ISSN 2307-8960 (online)

World Journal of *Clinical Cases*

World J Clin Cases 2024 February 16; 12(5): 872-1038

Published by Baishideng Publishing Group Inc

World Journal of Clinical Cases

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World Journal of Clinical Cases

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RESPONSIBLE EDITORS FOR THIS ISSUE

NAME OF JOURNAL
World Journal of Clinical Cases

ISSN
ISSN 2307-8960 (online)

LAUNCH DATE
April 16, 2013

FREQUENCY
Thrice Monthly

PUBLICATION DATE
February 16, 2024

World Journal of Clinical Cases

Submit a Manuscript: https://www.f6publishing.com

World J Clin Cases 2024 February 16; 12(5): 1004-1009

DOI: 10.12998/wjcc.v12.i5.1004

ISSN 2307-8960 (online)

CASE REPORT

Neuroimaging features in a patient with non-ketotic hyperglycaemic seizures: A case report

Jing Wu, Huijie Feng, Yaxiong Zhao, Junfeng Li, Ting Li, Kefeng Li

Specialty type: Neuroimaging

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Tuncyurek O, Cyprus; Yarmahmoodi F, Iran

Received: October 27, 2023
Peer-review started: October 27, 2023
First decision: November 28, 2023
Revised: December 27, 2023
Accepted: January 17, 2024
Article in press: January 17, 2024
Published online: February 16, 2024

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Abstract

BACKGROUND

Non-ketotic hyperglycaemic (NKH) seizures are a rare neurological complication of diabetes caused by hyperglycaemia in non-ketotic and non-hyperosmotic states. The clinical characteristics of NKH seizures are atypical and lack unified diagnostic criteria, leading to potential misdiagnoses in the early stages of the disease.

CASE SUMMARY

This report presents a rare case of NKH seizures in a 52-year-old male patient with a history of type 2 diabetes mellitus. We performed comprehensive magnetic resonance imaging (MRI) studies at admission, 12 d post-admission, and 20 d post-discharge. The imaging techniques included contrast-enhanced head MRI, T2-weighted imaging (T2WI), fluid-attenuated inversion recovery (FLAIR), diffusion-weighted imaging, susceptibility-weighted imaging, magnetic resonance spectroscopy (MRS), and magnetic resonance venography. At the time of admission, T2WI and FLAIR of the cranial MRI showed that the left parieto-occipital cortex had gyrus-like swelling and high signal, and subcortical stripes had low signal. MRS showed a reduced N-acetylaspartate peak and increased creatine and choline peaks in the affected areas. A follow-up MRI 20 d later showed that the swelling and high signal of the left parieto-occipital cortex had disappeared, and the low signal of the subcortex had disappeared.

CONCLUSION

This case study provides valuable insights into the potential pathogenesis, diagnosis, and treatment of NKH seizures. The comprehensive MRI findings

highlight the potential utility of various MRI sequences in diagnosing and characterizing NKH seizures.

Key Words: Non-ketotic hyperglycaemia seizures; Magnetic resonance imaging; Magnetic resonance spectroscopy; Diabetes; Case report

Core Tip: This study presents a rare case of non-ketotic hyperglycaemic (NKH) seizures in a patient with type 2 diabetes. These seizures are a complication of diabetes, though they lack specific diagnostic criteria and are often misdiagnosed. In particular, the magnetic resonance imaging (MRI) findings of these manifestation have rarely been described in the literature, and previous reports are inconsistent. In this report, we describe the comprehensive findings in several MRI sequences, including T2-weighted images, fluid-attenuated inversion recovery, diffusion-weighted imaging, susceptibility-weighted imaging, and magnetic resonance spectroscopy and venography. We believe that our study makes a significant contribution to the literature because these findings can help elucidate the pathogenesis, diagnosis, and treatment of this rare condition. Further, we believe that this paper will be of interest to the readership of your journal because this case report expands the clinical knowledge on NKH seizures, a rare but severe complication of diabetes.

Citation: Wu J, Feng H, Zhao Y, Li J, Li T, Li K. Neuroimaging features in a patient with non-ketotic hyperglycaemic seizures: A case report. *World J Clin Cases* 2024; 12(5): 1004-1009
URL: https://www.wjgnet.com/2307-8960/full/v12/i5/1004.htm
DOI: https://dx.doi.org/10.12998/wjcc.v12.i5.1004

INTRODUCTION

Non-ketotic hyperglycaemia (NKH) is a rare clinical syndrome characterised by hyperglycaemia, serum hyperosmolarity, and intracellular dehydration with no ketoacidosis. NKH mainly affects patients with type 2 diabetes over 50 years of age and is often considered a complication of this metabolic disease in patients with poor glycaemic control or in undiagnosed patients as a first symptom[1].

