Tetrabenazine for Hyperglycemic-Induced Hemichorea–Hemiballismus

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Video 

Abstract: **We reported a 74-year-old woman with new-onset diabetes mellitus who presented with the sudden onset of mild left hemiparesis and marked left hemichorea–hemiballismus. Brain CT scan and MRI showed T1W, T2W, and DWI lesions in the right putamen and caudate, which have been previously reported in cases of hyperglycemic-induced hemichorea–hemiballismus (HIHH). The patient dramatically responded to tetrabenazine within a day. Subsequent dose reductions lead to a reemergence of symptoms. Tetrabenazine improves a variety of hyperkinetic movement disorders but, to our knowledge, its use has never been reported for HIHH.** © 2006 Movement Disorder Society

Key words: hyperglycemia; chorea; ballismus; tetrabenazine

Hemichorea–hemiballismus (HCHB) is a continuous, involuntary, random movement involving proximal and/or distal muscles on one side of the body, including the face in some cases.[1,2] It is usually associated with structural brain lesions but can occur with metabolic abnormalities.[1,2] There are many reports of nonketotic hyperglycemia provoking hemichorea–hemiballismus with characteristic brain imaging, including hyperdensity of the contralateral basal ganglia on brain CT scan and increased signal intensity on T1W MRI.[3–8] Hyperglycemic-induced hemichorea–hemiballismus (HIHH) may resolve in days or persist.[6,7,9,10] Chronic cases were reported to have slight or incomplete response to medical treatment.[11] We report a persistent HIHH case who dramatically responded to tetrabenazine (TBZ).

CASE REPORT

A 74-year-old Nigerian woman with medical histories of hypertension, hypercholesterolemia, and bradyarrthymia came to the Unites States for cardiac pacemaker placement. The patient developed polyuria. Her evaluation revealed blood glucose of 301 mg/deciliter and she was diagnosed with new-onset diabetes mellitus. The patient received initial treatment with insulin injections but then changed to oral hypoglycemic drugs. One month later, she developed left hand and foot jerking after she woke up in the morning. This quickly progressed to involve her entire left side, including face. She did not see a physician until 3 days after symptom onset. She was started on aspirin and clopidogrel. A brain MRI done 5 days after the onset showed T1W hyperintensity, T2W hypointensity, and nonrestricted DWI of the right caudate and putamen (Fig. 1A–C). It was initially thought to be suspicious for intracerebral hemorrhage, so aspirin and clopidogrel were stopped. Repeated brain CT scan 10 days after the onset showed a mild hyperdensity at the right caudate and putamen corresponding to the abnormal MR signal (Fig. 1D). She restarted aspirin and clopidogrel. The left-side chorea/ballismus continued to worsen over 1 month. It did resolve in sleep. She developed pain in her left wrist, elbow, and ankle and felt depressed. The patient was started on clonazepam and the dose was escalated to 1 mg two times a day without any improvement.

The initial examination at Baylor College of Medicine Movements Disorders Clinic revealed mild dysarthria and a slightly decreased left nasolabial fold. The involuntary movements were not suppressible (see Video, Segment 1) Her Abnormal Involuntary Movement Scale (AIMS) was 21.[12] The volitional motor examination was otherwise mitigated by the marked hemichorea. An underlying bradykinesia was difficult to assess but there were clearly no other parkinsonian signs. Visual fields were normal. She did demonstrate decreased deep tendon reflexes. The patient was diagnosed with HIHH based on her history, examination, and classic radiographic features.

She was prescribed TBZ 12.5 mg two times a day for 5 days, with a slow titration to 25 mg three times a day. Within 2 hours of the first dose, she reported marked improvement, and by 3 days reported almost complete resolution of her HCHB. She denied any adverse effects of TBZ. The patient followed up in our clinic 1 month later. Examination revealed only very mild intermittent choreiform movement of her left foot (AIMS = 1), without any other abnormality (see Video, Segment 2). Per patient report, over the next 3 months, the left HCHB

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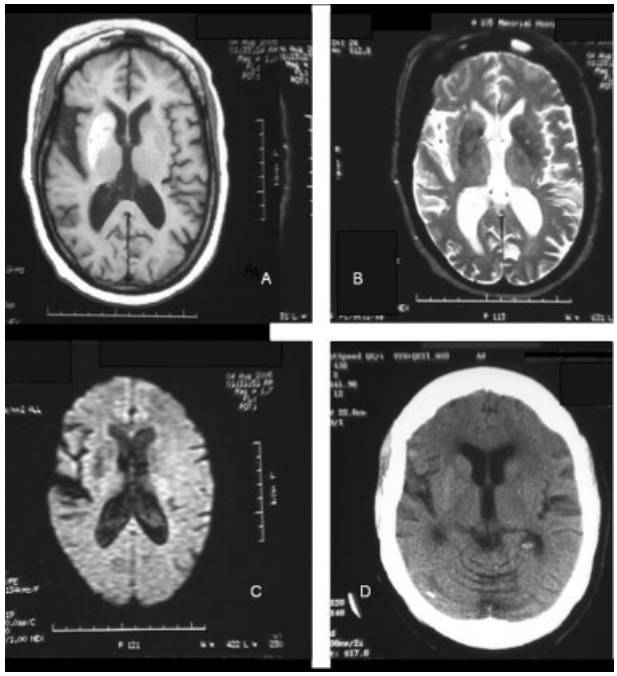

