Resolution of Acute Onset Hemichorea–Hemiballismus After Treatment With Intravenous Tissue Plasminogen Activator

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Abstract

Hyperkinetic movement disorders are uncommon after acute ischemic stroke. Since these movement disorders are rarely the initial manifestation of acute cerebral ischemia, their presence may result in diagnostic uncertainty or it may inappropriately delay intravenous thrombolytic therapy for ischemic stroke. Hemichorea–hemiballismus (HC-HB) is one of the more frequently encountered hyperkinetic movement disorders occurring in conjunction with stroke. Although HC-HB may result from a stroke mimic, the acute onset should prompt rapid evaluation and consideration for the presence of stroke along with its time-dependent therapies including recombinant tissue plasminogen activator (rtPA). In this article, we describe a case of a patient with acute cerebral ischemia presenting clinically with HC-HB, who was given intravenous rtPA therapy despite an initially negative, early diffusion-weighted magnetic resonance imaging (MRI). Follow-up brain MRI performed 24 hours after the initiation of thrombolytic therapy confirmed acute infarction in the contralateral striatum. The patient had near-complete resolution of her HC-HB on discharge and had no complications related to the administration of intravenous rtPA.

Keywords

stroke, cerebrovascular disorders, stroke and cerebrovascular disease, clinical specialty, chorea, movement disorders, dyskinesias, movement disorders, imaging, techniques

Introduction

Poststroke hyperkinetic movement disorders have an incidence of 0.08%.¹⁻³ Hemichorea (HC) is a unilateral continuous, random, and distally predominant jerking movement that may involve proximal muscles. Hemiballismus (HB) is a unilateral, involuntary, and large amplitude proximal movement.^{1,4} The most common poststroke hyperkinetic movement disorders are HC-HB and asterixis.^{3,5} Slow writhing athetoid movements have also been described.¹ The development of poststroke chorea is variable with an estimated average onset of 4.3 days poststroke, although 12.5% (7 of 56) of the patients develop HC-HB <24 hours after stroke onset.⁶ Robust estimates of HC-HB as a manifestation of acute ischemic stroke (AIS) are lacking. Recognition of HC-HB as a presentation of AIS can facilitate accurate diagnosis and ensure timely consideration of reperfusion therapy. This report describes a case of acute onset HC-HB as the initial manifestation of AIS with resolution after treatment with intravenous recombinant tissue plasminogen activator (rtPA).

Case Description

A 79-year-old woman was evaluated 90 minutes after the sudden onset of “twitching.” She abruptly developed involuntary, irregular movements of her left side while at home. There was no headache, language difficulty, visual disturbance, or alteration to consciousness. Past history revealed hypertension, dyslipidemia, and essential thrombocytosis. Medications included lisinopril, pravastatin, hydroxyurea, and

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Figure 1. A, Initial diffusion-weighted sequences at presentation showing the absence of restricted diffusion. B, Diffusion-weighted sequences 24 hours later showing restricted diffusion in the right caudate and lentiform nuclei.

aspirin. Hydroxyurea and aspirin were discontinued several weeks prior for an upcoming dental procedure.

The initial neurological examination noted frequent irregular large amplitude movements of the proximal left arm and leg with smaller amplitude writhing movements of the left hand and foot. Infrequent involuntary muscle contractions were noted in the left face. Flattening of the left nasolabial fold, drift of the left arm and leg, and reduced superficial pain sensation in the left face, arm, and leg were observed. The National Institutes of Health Stroke Scale (NIHSS) score was 4. The electrocardiogram demonstrated normal sinus rhythm with nonspecific T-wave abnormalities in the lateral leads. Initial laboratory testing revealed a platelet count of

$812 \times 10^3/\mu\text{L}$. The complete blood count, coagulation studies, blood viscosity, electrolytes, renal profile, and glucose were normal.

