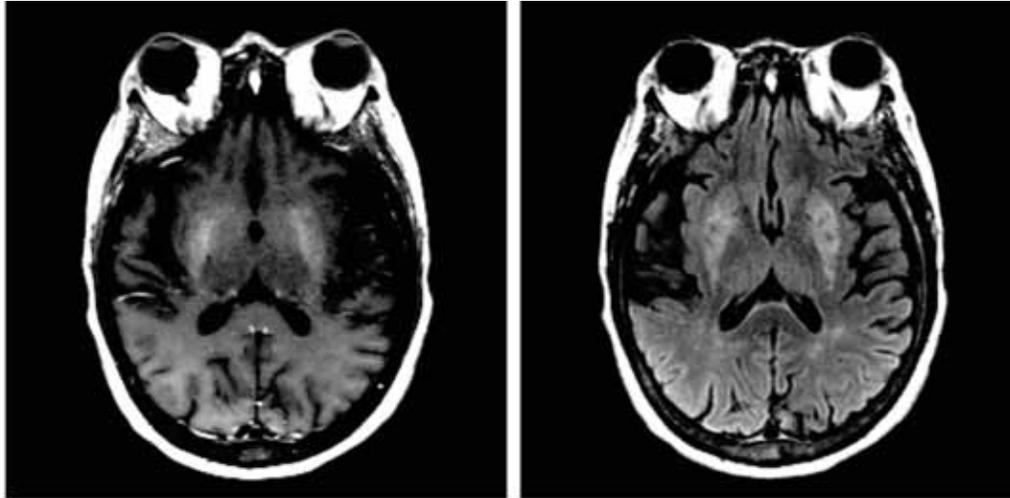
ketone formation and associated with hyperosmolarity. A variety of neurologic abnormalities have been known to accompany NKH, including delirium and coma, focal and generalized seizures, aphasia, hemiparesis, hemisensory loss, nystagmus, and hemianopia. An association between NKH and hemichorea was first described in 1960,[12] and by 1982, authors confirmed that the spectrum of focal neurologic deficits in NKH may include choreoathetosis and ballism.[4]

Clinical Characteristics and Presentation

Patients affected by this condition are predominantly elderly women with poorly controlled diabetes.[6,8] Interestingly, the majority of reported cases are patients of Asian descent.[5] A review of 53 cases of chorea associated with nonketotic hyperglycemia revealed a mean age of 71.1 years (range= 22-92 years) with a female to male predisposition of 1.8:15. Laboratory findings in these cases included the following: mean serum glucose upon admission 481.5mg/dl (range= 169-1264mg/dl), mean HbA1c 14.4% (range= 9.9-19.2%), and mean serum osmolarity 305.9mOsm/l (range= 291-335 mOsm/l); additional studies have confirmed these average glucose and osmolarity values.[8] In this series of patients, 88.6 percent had hemichorea vs. 11.4 percent who reported bilateral chorea; the majority found both upper and

lower extremities affected, while a small group also had facial involvement.[5]

Radiographic Findings

The characteristic radiographic finding in NKH patients with chorea is a high signal intensity basal ganglia lesion on the T1-weighted brain MRI.[2,7] All patients in the previous series of 53 cases, as well as two additional series of seven and eight cases respectively, demonstrated this finding.[5,6,15] The putamen was involved in all cases, while 42 percent had additional involvement of either the caudate nucleus or globus pallidus.[5] In cases of hemichorea, the high intensity lesion was located in the contralateral basal ganglia, while bilateral lesions were present in patients with generalized chorea. The differential for this hyperintense signal on T1 images includes the following: manganese toxicity in long-term parenteral nutrition, chronic liver failure, calcium metabolism abnormalities, Wilson's disease, neurofibromatosis, and hypoxic brain injury.[2] Findings on T2-weighted images are much more variable.[5,15]

SPECT studies have been performed in a small subset of patients with NKH and chorea to assess blood flow to the striatum. One small study[13] compared SPECT in six such cases with 10 age matched controls with a similar degree of hyperglycemia, but without chorea. In all chorea cases,

brain SPECT showed decreased perfusion of the striatum contralateral to the affected side on both visual and semiquantitative analysis. On the other hand, no perfusion defects were detected in the control group. This raises the possibility that striatal hypoperfusion and hence striatal hypometabolism may contribute to the pathogenesis of NKH-associated chorea, as is well-established in the chorea of Huntington's disease.[13]

