Chorea-ballismus with nonketotic hyperglycemia in primary diabetes mellitus.

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Chorea and ballism can result from a variety of conditions, including cerebrovascular dis-
Several case reports have described variable computed tomographic (CT) findings in this disorder, including no abnormalities (4–9), high density in the caudate (10), high density in both the caudate and putamen (11, 12), and high density in just the putamen (13, 14). Three case reports have described magnetic resonance (MR) imaging findings of high-intensity lesions in the basal ganglia on T1-weighted images (13–15). It is probable that some patients with chorea-ballismus on admission might have coincidental hyperglycemia caused by secondary diabetes mellitus in conjunction with other disease processes. Positive neuroimaging findings may help the physician identify structural lesions that could cause chorea and may also facilitate an earlier diagnosis of true primary diabetes with hyperglycemia and prompt appropriate therapy. Our purpose was to study the CT, MR, and single-photon emission CT (SPECT) findings in a series of patients with chorea-ballismus associated with nonketotic hyperglycemia in primary diabetes mellitus and to correlate these imaging findings with the clinical presentation.

### Materials and Methods

Over a period of 4 years, we conducted a retrospective review of the records of 10 men with chorea-ballismus associated with nonketotic hyperglycemia in primary diabetes who had CT and/or MR imaging of the brain. These 10 patients were 59 to 78 years old (mean, 70 years); none had a family history of movement disorders; and none had taken any medication that could cause chorea-ballismus (eg, neuroleptic drugs, metoclopramide hydrochloride, or levodopa). Other causes of chorea, including Wilson disease, thyroid disease, and systemic lupus erythematosus, were also excluded. No patient had evidence of previous infarction in the region of the basal ganglia on CT and/or MR imaging studies.

MR imaging (performed in five patients; cases 1 to 5, see the Table) was done on a 1.5-T superconducting system. Spin-echo T1-weighted images with parameters of 600/20/2 (repetition time/echo time/excitations) and proton density- and T2-weighted images with parameters of 2500/15,90/1 were obtained in the axial plane. Gradient-echo T2*-weighted images were obtained with parameters of 750/50/1 and a 10° flip angle. Images were 5 mm thick with a 2.5-mm gap between sections. The acquisition matrix was 256 × 256, with a 20-cm field of view. Three patients (cases 1 through 3) received follow-up MR examinations at 2 and 6 months, and one patient (case 1) also had a follow-up study at 1 year. The signal intensity of the basal ganglia (caudate nucleus, putamen, globus pallidus) was compared with the signal of the gray matter.

CT studies of the brain were obtained in the axial plane by using 8-mm-thick contiguous sections. Noncontrast CT scans were available in all patients. Three patients (cases 1 through 3) received follow-up CT examinations at 2 and 6 months, and one patient (case 1) also had a follow-up study at 1 year. The abnormal density of the basal ganglia was evaluated as hyperdensity, isodensity, or hypodensity relative to gray matter. Measurements of Hounsfield units (HU) in both basal ganglia were taken in every CT examination. CT scans were obtained from 3 to 7 days after the onset of symptoms, and all MR images were obtained within 3 days after CT. Two experienced neuroradiologists, trained in MR imaging and CT and blinded to the clinical status of the patient, evaluated all images for lesion location, attenuation abnormalities on CT scans, and signal changes on MR images, and reached a consensus as to the final interpretation.

Three patients (cases 1, 3, and 7) were examined with SPECT at 8 days and at 4 months in case 1, and at 14 days in cases 3 and 7, after the onset of chorea. Technetium Tc
99m hexamethylpropyleneamine oxime (HMPAO) brain SPECT, done to evaluate regional blood flow, was performed 10 minutes after an intravenous injection of 370 MBq of $^{99m}$Tc HMPAO. Scanning equipment consisted of a rotating, large-field-of-view gamma camera fitted with a low-energy, high-resolution collimator. Sixty images were acquired for 10 seconds each during a 360° camera rotation. Each image was stored in a $64 \times 64$-pixel matrix. Reconstruction of the image was performed with attenuation correction, using Hanning filters to produce transaxial sections.

