Non-Ketotic Hyperglycemia Induced Hemichorea-Hemiballism May Represent Glioma-Like Pattern On Multimodal Magnetic Resonance Imaging: Can ^{1}H Spectroscopy Help In The Differentiation?

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Case report

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Abstract

Background: Non-ketotic hyperglycemia (NKH) induced hemichorea-hemiballismus (HC-HB) is a rare reversible condition predominantly found in elderly patients with poorly controlled diabetics. Here, we describe two cases of NKH induced HC-HB with distinctive morphological and functional changes on conventional magnetic resonance imaging (MRI), diffusion-weighted imaging (DWI) and ^{1}H magnetic resonance spectroscopy (MRS).

Case presentation: In case 1 with NKH induced HC-HB, computer tomography depicted increased attenuation in the left putamen and caudate nucleus. Focal T2-hyperintensity, obvious mass effect and ring-like enhancement were revealed on conventional MRI, suggesting the imaging findings of glioma. DWI indicated the lesion with unrestricted diffusion of water molecule. MRS further illustrated markedly increased lactate (Lac) and lipids (Lip), slightly elevated choline (Cho), and slightly decreased N-acetylaspartate (NAA) within the lesion. In case 2, baseline and follow-up MRI showed a lesion with typical reversible signal intensity in the right putamen without mass effect.

Conclusions: This report emphasizes that NKH induced HC-HB may exhibit a unique appearance mimicking glioma. Slightly elevated Cho/NAA ratio with marked increased Lac peak on MRS may help to exclude neoplastic diseases.

Background

Diabetes mellitus is associated with pathological changes in the central nervous system that lead to impairments in neurobiology, cognition, and behavior. Non-ketotic hyperglycemia (NKH) induced hemichorea-hemiballismus (HC-HB) is a rare reversible condition predominantly found in elderly patients with poorly controlled type 2 diabetics [1].

Though the overall prognosis of NKH induced HC-HB is excellent and the radiological abnormalities are generally reversible, timely neuro-imaging and accurate diagnosis are vital for such patients with acute involuntary symptoms to rule out stroke, infection or even tumor [2, 3]. Typical imaging findings are increased attenuation within unilateral basal ganglia on computer tomography (CT) and corresponding increased signal intensity on T1-weighted image (T1WI) of magnetic resonance imaging (MRI) [2, 4, 5]. In the previous literature, functional MRI techniques including diffusion-weighted imaging (DWI) and ^{1}H magnetic resonance spectroscopy (MRS) were rarely used in the diagnosis and follow-up of NKH induced HC-HB.

We describe here two cases of NKH induced HC-HB with distinctive morphological and functional changes on conventional MRI, diffusion-weighted imaging (DWI) and ^{1}H magnetic resonance spectroscopy (MRS).

Case Presentation

Case 1

A 70-year-old male with a 20-year history of diabetes presented with severe involuntary movement of the right lower extremity for 2 days. The patients did not regularly take hypoglycemic drugs and monitor blood glucose. His baseline non-fasting plasma glucose was 9.08 mmol/L, serum osmolality was 307.10 mOsm/L, urinary ketone was negative.

Brain CT scan showed increased attenuation in the left putamen and caudate nucleus. Further MRI indicated the corresponding areas with heterogeneous hyperintensity on T1WI. T2 weighted image (T2WI) and fluid-attenuated inversion recovery (FLAIR) sequence suggested an irregular hyperintensity lesion in the caudate nucleus with distinct mass effect (indicated by the effacement of anterior horn of lateral ventricle). Interestingly, the focal lesion revealed evident ring-like enhancement on contrast-enhanced T1WI, which suggested the imaging findings of glioma (Fig. 1).

