

Clinical Reasoning: A 52-year-old woman with subacute hemichorea

Sarah M. Kranick, MD
Raymond S. Price, MD
Sashank Prasad, MD
Howard I. Hurtig, MD

Address correspondence and
reprint requests to Dr. Sarah
Kranick, Department of
Neurology, Hospital of the
University of Pennsylvania, 3
West Gates Bldg., 3400 Spruce
St., Philadelphia, PA 19104
sarah.kranick@uphs.upenn.edu

SECTION 1

A 52-year-old Korean woman with a history of poorly controlled Type 1 diabetes presented for evaluation of abnormal movements of her right arm and leg. The movements began insidiously in her right hand and arm, progressing over several months to involve the right foot as well. She was unaware of the movements until her husband noticed them. Over time the movements became more violent, eventually leading to severe flinging movements in the right arm. The movements interfered with activity. They were neither suppressible nor associated with any unpleasant internal sensation. In retrospect, her husband felt that the onset had been heralded by several months of subtle personality change: he described her as more quiet, and no longer “the life of the party.”

She was known to the clinic, having presented the year prior with several years of progressive numbness and paresthesias in the feet, lower legs, and hands. An EMG at that time revealed severe sensorimotor polyneuropathy, attributed to her long-standing diabetes. She had no other known medical illnesses. Her only medication was insulin and she was never treated with antipsychotic, antiemetic, or hormone replacement therapies. She denied the use of herbal or over-the-counter medications. There was no history of any toxic exposures. She was married without children and was a homemaker. She was adopted.

Question for consideration:

What is the differential diagnosis of hemichorea/hemiballismus?

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From the Department of Neurology, University of Pennsylvania Medical Center, Philadelphia.

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SECTION 2

This patient presents with excess writhing movements on one side of the body, with occasional superimposed sudden large-amplitude excursions, most consistent with hemichorea, hemiathetosis, and hemiballismus. These three terms describe a range of excessive uncontrollable movement, ranging in speed and amplitude from athetosis to ballismus; this continuum is often seen in the same patient.

Initial important considerations in the history are the acuity of presentation, progression over time, and associated cognitive or behavioral symptoms. Any recent medications are of critical importance given the common occurrence of medication-induced hyperkinetic disorders, such as those associated with levodopa or with estrogen replacement therapy. Remote medication history is also relevant for the possibility of tardive dyskinesia. Family history is important in ascertaining the risk of any inherited neurodegenerative disorder. Concurrent medical conditions must also be noted as the movement disorder may be secondary to a systemic medical illness.

In this patient, the history of severe polyneuropathy suggests the possibility of pseudoathetosis, a writhing movement of the limbs due to decreased proprioceptive input, although this is not usually as severe as hemiballismus. The unilaterality of the movements suggests either a structural lesion (such as a tumor, vascular malformation, or ischemic insult) or an asymmetric presentation of a process affecting both basal ganglia. The subacute nature of her presentation would make an insidious process more likely and argue against a vascular event such as a hemorrhage or infarct.

Diagnostic possibilities include neurodegenerative disorders, toxic-metabolic derangements, and systemic inflammatory or infectious processes. Neurodegenerative disorders that may present with hyperkinesia include Huntington disease, Wilson disease, pantothenate kinase-associated neurodegeneration, Fahr disease, chorea-acanthocytosis, X-linked McLeod syndrome, Huntington disease-like 2, spinocerebellar ataxia (types

2, 3, and 17), aceruloplasminemia, neuroferritinopathy, dentatorubral-pallidoluysian atrophy, and new variant Creutzfeldt-Jakob disease. Benign hereditary chorea is a non-neurodegenerative condition to be considered. Toxic and metabolic insults to the basal ganglia have been described in carbon monoxide poisoning and hyperglycemia. Systemic processes associated with chorea include lupus and antiphospholipid antibody syndrome, uremia, poststreptococcal (Sydenham) chorea, hyperthyroidism, celiac disease, and HIV infection. Although chorea only rarely manifests in paraneoplastic syndromes, the possibility of an underlying malignancy makes this diagnosis an important consideration. Finally, the possibility of a psychogenic movement disorder should be considered in cases marked by the sudden onset of symptoms in the setting of emotional stress.