NKH seizures are associated with various neurological manifestations, including epilepsy, headache, consciousness and vision alterations, and movement disorders. Magnetic resonance imaging (MRI) is a valuable tool for the accurate diagnosis of NKH seizures; however, findings from head imaging studies are inconsistent. Some researchers have suggested that unilateral subcortical hypointensities in T2-weighted imaging (T2WI) or fluid-attenuated inversion recovery (FLAIR) sequences are a characteristic MRI feature of NKH seizures, whereas others did not observe these findings[2,3]. Other MRI features reported in the literature include subcortical hypointense shadows on susceptibility-weighted imaging (SWI), focal enhancement of the pia mater and local cortex, and in arterial spin labelling sequences, enhancement of focal cerebral parenchyma perfusion[3-5]. Nevertheless, more extensive MRI evidence with multiple sequences is necessary to characterise and comprehensively understand the pathogenesis of NKH seizures.

Here, we present a rare case of NKH seizures in a patient. We also review the comprehensive MRI characteristics of this patient, including contrast-enhanced head MRI, T2WI, FLAIR, diffusion-weighted imaging (DWI), SWI, magnetic resonance spectroscopy (MRS), and magnetic resonance venography (MRV).

CASE PRESENTATION

Chief complaints

Dizziness for three days, aggravated with general convulsions for two hours.

History of present illness

A 52-year-old man with a one-year history of type 2 diabetes mellitus developed dizziness of unknown aetiology, accompanied by lethargy, poor mental status, and delayed reactions. The patient self-administered 'cold and flu capsules', although the dizziness symptoms persisted. On the second day, the patient experienced weakness and numbness in the right upper limb during work, accompanied by dizziness. This right upper extremity symptom manifested as weakness/difficulty in fine movements, such as holding chopsticks, with conserved lifting ability. The upper extremity and dizziness symptoms were not accompanied by altered consciousness or convulsions and resolved spontaneously after approximately one hour.

Three days later, the patient presented to the emergency room with worsening symptoms. During the consultation, the patient was in and out of consciousness, with delayed and inappropriate responses, subsequent involuntary lifting of the right upper limb, flexion and tonicity of the limbs with clonus, mouth foaming, upward gaze, and clenched teeth for more than 10 min. The symptoms were relieved with an intramuscular injection of sodium phenobarbital. Upon regaining full

consciousness, the patient was able to communicate and answer questions correctly.

The patient was admitted to the neurology department for further treatment. Admission vital signs and neurological examination were normal.

History of past illness

History of "diabetes mellitus" for 1 year, complaining of fair glycaemic control.

Personal and family history

No special notes.

Physical examination

Admission vital signs and neurological examination were normal.

Laboratory examinations

His admission blood glucose level was 329.4 mg/dL, and a cerebrospinal fluid sample showed a glucose level of 138.2 mg/dL, with negative tests for antibodies associated with autoimmune encephalitis and paraneoplastic syndrome. Blood glucose levels fluctuated between 129.6 and 351.0 mg/dL after admission.

Imaging examinations

A head MRI at admission showed a slight hyperintensity in the left parieto-occipital cortex and a subcortical hypointense line in T2WI and FLAIR images (Figure 1A and B). DWI revealed a limited diffusion-restricted signal in the same area and a reduced apparent diffusion coefficient (ADC map) (Figure 1C and D). MRS revealed a reduced N-acetylaspartate (NAA) peak and increased creatine and choline peaks in the left parietal-occipital cortex and subcortical areas, suggesting neuronal damage and metabolic encephalopathy (Figure 1E–H). Contrast-enhanced MRI showed swelling of the left parieto-occipital gyrus and localized soft meningeal enhancement in the parietal lobe (Figure 1I and 1J). No significant alterations were noted on SWI (Figure 1K) and MRV. Non-ketotic hyperglycaemia-associated epilepsy is difficult to identify and is even misdiagnosed in the emergency medical setting. It is distinguished from major acute infarction stroke, reversible posterior encephalopathy syndrome, encephalitis, and meningitis by the richness of cranial nuclear magnetic sequence manifestations in conjunction with clinical test indices. On day 5 of hospitalization, an electroencephalogram (EEG) revealed bilateral spike emanations in the frontal and central regions, asynchronous left and right sides, and multiple slow-wave activities in the left parietal, occipital, and temporal regions. These EEG alterations were consistent with the cortical swelling seen on MRI.

FINAL DIAGNOSIS

Non-ketotic hyperglycaemia-associated epilepsy.