Clinical and Laboratory Data

Six patients had abnormal movements on the right side (cases 1 and 3 through 7), one patient had abnormal movements on the left side (case 8), and three patients had bilateral abnormal movements (cases 2, 9, and 10) noted for several (3 to 7) days at the initial presentation (Table). All patients were conscious except one (case 9), who was comatose. This patient died of acute neurologic deterioration and respiratory arrest of unknown cause 3 days after admission. Autopsy studies were not available. In the nine conscious patients, chorea resolved within 2 days after correction of the hyperglycemia. A history of diabetes mellitus was established in six patients (cases 1, 2, 5 through 7, and 9); the other four had no such history, although they were subsequently proved to have diabetes mellitus during their hospital stay. Initial blood sugar levels ranged from 200 to 560 mg/dL on admission. A history of hypertension could be traced in four patients (cases 4, 7, 8, and 10); however, all patients were normotensive during the hospital course. There were no ketones in the serum, and calculated serum osmolarity ranged from normal to mild hyperosmolarity (285 to 325 mOsm/kg) in all patients except case 9, who had severe hyperosmolarity (360 mOsm/kg).

Results

Initial CT and MR Examinations

The lesions were located in the putamen unilaterally in four patients (cases 1, 3, 5, and 8), in the putamen and caudate unilaterally in 3 patients (cases 4, 6, and 7), in the putamen and caudate bilaterally in two patients (cases 9 and 10), and in the putamen and caudate and lateral portion of the globus pallidus bilaterally in one patient (case 2).

On CT scans, 9 of 10 patients had slightly increased density in the involved caudate nucleus and/or putamen (Figs 1A and 2A). Tissue density was found to be 40 to 51 HU for the areas of increased attenuation in the involved basal ganglia. In the comparatively normal areas of the basal ganglia, tissue density was 33 to 36 HU. One patient (case 5) had normal CT findings.

At MR imaging, all patients (including the patient with a normal CT study) had increased signal intensity in the involved basal ganglia on T1-weighted images (Figs 1B, 2B and C). Abnormalities were delineated better and were more often conspicuous on the MR images than on the CT scans. Proton-density T2-weighted images showed slightly hyperintense signal relative to the contralateral side (Fig 1C), and gradient-echo T2*-weighted images revealed no significant signal alternation in case 1. Proton-density T2-weighted and gradient-echo T2*-weighted images showed no significant signal alternation in the other four patients (cases 2 through 5).

In all patients, the manifestation of chorea-ballismus correlated well with the neuroimaging findings. In the six patients with right-sided symptoms, a lesion was noted on CT scans and/or MR images in the contralateral left basal ganglia. In the one patient with left-sided symptoms, a lesion was found in the right basal ganglia. In the three patients with bilateral chorea-ballismus, CT scans and/or MR images showed lesions in the basal ganglia bilaterally.

Follow-up CT and MR Examinations

In case 1, CT scans showed that the high attenuation in the left putamen had completely resolved after 2 months (Fig 1E), and there was no change at 1 year. T1-weighted MR images in this patient revealed that the hyperintensity had decreased within 6 months and had completely resolved at 1 year (Fig 1F and I). The patient remained well during the year after resolution of chorea-ballismus. In case 2, CT scans showed decreased attenuation and T1-weighted MR images showed decreased signal intensity bilaterally in the abnormal basal ganglia at 2 months. The 6-month follow-up imaging studies showed normal density on CT scans and more decreased signal intensity on MR images. The patient remained well, although bilateral chronic subdural hematoma was noted incidentally (Fig 2D). The third patient (case 3) returned about 2 months later, when a second episode of diabetic hyperglycemia occurred, with hyperkinetic movements of the right arm. Increased signal intensity was noted in the left putamen on T1-weighted images as compared with the first MR
Case 1: 66-year-old man with diabetes and abrupt onset of involuntary movements involving right limbs. CT scans were obtained 4 days after hemichorea; MR images at 6 days. (All CT scans were acquired with identical center and window level. All MR images were acquired with identical imaging parameters and were photographed with identical window and level settings.)

