

TRODAT-1 and Tc-99m ECD observations in hyperglycemia hemichorea

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Abstract

We describe two cases of right hyperglycemia hemichorea (HGHC) with identical Tc-99m TRODAT-1/Tc-99m ECD scan findings. While the brain MRI showed signal alterations within the left putamen, there was evidence of hyperperfusion on Tc-99m TRODAT-1 but hypoperfusion on Tc-99m ECD within the left putamen, in association with hyperperfusion within left thalamus on Tc-99m ECD. The discrepancy between the Tc-99m TRODAT-1 and Tc-99m ECD scan provides insight into the imbalance between direct and indirect circuits along the nigrostriatal pathway, as the fundamental genesis of HGHC. Furthermore, the hyperperfusion at the left thalamus represents thalamic disinhibition secondary to loss of pallidal negative control, which ultimately leads to HGHC through re-entrant outflow to the motor cortex.

INTRODUCTION

Hyperglycemia hemichorea (HGHC) is a rare syndrome characterized by unilateral chorea in the context of a hyperglycemic state and characteristic neuroradiological findings within the contralateral striatum.¹ Patchy hyperintensities within the putamen and/or caudate nucleus in T1 weighted imaging of magnetic resonance imaging (MRI) are regarded as the main radiological features.¹ Although HGHC has been recognized as a unique clinical-radiological syndrome for years, its mechanisms have remained obscure.²⁻⁴ While histological studies using biopsy specimens have described gemistocytic astrocytosis², autopsy cases of more complicated clinical profiles have shown infarct³, reactive astrocytosis³, or inconsistent mineral deposits.⁴ Studies dedicated to structural neuroimaging once proposed microhaemorrhage⁴, mineral deposition⁵, ischemic insults⁶, and altered hemodynamics from a venous anomaly⁷ as the favored causes of HGHC. However, there have been few functional imaging reports in the literature.^{8,9} We herein elaborate two cases of HGHC and probe its underlying pathogenesis by incorporating MRI findings with observations from a Technetium-99m TRODAT-1 scan (Tc-99m TRODAT-1) and Technetium-99m ethyl cysteinate dimer (Tc-99m ECD).

CASE REPORTS

Patient 1

A 77-year-old man with a 5-year history of diabetes mellitus presented abrupt onset and persistent involuntary movement of the right limbs for 2 weeks. The twisting motions, initially witnessed at the right foot, turned to involve the right hand days later. Hyperglycemia (321 mg/dL) with hyperosmolarity (307 mOsm/Kg) was noted. Comprehensive screens for heavy metal, autoimmune, and thyroid function were all unremarkable. Both family and drug histories were excluded. Neuroimaging studies were completed 17 days after the onset of right hemichorea. Brain MRI showed patchy hyperintensity on the T1-weighted image and hypointensity on the T2-weighted image within the left putamen (Figure 1 A, B). Diffusion weighted images were normal. During the attack of chorea, surveillance SPECT was arranged to elucidate its underlying mechanism. The Tc-99m TRODAT-1 scan showed relatively-increased uptake in the left basal ganglia, mostly within the putamen (Figure 1 C). The Tc-99m ECD showed hypoperfusion at the left putamen and relative hyperperfusion within the left thalamus (Figure 1 D). Under the treatment of risperidone 3 mg/day in line

of euglycemia achieved by insulin therapy, the hemi-chorea gradually resolved 3 weeks after the onset of chorea.

Patient 2

A 75-year-old woman with a 10-year-history of diabetes mellitus was referred to our hospital due to involuntary movement of the right limbs for 3 days. The choreiform movements, increased with emotional tension, were witnessed. Laboratory data on admission showed extremely high sugar level (573 mg/dL) and hyperosmolarity (313 mOsm/Kg). She had no related family history or prior use of dopamine antagonist or estrogen. Lupus anticoagulants, anticardiolipin antibodies, anti-β2glycoprotein antibodies, antinuclear antibodies, C3, C4, and thyroid function were all within reference range. Neuroimaging studies were completed 12 days after the onset of right hemichorea. Brain MRI showed faint hyperintensity on the T1-weighted image and hypointensity on T2-weighted image within the left putamen (Figure 1 E, F). No changes in the diffusion weighted images were identified.

Diagnosis of HGHC was made on the basis of clinical context and pathognomonic signal changes of brain MRI. Identical to the SPECT observations in Patient 1, left basal ganglia showed increased activities on the Tc-99m TRODAT-1 but decreased activities on the Tc-99m ECD (Figure 1 G, H). Hyperperfusion in the left thalamus was also noted on the Tc-99m ECD (Figure 1 H). Under intensive sugar control with treatment of haloperidol (5 mg/day), her chorea resolved 15 days after the onset of chorea.