TREATMENT

Following admission, the patient was treated with antiepileptic drugs *via* an intramuscular injection of 200 mg of phenobarbital sodium and antidiabetic therapy consisting of 10 mg of dapagliflozin taken orally once a day, 0.5 g of metformin hydrochloride extended-release tablets taken twice a day, and 4–6 IU of subcutaneous insulin given once a day in case of poor glycaemic control, as well as fluid supplementation to improve blood circulation.

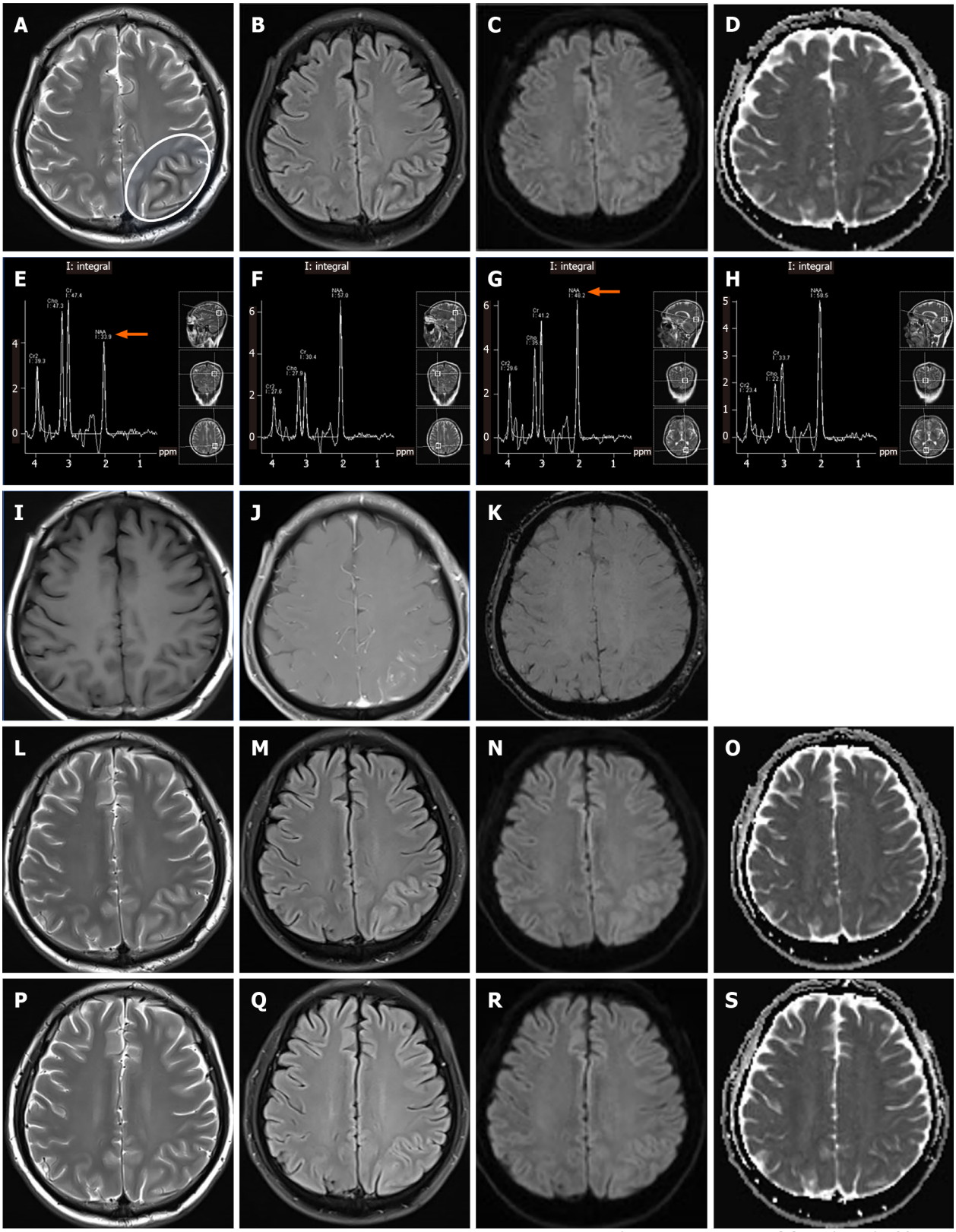
OUTCOME AND FOLLOW-UP

MRI after 12 d of treatment showed alleviation of the subcortical hypointense T2 signal (Figure 1L). The hyperintensity observed on FLAIR images in the left parieto-occipital cortex was more pronounced than that seen on the MRI upon admission (Figure 1M). The performance of DWI and ADC did not change significantly from the images taken on admission (Figure 1N and O).

The patient did not experience any further seizures after admission and was discharged after 2 wk, continuing the diabetes treatment and blood glucose monitoring at home. A follow-up MRI 20 d later showed disappearance of the swelling and hyperintensity in the left parieto-occipital cortex and of the subcortical hypointensities seen on T2WI and FLAIR images (Figure 1P and Q).