As an advanced MRI technology, DWI showed the lesion with iso-intensity or hypo-intensity (indicating unrestricted diffusion of water molecules within the lesion). In addition, single-voxel ^{1}H MRS further illustrated markedly increased lactate (Lac) level and lipids (Lip) level, slightly elevated choline (Cho) level, slightly decreased N-acetylaspartate (NAA) level and basically stable creatine (Cr) level. The Cho/NAA ratio, Cho/Cr ratio, NAA/Cr ratio, and (Lac+Lip)/Cr ratio were 0.675, 1.04, 1.54, and 1.34, respectively (Fig. 1).

The patient's symptoms gradually improved over days after hypoglycemic and antiepileptic treatment. Three months later, follow-up MRI showed an obvious resolution of the glioma-like abnormalities in the caudate nucleus, while patchy T1-hyper-intense area still existed in the basal ganglia region (Fig. 1).

Case 2

An 84-year-old female presented with weakness and involuntary movement of the left extremity for 20 days. His baseline non-fasting plasma glucose was 16.21 mmol/L, serum osmolality was 307.39 mOsm/L, urinary ketone was negative, glycosylated hemoglobin was up to 131 mmol/mol.

The patient represented increased attenuation in right putamen on CT. Corresponding T1-hyper-intensity and T2-hypo-intensity were revealed on MRI without mass effect. No obvious restricted diffusion was found on DWI in the corresponding area. Her symptoms improved after immediate hypoglycemic and neuroprotective treatment. After 2 months of follow-up, CT displayed a complete resolution of the previously described lesion (Fig. 2).

Discussion And Conclusions

Bedwell firstly described HC-HB in the year 1960 as an unusual movement disorder induced by poorly controlled diabetes. NKH induced HC-HB were sporadically reported in cases with east Asian origin, which

suggested hyperglycemia as a rare cause (only 1%) of chorea with a possible genetic disposition [1, 6].

Although the precise mechanism of NKH induced HC-HB remained controversial, the mainstream theory holds that hyperglycemia causes the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) to be consumed as an alternative energy source in the affected parenchyma [1, 7]. Consequently, reduction of GABA signaling in the thalamus could lead to increased excitatory thalamocortical drive and secondary involuntary movements on the contralateral side [7].

The cause-and-effect relationship of NKH induced HC-HB between hyperglycemia state and imaging patterns has not yet been fully proved. The T1-hyper-intensity was initially thought to be due to focal hemorrhage, demyelination, or calcification after “ischemic events”, but currently attributed to presence of gemistocytes (special reactive astrocytes) that could accumulate manganese (causing T1 shortening effect) after chronic ischemia [1–4, 6].

The glioma-like appearance in the first case, as an unexpected discovery, was mainly ascribed to the obvious enhancement on T1WI after injection of paramagnetic contrast agent. We assumed that the abnormal contrast enhancement may be due to high-glucose-induced inflammatory responses and increased blood-brain barrier permeabilities under hyperglycemia conditions [3, 7]. It should also be noted that DWI revealed no evidence of cytotoxic edema or active cell proliferation (presented as restricted diffusion in patients with acute cerebral infarction or high-grade glioma) in the corresponding area.

MRS is a non-invasive method used for identifying specific metabolic markers of seizure-induced neuronal damage, which has not been systematically reported in patients with NKH induced HC-HB [8]. Excessive activation of various molecular pathways could lead to loss of balance between anaerobic glycolysis and oxidative metabolism (which produces large quantities of Lac) in such cases [2]. Thus, in-situ Lac level as illustrated by MRS could be applied in assessing possible “ischemic damage” of NKH induced HC-HB [3, 8]. Besides, the quantitative parameter Cho/NAA ratio of MRS is widely used in the differentiation of brain tumors and non-tumor diseases. In the vast majority of gliomas (especially glioblastoma), Cho peak markedly increased (suggesting increased cell membrane synthesis) and NAA peak markedly decreased (suggesting neuronal damage). By contrast, a relatively low Cho/NAA ratio (<1) suggested the diagnosis of a metabolic/reversible disease as revealed by our case.