The movements diminished after administration of 1 mg intravenous lorazepam to facilitate emergent brain magnetic resonance imaging (MRI) 2 hours after symptom onset. No acute abnormalities were noted on diffusion-weighted imaging (Figure 1A), and no hemorrhages were identified. Despite negative diffusion-weighted imaging, AIS was considered the most likely diagnosis. The patient was treated with 0.9 mg/kg of alteplase (61.2 mg total dose: 6.12 mg as bolus over 1 minute followed by 55.08 mg over 1 hour) 165 minutes after the symptom onset.⁷

The patient was admitted to the neurological intensive care unit for postthrombolysis management. The patient remained neurologically stable during the initial 24-hour period and follow-up clinical evaluation revealed choreoathetoid movements of the distal left arm. The MRI repeated at 24 hours postthrombolysis demonstrated interval development of restricted diffusion within the right caudate and lentiform nuclei (Figure 1B) consistent with AIS. By hospital day 3, the patient's symptoms resolved (NIHSS = 0) and she was discharged without any functional disability.

Discussion

Hemichorea–hemiballism is a hyperkinetic movement disorder uncommonly reported with AIS. The incidence of HC-HB in acute stroke ranges between 0.4% and 0.54%,^{2,3} with a prevalence of 1%.³ Typical lesions are isolated to 1 hemisphere and contralateral to the movement disorder.³ The hyperkinetic movements involve the face, arm, or leg on the same side.^{2,3}

The basal ganglia form a complex network with reciprocal connections to several distinct brain regions. Disruption of this functional connectivity is postulated to produce the characteristic movements of HC-HB.^{2,3} Although damage to the subthalamic nucleus is classically associated with HC-HB, lesions of the contralateral striatum are more common.^{2,3} Other localizations of HC-HB include the thalamus, posterior limb of the internal capsule, corona radiata, frontal and parietal cortices, external capsule, and pons.¹

The most common vascular territories affected in HC-HB are the middle cerebral artery (M1, M2, and lateral lenticulostriate arteries), posterior cerebral artery (thalamoperforating, thalamogeniculate, and choroidal arteries), and rarely the anterior cerebral artery (recurrent artery of Huebner and leptomeningeal arteries).^{1,3} The most common pathophysiology is small vessel disease with lacunar infarction (<1.5 mm) accounting for two-thirds of patients who develop poststroke hyperkinetic movement disorders, while large and medium vessel atherothrombosis, cardioembolism, and hemorrhage account for one-third.¹⁻³ In our patient, we hypothesize that the lenticulostriate arteries are the vascular distribution responsible for the diffusion-weighted changes

on MRI due to involvement of both the lentiform and caudate nuclei. Although this does not account for sparing of the anterior portion of the internal capsule, skip lesions involving the lenticulostriate arteries with preferential involvement of the gray matter separated by areas of preserved white matter (anterior limb of internal capsule) are well described. Proposed mechanisms include selective vulnerability of gray matter to ischemia, embolic phenomena involving independent lenticulostriate arteries for gray and white matter, or variation in tissue oxygen consumption of the basal ganglia and internal capsule.⁸

Most strokes affecting the basal ganglia do not produce HC-HB suggesting unique predisposing factors for this rare clinical phenotype.⁹ Advanced age, female gender, Asian ethnicity, vascular stenosis, and medical comorbidities (eg, uncontrolled diabetes mellitus) may predispose to post-stroke HC-HB.¹⁰ Other factors including hyperosmolarity, hyperviscosity, and underlying cerebrovascular disease may contribute by creating relative ischemia and metabolic dysregulation within the functional network of the basal ganglia.^{11,12}