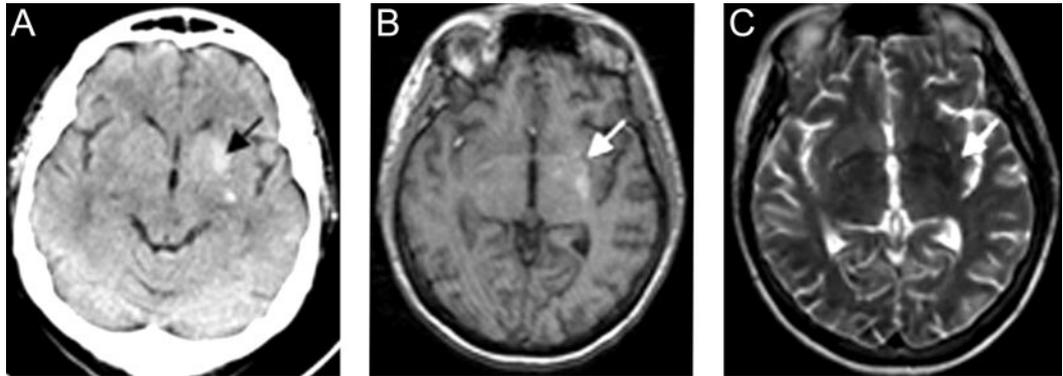
Clinical course. On examination, our patient was afebrile, with a blood pressure of 200/100 mm Hg and a heart rate of 120 beats/minute. While she was alert and oriented with fluent language, she demonstrated some impulsivity and required frequent redirection. Primitive reflexes were absent. She correctly performed Luria gestures. Her cranial nerves, strength, and coordination were intact, and the movements did not interfere with walking. Sensation of pain, temperature, and vibration was symmetrically diminished to the mid-thighs and the wrists. Reflexes were absent at the ankles, 1+ at the knees, and 2+ in the arms. Plantar responses were flexor. She had frequent writhing, twisting movements of the right shoulder, arm, and hand, as well as the right foot. These movements were particularly noticeable during voluntary movement. She would occasionally incorporate the writhing movements into semi-purposeful movement; for example, after twisting her arm into the air, she would run her hand over her hair or wave at the people in the room.

Question for consideration:

What testing would you pursue?

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Figure (A) CT of head showing hyperintensity in left putamen, (B) T1-weighted MRI of brain showing increased signal in left putamen, and (C) T2-weighted MRI of brain showing decreased signal in left putamen



SECTION 3

Initial evaluation should include neuroimaging with contrast to rule out mass lesions or ischemia. In addition, laboratory testing should include basic serum chemistries for metabolic abnormalities, and, depending upon the results, HIV, ANA, ceruloplasmin, thyroid function, serum ferritin, and paraneoplastic antibodies. Further testing could include creatine kinase, liver enzymes, and peripheral blood smear for neuroacanthocytosis. Genetic testing for Huntington disease and pantothenate kinase-associated neurodegeneration can be obtained with the appropriate clinical presentation, even in the absence of family history, although this must be accompanied by thorough genetic counseling as no cure exists for these disorders.

Clinical course. The patient was admitted to the hospital for further evaluation. Initial laboratory results revealed serum glucose of 575 mg/dL. Her anion gap

was normal and measured serum osmolality was 310 mosm/kg.

A CT scan of the head revealed a hyperintensity in the left putamen (figure, A). MRI of the brain showed increased signal in the left putamen on T1-weighted images with corresponding decreased signal on T2-weighted images, without diffusion restriction, mass effect, or contrast enhancement (figure, B and C). Both imaging studies were done during the initial evaluation, while the movements were still occurring.