FIG. 1. Brain magnetic resonance imaging showed hyperintensity T1-weighted (**A**), hypointensity T2-weighted (**B**), and nonrestricted diffusion-weighted imaging (**C**) of right caudate and putamen. Axial brain CT scan (**D**) showed hyperdensity of right caudate and putamen.

recurred shortly after stopping TBZ on two occasions and resolved within the first dose of reinstituting it. She currently remains on the relatively low dose of 12.5 mg per day with continued excellent control.

DISCUSSION

We report a case of an elderly woman who developed left HCHB 1 month after the diagnosis of a new-onset diabetes mellitus. The distinction between hemichorea and hemiballismus is phenomenological and likely represents a matter of severity.[1,2] Hyperglycemia was the second most common reported cause of HCHB on Asian series.[6,9–11,13] HIHH tends to present in elderly women.[2] The Asian preponderance of reports may suggest some genetic contribution.[2,3,5,6,9,14,15]

Brain CT in our patient showed a hyperdensity of left putamen and caudate, and an increased intensity on T1W MRI as previously reported.[7,13,16] Most cases involve the putamen and caudate and some involve the globus pallidus with sparing of the anterior limb of internal capsule.[3,5–7,13,15,16] These findings can be observed in other diseases, including chronic hepatic encephalopathy, postcardiac arrest encephalopathy, hypoglycemic coma, and possibly focal ischemia.[6] The high signal intensity in basal ganglia on T1W MRI may resolve, coinciding with the improvement of chorea.[5,6,13]

The brain pathology of HIHH was reported to demonstrate selective neuronal loss, reactive astrocytosis of the striatal area, but no hemorrhage.[6,17] The exact mechanism of HIHH remains speculative. This literature is complicated by early reports that include a heterogeneous collection of causes, including petechiae hemorrhage,[11,16] calcification,[16] demyelination,[14] regional metabolic failure from cerebral vascular insufficiency and metabolic derangement,[15] and protein desiccation in the course of Wallerian degeneration.[7] Some have also combined this with the dystonic and choreatic movements seen in nonketotic hyperglycemia, which resolve immediately upon glucose correction.[2,10,18]

There is, however a pure idiopathic form without other diabetes-associated pathologies. The mechanism is not known. One group speculated that the predominance of HIHH in older women suggests that the relative estrogen deficiency after menopause, which may reduce inhibition of dopamine function in the nigrostriatal system, contributes to supersensitivity in the striatal dopamine receptor.[9] Altered neurotransmitters are also speculated to contribute to HIHH. Hyperglycemia induces deficiencies of GABA and acetylcholine may lead to HCHB.[4,6] However, this would not explain persistent movements. It was also speculated that the damage of GABA-inhibitory neurons in the striatum leaded to the disinhibition of the external segment of the globus pallidus (GPe) and subthalamic nucleus.[3] The rapid and dramatic response from TBZ is not necessarily inconsistent with these, but dose suggest a direct dopaminergic, or less likely adrenergic, contribution to the pathophysiology.

TBZ inhibits vesicular monoamine transporter 2 (VMAT2), which in turn prevents the release of monoamines. It is also a mild dopamine receptor blocker.[19–21] There are many reports using TBZ in hyperkinetic movement disorders, including tardive sterotypy, myoclonus, Huntington's disease, tardive dystonia, idiopathic dystonia, Tourette's syndrome, and hemiballismus from structural lesions around the subthalamic nucleus.[19,21] We could not find any previous report of attempting TBZ in HIHH. We have used TBZ for typical structural hemiballismus in at least 18 cases but have never seen this dramatic of a response, possibly suggesting that the two conditions may differ physiologically. One case of HIHH with a 3-month onset of chorea and classic MRI changes was reported to improve with thalamic deep brain stimulation after failing medical therapy with haloperidol, clonazepam, and tiapride for 4 months.[8] We would recommend considering TBZ in persistent HIHH before resorting to neurosurgical procedures.

LEGENDS TO THE VIDEO

Segment 1. Pretreatment 30 days after symptom onset: left facial movements and left hemichorea and ballismus (AIMS = 21).

Segment 2. Posttreatment 29 days after starting TBZ and 59 days after symptom onset: only slight chorieform movement of left foot (AIMS = 1).

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