

Tetrabenazine in Hyperglycemic Induced Hemichorea Hemiballismus

Oraporn Sitburana, M.D. and William G Ondo, M.D.

Parkinson's Disease Center and Movement Disorders Clinic, Department of Neurology, Baylor College of Medicine, Houston, Texas

ABSTRACT

OBJECTIVE: To report a case of hyperglycemic induced hemichorea hemiballismus (HIHH) successfully treated with tetrabenazine (TBZ). **BACKGROUND:** HIHH is a rare condition manifest by acute onset hemichorea, associated with characteristic unilateral MRI hyper-intensities in the striatum. The exact pathology is not known. TBZ is a monoamine depletory that treats a variety of hyperkinetic movement disorders but has never been evaluated for HIHH. **METHODS:** A 74-year old woman presented with the sudden onset of left hemiparesis and left hemichorea-hemiballismus shortly after the diagnosis of new-onset diabetes mellitus. She was treated with clonazepam 1 mg two times a day without benefit. The intensity was stable for one month prior to evaluation and resulted in marked functional disability. Neurological examination at presentation was normal except for the involuntary movements. Her Abnormal Involuntary Movement Scale (AIMS) was 21. CT scan and MRI imaging of the brain showed well delineated hyperintensity of the right lentiform nucleus and caudate, consistent with previous reports of HIHH. **RESULTS:** The patient was started with TBZ one month after the onset of HIHH at 12.5 mg two times a day for 5 days and titrated to 25 mg three times a day. Within 2 hours of the first dose she reported marked improvement, and by three days had almost complete resolution of the movements. She denied any adverse events. Examination on TBZ showed only very mild intermittent right foot chorea (AIMS =1). The dose was reduced back to 12.5 mg two times a day with continued benefit. **CONCLUSION:** TBZ dramatically improved this case of HIHH. This was much more robust than when TBZ is used to treat hemichorea-hemiballismus associated with lesions of the sub-thalamic nucleus, suggesting a different pathophysiological mechanism.

INTRODUCTION

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. [Dewey and Jankovic, 1989] It is usually associated with structural brain lesions but can occur with metabolic abnormalities. [Dewey and Jankovic, 1989] 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. [Hashimoto et al., 1999; Oh et al., 2002; Wintermark et al., 2004; Nakano et al., 2005] Hyperglycemic induced hemichorea-hemiballismus (HIHH) may resolve in days, or persist. [Oh et al., 2002; Wintermark et al., 2004; Lin and Chang, 1994; Ilergane et al., 2001] Chronic cases were reported to have slight or incomplete response to medical treatment. [Ahlskog et al., 2001] We report a persistent HIHH case who dramatically responded to TBZ.

METHODS

- A 74-year old Nigerian woman with medical histories of hypertension, hypercholesterolemia, and bradycardia developed polyuria. She has been diagnosed with new-onset diabetes mellitus.
- One month later she developed left hand and foot "jerkling" after she woke up in the morning. This quickly progressed to involve her entire left side, including face.
- A brain MRI done 5 days after the onset showed T1W hyperintensity, T2W hypointensity and non-restricted DWI of the right caudate and putamen. (Figure 1A, 1B, 1C)
- 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. (Figure 1D) She was treated with aspirin and clopidogrel.
- 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 (Video Segment 1A) Her Abnormal Involuntary Movement Scale (AIMS) was 21. [Munetz and Benjamin, 1988] The volitional motor examination was otherwise mitigated by the marked hemichorea.
- The patient was diagnosed with HIHH based on her history, examination, and classic radiographic features.
- She was prescribed TBZ 12.5 milligrams two times a day with a slow titration to 25 milligrams three times a day. Within 2 hours of the first dose she reported marked improvement.
- Examination revealed only very mild intermittent choreiform movement of her left foot (AIMS = 1) without any other abnormality. (Video Segment 1B)
- Over the next three months, the left HCHB recurred shortly after stopping TBZ on two occasions.
- She currently remains on the relatively low dose of 12.5 milligrams per day with continued excellent control.



CONCLUSIONS

We report a case of an elderly woman who developed left HCHB one 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. [Dewey and Jankovic, 1989]

Hyperglycemia was the second most common reported cause of HCHB on Asian series. [Oh et al., 2002; Chu et al., 2002; Ahlskog et al., 2001] HIHH tends to present in elderly women. The Asian preponderance of reports may suggest some genetic contribution. [Hashimoto et al., 1999; Oh et al., 2002; Hsu et al., 2004]

The brain pathology of HIHH was reported to demonstrate selective neuronal loss, reactive astrocytosis of the striatal area, but no hemorrhage. [Oh et al., 2002; Ohara et al., 2001] The exact mechanism of HIHH remains speculative. This literature is complicated by early reports that include a heterogeneous collection of causes including petechial hemorrhage [Ahlskog et al., 2001; Shan, 2005] calcification [Shan, 2005], demyelination [Lai et al., 1996], regional metabolic failure from cerebral vascular insufficiency and metabolic derangement [Hsu et al., 2004], and protein desiccation in the course of Wallerian degeneration [Wintermark et al., 2004]. Some have also combined this with the dystonic and choreatic movements seen in non-ketotic hyperglycemia, which resolve immediately upon glucose correction. [Rector et al., 1982]

Tetrabenazine (TBZ) inhibits vesicular monoamine transporter 2 (VMAT2) which intern prevents the release of monoamines. It is also a mild dopamine receptor blocker. [Jankovic and Beach, 1997] There are many reports using TBZ in hyperkinetic movement disorders including tardive stereotypy, myoclonus, Huntington's disease, tardive dystonia, idiopathic dystonia, Tourette's syndrome, and hemiballismus from structural lesions around the STN. [Jankovic and Beach, 1997]

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 three-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 four months. [Nakano et al., 2005] We would recommend considering TBZ in persistent HIHH before resorting to neurosurgical procedures.

VIDEO ILLUSTRATION

- Segment 1: Pre-treatment 30 days after symptom onset: left facial movements and left hemichorea and ballismus (AIMS = 21)
- Segment 2: Post-treatment 29 days after starting TBZ and 59 days after symptom onset : only slight choreiform movement of left foot. (AIMS = 1)

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