In conclusion, a combination of long-term uncontrolled hyperglycemia, unilateral involuntary movements and contralateral basal ganglia abnormalities may suggest the diagnosis of NKH induced HC-HB. In addition to the classic T1-hyper-intensity characteristic, this report emphasizes the reversible focal neurological disorder may exhibit a unique appearance mimicking glioma. Slightly elevated Cho/NAA ratio with marked increased Lac peak on MRS may help to exclude neoplastic diseases.

Abbreviations

NKH: Non-ketotic hyperglycemia; HC-HB: Hemichorea-hemiballismus; CT: Computer tomography; MRI: Magnetic resonance imaging; T1WI: T1-weighted image; T2WI T2-weighted image; DWI: Diffusion-

weighted imaging; MRS: Magnetic resonance spectroscopy; Lac: Lactate; Lip: Lipids; Cho: Choline; NAA: N-acetylaspartate.

Declarations

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Author contributions Yu Lin contributed to literature search, clinical analysis, and writing the initial manuscript. Xiaoxiao Zhang contributed to CT/MRI analysis and writing the original manuscript. Xin Yue contributed to conception and design of the investigation. Jinan Wang contributed to data interpretation and study supervision.

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Conflict of interest The authors declare no conflict of interest regarding the report.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

Availability of data and material The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