The patient was started on IV fluids and insulin infusion. Her serum glucose returned to a normal level within 6 hours; by the next morning her movements had almost completely disappeared, and resolved entirely by the time of discharge. Her HgbA1c was found to be 17.7%.

Question for consideration:

What is the diagnosis and prognosis?

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SECTION 4

In this patient, the resolution of hemichorea with glucose control, as well as characteristic imaging findings, support the diagnosis of nonketotic hyperglycemia-induced chorea-ballism. When properly identified and treated, the condition has an excellent prognosis and may be completely reversible.

DISCUSSION Chorea occurs less frequently than other neurologic manifestations of hyperglycemia, and it usually occurs in the setting of nonketotic hyperglycemic syndrome. In a review of 53 published cases of nonketotic hyperglycemic hemichorea/hemiballism, the mean age was 71 years with a female to male ratio of 1.8:1.¹ The majority of cases have been reported in Asian women, suggesting a genetic predisposition. Patients typically present with hemichorea with or without hemiballism developing over days to months in the setting of elevated serum glucose, hemoglobin A1c (mean 14%), and osmolality. This syndrome can complicate long-standing type 1 or type 2 diabetes, and has also been described as the presenting symptom of new-onset diabetes.² Given that the symptoms are related to a temporary metabolic disturbance, the abnormal movements usually subside as glucose is corrected. In cases where chorea persists despite glucose normalization, medications (including benzodiazepines, neuroleptics, antiepileptics, and tetrabenazine) may be helpful.^{3,4}

Altered personality has not been previously reported to accompany the syndrome of hyperglycemic hemichorea. We hypothesize that focal basal ganglia dysfunction in this case led to disruption of the frontal-basal ganglionic circuits mediating behaviors such as motivation and organization.⁹ Our patient's improvement after correction of the metabolic derangement suggests that these circuits were reversibly damaged.

The imaging findings in this case are classic for nonketotic hyperglycemia hemichorea. The overwhelming majority of patients with this syndrome will have hyperintensities of the contralateral basal ganglia on T1-weighted MRI sequences with corresponding hypointensities on T2-weighted MRI and hyperdensities on CT.⁵ While multiple locations in the basal ganglia may demonstrate abnormal signal, the putamen is invariably affected.¹ The differential diagnosis of these MRI findings also includes subacute hemorrhage, mild focal ischemia, hypoxic-ischemic encephalopathy, chronic hepatic encephalopathy, manganese toxicity (including long-term total parenteral nutrition), and severe hypoglycemia. An important imaging characteristic of this syndrome is the resolution of signal abnormality on follow-up imag-

ing, although this may lag considerably behind clinical improvement.⁵

The exact mechanisms by which hyperglycemia can cause abnormal movements and characteristic imaging abnormalities remain unclear. Ischemia seems to be a likely etiologic factor, but neural injury from hyperglycemia may also be due to subacute hemorrhage.⁶ Although one autopsy report of a patient with hyperglycemic hemichorea showed basal ganglia gliosis without hemorrhage,⁷ a more recent series demonstrated unilateral focal microhemorrhages.⁸ It seems, therefore, that a spectrum of pathophysiology underlying this disorder likely exists. Furthermore, the etiology by which hyperglycemia induces chorea may differ between patients who recover fully and patients who do not. The infrequent availability of tissue specimens in these cases, particularly those with favorable outcomes, makes this delineation extremely difficult.

Clinical course. Several days after discharge, the involuntary movements reappeared despite a normal serum glucose. The movements slowly worsened over several weeks but did not reach the severity of her initial presentation. She was treated with clonazepam 0.25 mg TID and the movements resolved. She has had no further relapses, although she has persistent mild weakness on the right. Her personality gradually returned to normal.

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