The underlying pathophysiology of HC-HB is incompletely understood. One proposed mechanism postulates that lesions of the contralateral striatum interrupt γ -aminobutyric acid (GABA) pathways to the globus pallidus externa (GPe) resulting in increased GPe neuronal activity.² The increased GPe neuronal activity causes greater inhibition of neurons within the subthalamic nucleus. Increased inhibition within the subthalamic nucleus leads to a loss of control over the globus pallidus interna causing disinhibition of the motor thalamus. Dopamine may also contribute to HC-HB and may account for the elderly female predominance. Estrogen decreases dopamine's efficacy within the nigrostriatal system, causing an increase in dopamine receptor density.¹¹ Postmenopause, estrogen decreases leading to increased sensitivity of existing dopamine receptors. The increased dopaminergic stimulation with decreased inhibitory reserve may contribute to the clinical development of HC-HB.^{2,11,12}

Prognosis of HC-HB is favorable and may be related to lesion localization. The HC-HB due to cortical lesions resolves in 85% of patients, whereas subthalamic lesions result in persistent impairment.¹⁻³ Complete symptom resolution occurs in 50% of the cases.¹⁻³ Persistent HC-HB is treated pharmacologically with neuroleptics (ie, haloperidol, perphenazine, etc).^{1,4} Atypical neuroleptics may be effective with less extrapyramidal side effects. Other medications with efficacy include tetrabenazine, reserpine, benzodiazepines, sodium valproate, gabapentin, and topamax.^{4,13}

In our patient, predisposing factors for HC-HB include advanced age, female gender, and untreated essential thrombocytosis. Recent discontinuation of aspirin therapy likely contributed to a prothrombotic state. Acute symptom onset suggested a vascular etiology and there were no contraindications to thrombolytic therapy. Although MRI is not our local standard for evaluating AIS, a more detailed investigation was pursued due to the patient's presentation,

medical comorbidities, and early arrival after the symptom onset. The initial MRI did not show T1, T2, fluid-attenuated inversion recovery (FLAIR), or diffusion-weighted imaging changes. Since restricted diffusion is closely associated with irreversible ischemia, we hypothesize that the neurological symptoms at the time of initial imaging were due to hypoperfusion that had not reached the critical threshold for infarction (ie, ischemic penumbra). Lorazepam was administered due to clinical convenience, intravenous preparation, and concomitant anxiolytic effect. The benefit of lorazepam is postulated to be due to its GABA mimetic effect within the GABA pathways to the GPe as mentioned above.¹⁴ Our literature review identified 1 report of intravenous rtPA administered for AIS in a patient presenting with HC-HB.¹⁵ The patient from this previous case report had complete resolution of HC-HB during infusion of rtPA and negative follow-up MRI. Our patient had similar improvement after rtPA infusion. Neither our patient nor the previous patient reported had any adverse effects from rtPA administration.

Stroke mimics were considered, especially given comorbid essential thrombocytosis in our patient. Typical neuroimaging of HC-HB due to essential thrombocytosis or non-ketotic HC-HB reveals T1-weighted hyperintensities with corresponding low-signal intensity in T2-weighted imaging.^{16,17} Without T1- or diffusion-weighted MRI changes to assist in clinical decision making, we chose to initiate rtPA therapy based on our high clinical suspicion for AIS. Our therapeutic approach was supported by recent studies demonstrating safety of intravenous rtPA in patients with stroke mimics or neuroimaging negative cerebral ischemia.¹⁸ Follow-up imaging at 24 hours revealing diffusion-weighted and FLAIR hyperintensities with decreased apparent diffusion coefficient images and normal T1-weighted imaging supported our clinical diagnosis of AIS and helped justify our decision to administer rtPA. Since two-thirds of HC-HB is reportedly due to small vessel disease, and patients with small vessel disease treated with thrombolytic therapy have better neurologic outcomes and lower rates of spontaneous intracerebral hemorrhage and mortality, we believe that patients with HC-HB should be considered for intravenous rtPA therapy.¹⁹

Conclusion

Hemichorea-hemiballism is a hyperkinetic movement disorder uncommonly associated with AIS. Prompt recognition of this movement disorder in the appropriate clinical setting may reduce diagnostic uncertainty and facilitate treatment with reperfusion therapies to reduce the likelihood of poststroke functional impairment.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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