A, Unenhanced CT scan shows slightly increased attenuation in the left putamen.

B, Axial T1-weighted (600/20) MR image reveals increased signal intensity, mainly in the left putamen.

C, T2-weighted (2500/90) MR image, which corresponds to B, shows slightly higher signal intensity on the left (arrow) than on the right.

D, HMPAO brain SPECT scan obtained 8 days after hemichorea shows decreased perfusion in regions of the left basal ganglia.

E-H, CT and MR images obtained after 2 months. The high density is resolved on unenhanced CT scan (E). T1-weighted (600/20) MR image (F) shows reduction of hyperintense signal in left putamen. Corresponding T2-weighted (2500/90) MR image (G) shows mildly decreased intensity involving left putamen (arrows). Significant hypointense left putamen is also noted on gradient-echo T2*-weighted (750/50, 10° flip angle) MR image (H).

I, The abnormal signal intensity is completely resolved on T1-weighted (600/20) MR image obtained at same level 1 year later.
image. The chorea resolved after treatment, and the signal intensity was decreased at the 6-month follow-up examination. Increased hypointensity on T2-weighted and gradient-echo T2*-weighted images was observed on the sequential MR images in cases 1 to 3 (Fig 1G and H). Follow-up neuroimaging findings correlated well with the clinical course in these three patients. Nevertheless, resolution of the lesions noted on the imaging studies was slower than the clinical course.

Initial and Follow-up SPECT Examinations

The first HMPAO brain SPECT study (Fig 1D) revealed decreased regional blood flow in the area of the left basal ganglia, corresponding to CT and MR findings in all patients, and, in one patient, decreased regional perfusion was still noted on follow-up examinations 4 months later.

Discussion

The critical pathophysiological basis for chorea-ballismus associated with nonketotic hyperglycemia in primary diabetes mellitus is unknown. It is probable that underlying chronic focal cerebrovascular diseases in primary diabetes mellitus (16, 17) provide the basis for acute blood-brain barrier dysfunction (18) and synergetic metabolic effects during the hyperglycemic episode (17, 19). Hyperglycemia also produces a global decrease in regional cerebral
blood flow with maximal reduction in the basal ganglia. Thus, the reduction of cerebral blood flow may contribute to the reduction of local amounts of g-aminobutyric acid. Depletion of corpus striatal g-aminobutyric acid in nonketotic hyperglycemia may allow increased pallidal activity with resultant dyskinesia (17, 19).

The presence of lesions with increased signal intensity on spin-echo T1-weighted images is unusual; relatively few documented tissue abnormalities have been associated with such signal intensity (20–27). Hyperintense signal in the region of the basal ganglia on T1-weighted MR images has been noted by other investigators (20, 26–30), and has been associated with manganese toxicity in long-term parenteral nutrition (26), chronic liver failure (28), problems of calcium metabolism (20), Wilson disease (27), neurofibromatosis (29), and hypoxic brain changes (30). The lesions reported in connection with the first two conditions were located mainly in the globus pallidus, symmetrically. In the others, there were lesions in additional areas as well. In our series, chorea-ballismus with hyperglycemia was restricted largely to the putamen and/or caudate nucleus.

The differential diagnosis of acutely developing increased density on CT scans includes calcification and hemorrhage (31). An imaging abnormality that has an apparently rapid onset and that disappears within months more or less rules out calcium as a cause (32). In our patients, only slightly increased attenuation in the range of 40 to 51 HU was noted in the abnormal areas of the basal ganglia. Attenuation in the comparatively normal areas of the basal ganglia was about 33 to 36 HU. This finding could be explained by multiple petechial hemorrhages rather than an intracerebral hematoma.