Pathophysiology

The precise mechanism for chorea-ballism secondary to hyperglycemia is unknown; several theories have been proposed. Some have postulated that a dopamine hypersensitivity or hyperactive dopaminergic state exists in postmenopausal women, which explains their predisposition to this condition.[6,7] An impairment of GABAerigic or cholinergic neurons, which would normally inhibit dopaminergic activity in the nigrostriatal system may explain this hyperactive state. One postulated mechanism leading to dysfunction of GABAergic neurons is hyperviscosity.[15] Furthermore, cerebral hypoperfusion and a direct effect of hyperglycemia on cerebral metabolism result in depletion of Á-aminobutyric acid (GABA) in the corpus striatum.[2,5] With reduced levels of striatal GABA, increased pallidal activity results in dyskinesia.

Some debate also exists over the nature of the characteristic hyperintense MRI signal changes; suggestions include petechial hemorrhage, myelinolysis, or calcifications.[2,6] However, given the disappearance of these lesions on most follow-up MRI studies, it is much less likely that these lesions represent calcifications.[5] Petechial hemorrhages in the putamen, which is a leading hypothesis for NKH-chorea,[14] may result from compromise of the blood-brain barrier due to underlying chronic focal cerebrovascular disease in diabetes. The debate continues, as very few striatal tissue biopsies have been performed in patients with these MRI lesions, and the findings have been inconsistent.[3,6]

Treatment

The mainstay of treatment for chorea-ballism in

this syndrome is normalization of blood glucose[2,5]. In the largest case series, a subset of 16 patients who were treated only with blood sugar control had complete amelioration of their chorea.[5] The remaining patients in this series were treated with varying combinations of blood sugar control and medications, including haloperidol, tiapride, chlorpromazine, and diazepam. Treatment options for persistent chorea despite normalization of blood glucose include medications used to treat hemichorea-hemiballism of any cause. The most effective drug classes block postsynaptic dopamine D2 receptors.[16] Historically, typical antipsychotics, haloperidol or perphenazine, were most commonly used; however, given their increased risk for extrapyramidal symptoms, atypical antipsychotics, clozapine, risperidone, and olanzapine, have emerged as options. Some success has resulted with use of tetrabenazine, a dopamine depletor. Finally, medications with GABAergic properties, including benzodiazepines and topiramate, have been shown to improve hemichorea-hemiballism, with the latter studied in only a small number of cases.[16]

Clinical Course

One series reports that 74 percent of patients had complete resolution of chorea after a period ranging from one day to 10 months, with the large majority reaching a full recovery within six months.[5] An alternative case series of 10 patients reports dramatic resolution of dyskinesia within days after control of hyperglycemia in all but one patient.[2] In 86 percent of those patients who had a follow-up MRI after improvement in their chorea, the high signal intensity basal ganglia lesion on T1-weighted MRI images had resolved,[5] although radiographic resolution typically lags behind clinical progress. In the largest case series,[5] recurrence of chorea was reported in 13.2 percent of cases, mostly within two months. Hyperglycemia was present in all cases in which blood glucose was reported. In summary, reported cases illustrate that acute chorea-ballismus caused by hyperglycemia is treatable and carries a good prognosis.

Case Follow-Up

Our patient was managed with both titration of her insulin regimen to achieve euglycemia and simultaneously a course of Risperidal 2mg PO BID. She was discharged to acute inpatient rehab. She was seen in our endocrinology clinic within approximately three weeks of discharge from the hospital. At that time, she had complete resolution of her chorea-ballism; she was still taking Risperdal and she had excellent control of blood glucose on a regimen of Lantus (insulin glargine), metformin, and Prandin (repaglinide). She recently followed up with our movement disorders specialist and is in the process of a four week Risperidal taper. She will undergo a repeat brain MRI in the near future to assess for resolution of the bilateral basal ganglia hyperintensities. ■

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