threatening drug–drug interaction.[2] Effective treatment of leflunomide-induced interstitial lung disease using cholestyramine washout therapy has been reported. Eleven days of 8 g of cholestyramine three times daily is recommended to reverse effects of leflunomide; otherwise the long elimination half-life of 1 to 4 weeks make it impossible to detect subtherapeutic plasma levels for 2 years.[3] Alternative management might be the use of target-specific oral anticoagulants (TSOACs) instead of warfarin. It would probably have been a rational approach in the current case to switch to TSOACs because of their lack of leflunomide interaction, but this would have been a major challenge when absence of antidotes for TSOACs was considered in the case of gastrointestinal bleeding in such a high-risk individual. Low-molecular-weight heparin was started as a trusted method of anticoagulation. In conclusion, it was challenging to determine the best agent to maintain anticoagulation. Physicians should keep in mind that many factors influence warfarin metabolism and that alternative agents may be beneficial in selected cases.

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AN UNUSUAL CASE OF HEMIBALLISM-HEMICHOREA ASSOCIATED WITH NONKETOTIC HYPERGLYCEMIA IN ASSOCIATION WITH A CENTRUM SEMIOVALE STROKE

To the Editor: An 86-year-old man with a medical history of diabetes mellitus, hypertension, dyslipidemia, severe tobacco use (10 pack-years), and brain trauma was admitted to the hospital for a left-sided hemichoreoathetosis that had started suddenly 48 hours before. Family history was unremarkable for movement disorders.

On neurological examination, he was disoriented to time and space and presented with left-sided abnormal involuntary movements suggestive of hemichoreoathetosis associated with left facial spasms.

Brain computed tomography (CT) revealed spontaneous hyperdensity within the right striatum. Blood sample examination showed high fasting glucose (306 mg/dL, normal <126 mg/dL), high glycosylated hemoglobin (HbA1c; 11.9%, normal <6.5%), and high osmolarity (303.3 mOsmol/kg, normal 285–295 mOsmol/kg); urinary ketones were absent; and cerebrospinal fluid analysis revealed high glucose and lactate levels. On brain magnetic resonance imaging (MRI), the right striatum was hyperintense on T1-weighted images without contrast administration, suggestive of diabetic striatopathy. Focal hyperintensity on diffusion-weighted imaging within the right centrum semiovale suggested the presence of an associated recent ischemic stroke (Figure 1).

Diabetes mellitus decompensation, with fasting glucose levels reaching 540 mg/dL during the hospital stay, was treated with insulin, and platelet antiaggregation therapy for stroke treatment and recurrence prevention was started. As soon as blood glucose decreased toward normal values, hemichorea gradually subsided, making symptomatic treatment unnecessary; dramatic cognitive and motor improvement were obtained at discharge.

Clinical and MRI follow-up were performed. Hypersignal of right lenticular and caudate nuclei and recurrence of left hemichorea were evident until 9 months later in a context of not-yet-satisfactory glycemic control (HbA1c 9.1%). Imaging and clinical findings had disappeared at 24-month follow-up, when better control of diabetes mellitus was evident (HbA1c 8.3%), reinforcing the diagnosis of hyperglycemic hemichorea. He had three recurrent strokes during 24 months of follow-up in the deep territory of the left middle cerebral artery, the right cerebellar hemisphere, and the left medulla oblongata and right corona radiata.

This individual was characterized by the overlap of diabetic decompensation with hemichoreic symptomatology and ischemic stroke manifesting with confusion and postural instability. Hemichorea was recurrent during the

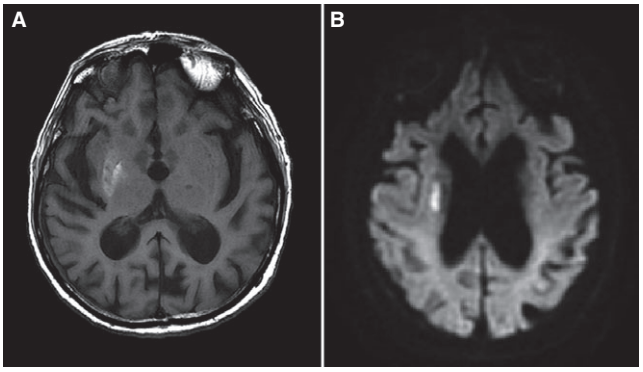

Figure 1. Brain magnetic resonance imaging revealing (A) T1-weighted hyperintensity of the right basal ganglia and (B) a diffusion-weighted hypersignal in the right centrum semiovale.

9-month period of persistence of basal ganglia abnormalities in the context of poor glycemic control. Diabetic striatopathy is a well-recognized but rare cause of hemiballism-hemichorea, associated with contralateral basal ganglia hyperdensity on CT and hyperintensity on T1-weighted MRI.[1–4] The cause of clinical and imaging abnormalities is unclear. Several mechanisms attributed to hyperglycemia have been proposed: transient ischemic injury with microhemorrhage resulting in hyperviscosity caused by hyperosmotic state, calcium deposition, gemistocytosis, altered GABAergic and dopaminergic neurotransmission,[5–8] paramagnetic mineral deposition including zinc-containing metallothionein expressed in swollen astrocytes,[9] and autoimmunity-mediated inflammation.[10]

This was the first case, to the authors' knowledge, of contemporary occurrence of hyperglycemia-related hemichorea and stroke. Two possible diagnostic hypothesis were taken into account: the first considered stroke to have played a central role in diabetes mellitus decompensation, which, in a context of cerebral frailty due to stroke, led to the development of hyperglycemia-related hemiballism-hemichorea; the second considered hyperglycemia as the trigger of stroke through an ischemic injury due to hyperviscosity.[5] The available anamnestic data did not help identify which of the two disorders first appeared. The proximity of the stroke lesion to the altered basal ganglia, both in the right middle cerebral artery area, is interesting; although this strengthens the hypothesis of the ischemic mechanism for imaging abnormalities associated to hyperglycemia, it seems in accord with the second hypothesis. It could also be related to the first hypothesis, if the abnormal basal ganglia is considered to enter the ischemic penumbra of the documented stroke. Moreover, a participating direct role of the documented ischemic stroke to the abnormal movements cannot be excluded given the existence also of vascular hemichorea-hemiballism typically associated with lesions of the basal ganglia and, as in this case, of the adjacent white matter.[1]

Difficulties in optimal glycemic control probably contributed to the persistence for several months of basal ganglia abnormalities accompanied by recurrence of hemichorea, both finally disappearing 24 months later when diabetes mellitus compensation was also evident.

Hyperglycemia-related hemiballism-hemichorea and the occurrence of four ischemic strokes during a 24-month period are rare in clinical practice. This man's case raises doubts also about the possible predictive role of hyperglycemia-related hemiballism-hemichorea for recurrence of stroke.

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COMMENTS/RESPONSES

GUIDELINES FOR THE CLINICAL DIAGNOSIS OF DIABETES MELLITUS–RELATED DEMENTIA

To the Editor: Type 2 diabetes mellitus (DM) has been shown to increase the risk of cognitive decline and dementia, such as Alzheimer's disease (AD) and vascular dementia.[1] Several mechanistic studies have indicated that vascular disease, glucose toxicity, and changes in insulin and amyloid metabolism underlie the pathophysiology of dementia.[2] A dementia subgroup with characteristics predominantly associated with DM-related metabolic abnormalities rather than AD or vascular pathology was identified in individuals with dementia associated with DM.[3] This type of dementia, showing neither cerebrovas-