MR examinations of our patients were obtained 6 to 10 days after onset of chorea. Methemoglobin has usually formed by the first week after a hemorrhagic event (24). The presence of methemoglobin from recent petechial hemorrhage, with blood interspersed between brain tissue, could theoretically account for the increased intensity seen at admission on T1-weighted images and for the absence of marked signal alternation seen on T2-weighted and gradient-echo T2*-weighted sequences in patients. The sequential resolution of hyperintense signal on T1-weighted images and the sequential presence of increased hypointensity on T2-weighted and gradient-echo T2*-weighted sequences in the basal ganglia with continuous resolution of high density on CT scans also suggest evolution of petechial hemorrhage with hemosiderin deposition.

A review of the neuroimaging findings in patients with chorea associated with hyperglycemia in primary diabetes mellitus (4–15) shows that 11 patients had CT studies only (4–12). Among them, 8 had normal findings (4–9) and the other 3 had high attenuation in the basal ganglia (10–12). Three patients had both CT and MR studies (13–15). Of these, 2 had hyperdense basal ganglia on CT scans (4 and 7 days, respectively, after onset of chorea) and hyperintense signal on T1-weighted MR images (14 and 18 days, respectively, after onset) (13, 14). The third patient had normal CT findings with hyperintense signal on T1-weighted MR images (both studies performed 3 months after onset) (15). There were different schools of thought about the cause of the imaging abnormalities. In three reports of positive CT findings in which there were no MR examinations, basal ganglia calcification (10) and hemorrhage (11, 12) were suggested. Hemorrhage was also considered as the cause of imaging abnormalities in two reports in which both MR and CT findings were positive (13, 14). In the article that reported normal CT findings in a patient with abnormal MR results, destroyed myelin in the basal ganglia was suggested as the cause of the high signal on T1-weighted images (15).

Among the 10 patients we studied, we believe the basal ganglia hemorrhage can explain the imaging findings in 9 cases. However, the MR imaging abnormalities in the one patient who had normal CT findings during the acute stage of chorea cannot be easily explained by basal ganglia hemorrhage. The abnormal MR signals may be the result of destroyed myelin. Release of lipids following a breakdown of the myelin sheath in some vascular and metabolic brain diseases can cause T1 and T2 shortening (30, 33, 34). However, we cannot exclude the possibility of the existence of some minute amount of blood that escaped detection by CT. Therefore, the imaging abnormalities may be attributed to petechial hemorrhage in the basal ganglia with some contribution of myelin destruction caused by the disease process.

We found that the locations of lesions shown on both MR images and CT scans correlated well with the initial presentation of the chorea (such as a right basal ganglia lesion with left
extremity chorea, bilateral lesions with bilateral chorea). In all our patients except one, hyperkinesia resolved dramatically after control of the hyperglycemia. This illustrates that acute chorea-ballismus caused by hyperglycemia is a treatable disorder with a good prognosis. Another interesting but important clinical finding is that all the patients reported in the literature, as well as the patients in our study, had primary diabetes mellitus. Indeed, even our four patients who had no history of diabetes were found to have primary diabetes mellitus during their hospitalization. It is possible for a patient with chorea-ballismus to have hyperglycemia at the initial presentation. The hyperglycemia could be the result of either primary or coincidental secondary diabetes mellitus stemming from any of a variety of diseases (16). A positive neuroimaging study should be an indication that the hyperglycemia is most likely due to underlying primary diabetes mellitus. The sequential neuroimaging findings in our patients also correlated well with the clinical course; however, resolution of the lesions on the imaging studies was slower than the clinical progress.

In conclusion, abnormal lesions in the basal ganglia display gradual resolution following treatment on follow-up CT and MR images. SPECT scans show hypoperfusion. Pathologic reports regarding chorea with hyperglycemia are scanty and inconclusive, since hyperglycemia is a treatable disease and most patients survive. However, our neuroimaging findings in this disease are noteworthy, and may shed light on the underlying pathophysiologic changes of this metabolic disorder.

References