DISCUSSION

The aim of this investigation was to probe the HGHC mechanism by integrating Tc-99m TRODAT-1 and Tc-99m ECD observations, as they reflect activity changes along the nigrostriatal pathway relevant to the genesis of hemichorea. Since neither of our cases showed evidence of acute stroke to explain their hemichorea, the diagnosis of HGHC was justified. Due to the pathognomonic signal alterations within the corpus striatum which might predate choreiform movement¹⁰, functional imaging

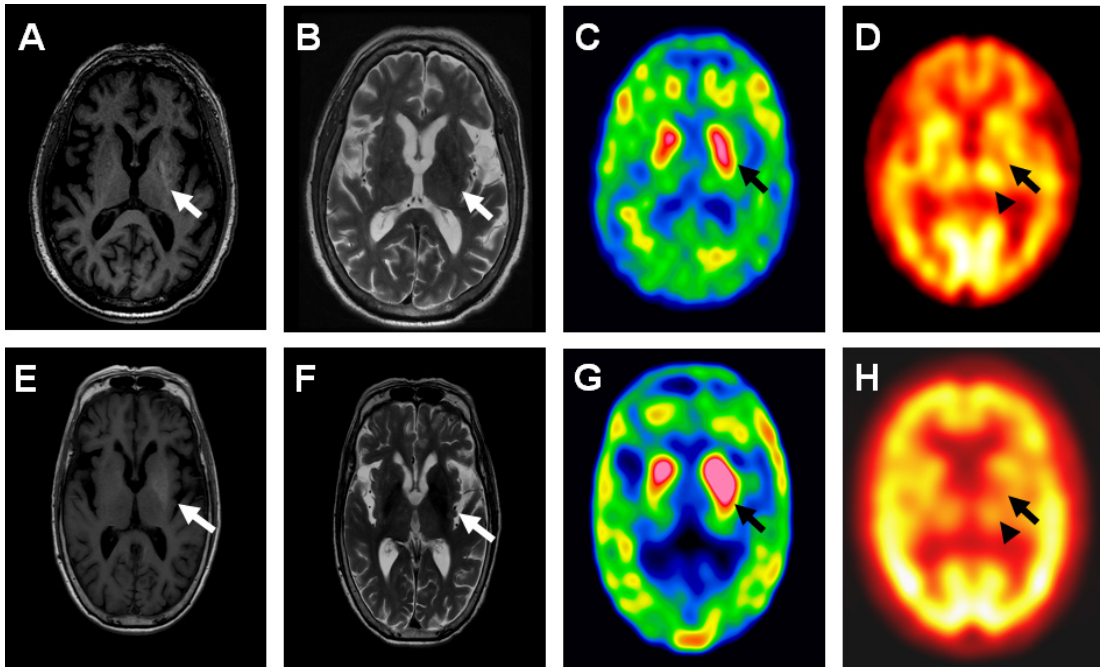


Figure 1. In both patients with right HGHC, T1-weighted image of brain MRI shows hyperintensity within left putamen (arrow) (A, E). T2-weighted image shows corresponding hypointensity (arrow) (B, F). During the attack of choreic movement, Tc-99m TRODAT-1 scan shows increased uptake in the left putamen (arrow), representing de novo upregulation of presynaptic dopamine receptors after structural damages (C, G). Tc-99m ECD shows hypoperfusion in the left putamen (arrow) and hyperperfusion in the left thalamus (arrow head), most likely due to loss of pallidal inhibitory input to the thalamus (D, H).
【Patient 1: (A-D). Patient 2: (E-H)】

might provide a more fascinating insight into relevant neurochemical and metabolic changes. As the striatal outputs are segregated into direct and indirect pathways, patchy but not complete damage may lead to an imbalance between these two circuits.² Coexistence of the activated direct pathway and the impaired indirect pathway has been conjectured to be the genesis of hemichorea-hemiballism.² From the Tc-99m TRODAT-1 in our patients, the increased uptake, mostly within the putamen, reflects the upregulation of presynaptic dopamine receptors as well as incomplete damage of corpus striatum. We therefore hypothesize that activation of the direct pathway in line of dopamine hypersensitivity contributes to the hemichorea movement. Some may speculate that the Tc-99m TRODAT-1 findings are the epiphenomena modified by risperidone or secondary to putamen structural damage. It is, however, the disproportionate signal asymmetry that makes such a consideration less likely. Our case report explores the utility of the Tc-99m TRODAT-1 in HGHC, as it identifies relevant neurotransmitter-specific information within an anatomic locus. To the best of our knowledge, few reports have applied the Tc-99m TRODAT-1 scan in the evaluation of HGHC.

The hypoperfusion of the putamen in the Tc-99m ECD turned out to be an interesting parallel compared with the Tc-99m TRODAT-1 findings. The microstructural changes plus a direct effect of hyperglycemia can negatively impact on the affected neuronal substrates, leading to energy depletion and hypoperfusion evident in the Tc-99m ECD. We therefore speculate that the hypoperfusion of the putamen represents the disintegration of the indirect pathway. It is also worth underpinning the hyperperfusion of the thalamus contralateral to the site of HGHC in our case, which reflects changes secondary to the putamen hypofunction, as the major downstream mechanisms corresponding to the hemichorea. From the literature on SPECT, signal asymmetry within basal ganglia, either hyper- or hypoperfused, develops during a certain period of HGHC.^{6,8,9} The asymmetric perfusion identified from SPECT indicates the dynamic changes within the striatum as a crucial mechanism. It is postulated that the hyperperfusion of the basal ganglia is the result of vascular autoregulation during the early course of damage. Hypoperfusion, on the other hand, reflects neuronal metabolic derangement due to hyperglycemia, vascular insufficiency, or both.⁹ Overall, the pathogenesis of HGHC is hypothesized as thalamic disinhibition

secondary to loss of pallidal negative control, which ultimately leads to hyperkinetic movement disorders through re-entrant outflow to the motor cortex.

In summary, we postulate that the pathophysiological bases of HGHC are (i) the imbalance between direct and indirect circuits in nigrostriatal pathway, and (ii) the loss of pallidal inhibitory input to the thalamus.

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DISCLOSURE

Conflict of interests: None.

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