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Figures

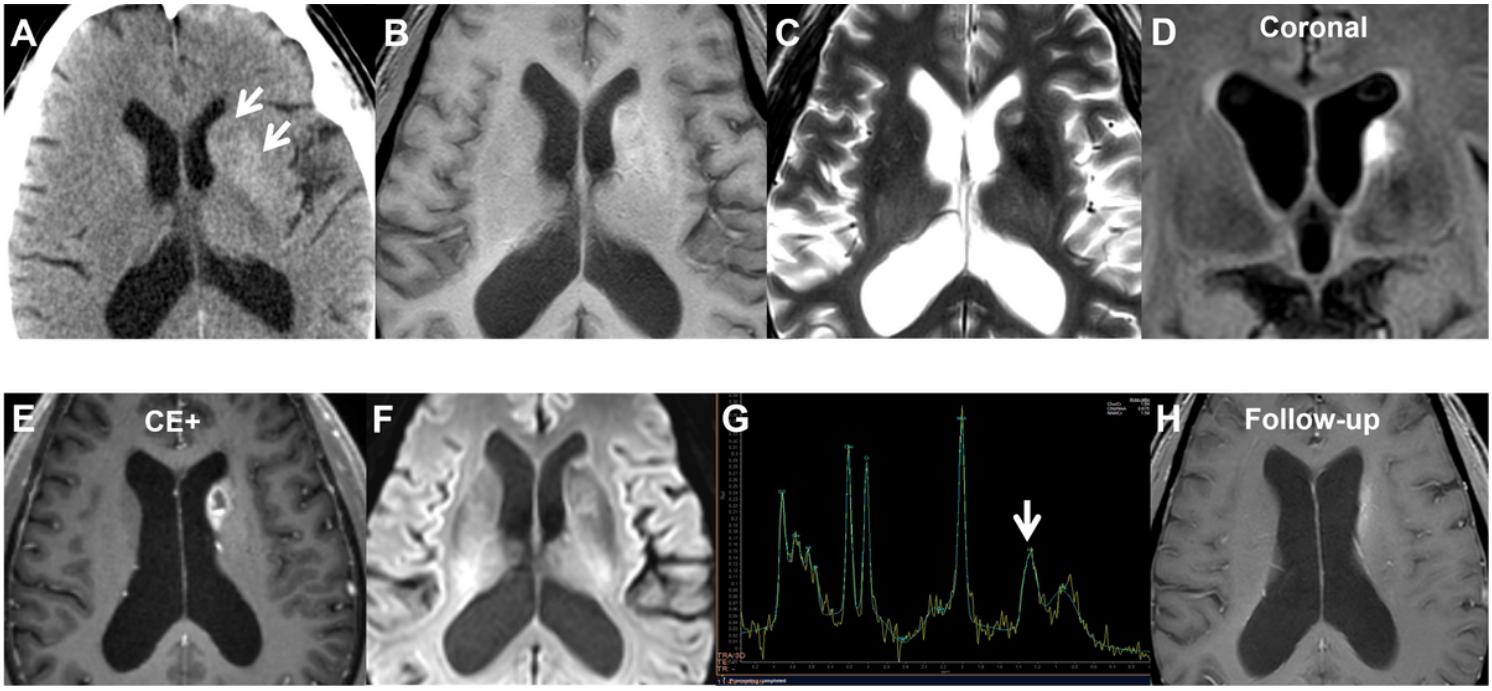

Figure 1

A 70-year-old male patient with non-ketotic hyperglycemia-induced hemichorea-hemisballismus. The lesions of the left putamen and caudate nucleus (arrows) showed hyperdensity on CT (a) and

hyperintensity on T1-weighted image (T1WI) (b). T2 weighted image (c) and coronal fluid-attenuated inversion recovery sequence (d) suggested an irregular hyperintense lesion in the caudate nucleus with mass effect. The corresponding lesion manifests ring-like enhancement on contrast-enhanced T1WI (e) and iso-intensity or hypo-intensity on the diffusion-weighted image (f). Magnetic resonance spectroscopy (g) showed markedly increased lactate peak (arrow) and slightly elevated choline peak. Follow-up contrast-enhanced T1WI (h) in 3 months showed an obvious resolution of the previous lesion.

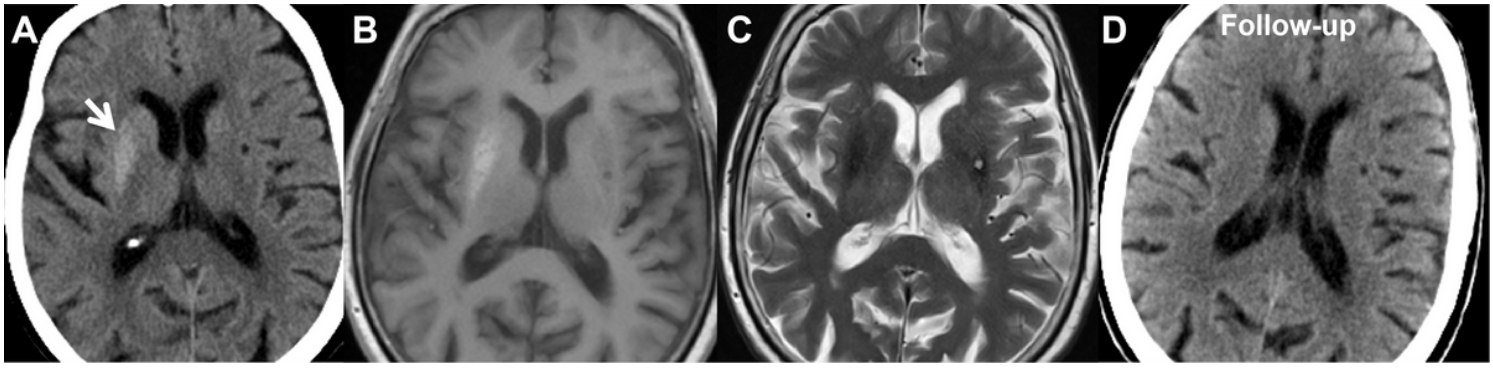

Figure 2

A 84-year-old female patient with non-ketotic hyperglycemia-induced hemichorea-hemisballismus. The lesions of the right putamen (arrow) show hyperdensity on CT (a), hyperintensity on T1-weighted image (b) and hypointensity on T2 weighted image (c). Follow-up CT (d) in 2 months showed a complete resolution of the previous lesion.