DISCUSSION

Currently, no diagnostic criteria for NKH seizures have been established. Previous case studies show that blood glucose, osmolality, and haemoglobin A1c levels are often elevated in patients with NKH seizures. However, the degree of



DOI: 10.12998/wjcc.v12.i5.1004

Figure 1 Head magnetic resonance imaging findings of a patient with non-ketotic hyperglycaemic seizures with hyperhomocysteinaemia. A-D: Images at admission, showing the left parieto-occipital cortex (white arrow) on (A) T2-weighted images (T2WI) and (B) fluid-attenuated inversion recovery (FLAIR) sequence with cortical swelling and hyperintense T2 signal. (C) Diffusion-weighted imaging (DWI) shows restricted diffusion in the left parieto-occipital cortex and (D) low signal in the apparent diffusion coefficient (ADC) map; E–H: Magnetic resonance spectroscopy (MRS) images on the day after admission, showing (E) decreased N-acetylaspartate (NAA) peaks (white arrows) in the left parieto-occipital subcortex, increased creatine (Cr) and choline (Cho) peak, and (F) no significant alterations in the right parieto-occipital subcortex. MRS also showed (G) decreased NAA peaks (white arrows) in the left parieto-occipital cortex, and increased Cr and Cho peaks, less evident than in the corresponding subcortex in panel (E). (H) The right parieto-occipital cortex showed no significant alterations; I–K: Contrast-enhanced magnetic resonance imaging (MRI) images on the day after admission, showing no significant alterations on (E) T1-weighted images, with swelling of the

left parieto-occipital gyrus and localized soft meningeal enhancement in the parietal lobe (J). No significant alterations were noted on susceptibility-weighted imaging (K); L–O: MRI findings after 12 d of treatment, showing alleviation of the subcortical hypointensities on (L) T2WI and (M) FLAIR images, with more pronounced hyperintensity in the left parieto-occipital cortex in the latter than at admission. (N) DWI and (O) ADC map showed no significant changes; P–S: Follow-up MRI images 20 d after discharge, showing normalisation of the left parieto-occipital cortex and subcortical areas on (P) T2WI and (Q) FLAIR images. (R) DWI and (S) ADC map showed no significant alterations.

elevation varies from case to case, with the majority of patients having only moderate hyperglycaemia, without significant hyperosmolality, and not meeting the diagnostic criteria for hyperosmolar hyperglycaemia syndrome (plasma glucose level of ≥ 600 mg/dL, serum osmolality of ≥ 320 mOsm/kg)[6]. This suggests that prolonged hyperglycaemia may lead to seizures rather than extreme hyperglycaemia, which is associated with an acute seizure[7].

In the present case, MRS revealed a decrease in NAA and an increase in creatine and choline in the affected cortical and subcortical regions compared to the contralateral regions. To our knowledge, these findings represent the first MRS report of non-ketotic hyperglycaemia-related epileptic brain lesions. NAA is a biomarker of neuronal density and survival, reflecting the functional status of neurones, whereas creatine is a biomarker of energy-dependent brain cell systems, which increases in low metabolic states. Choline is involved in cell membrane synthesis and metamorphosis, reflecting cell membrane renewal as a component of phospholipid metabolism[8]. Overall, these findings highlight the potential utility of MRS in the diagnosis and characterisation of NKH seizures.

Reversible subcortical T2WI/FLAIR hypointense areas are a specific manifestation of non-ketotic hyperglycaemia-related epilepsy, often attributed to iron deposition or free radicals[4]. The exact aetiology of this manifestation remains unclear; however, some patients present hypointensities in SWI sequences related to astrocyte dysfunction, which leads to iron deposition due to astrocyte involvement in the regulation of iron molecule inflow and outflow[9]. In the present case, no mineral-related hypointense alterations were found in the SWI sequence, suggesting that the short-term accumulation of free radicals due to axonal damage in excitatory neurones caused the lesions. This accumulation can cause T2 shortening effects, resulting in subcortical T2/FLAIR undersignalling[10].

Limited cortical diffusion signal and T2WI/FLAIR hyperintensities are common imaging signs of seizures. Decreased cortical diffusion signals reflect cytotoxic oedema, whereas T2WI/FLAIR cortical hyperintensity is associated with vasogenic oedema resulting from increased blood–brain barrier permeability. Vasogenic cerebral oedema is caused by increased capillary permeability due to damage and disruption of the blood–brain barrier, increased water exudation, and accumulation in the perivascular and intercellular spaces. The cerebral pia mater enhancement confirmed the altered permeability in the present case.

The current treatment of NKH seizures focuses on glycaemic control and maintaining stable blood glucose in an effort to prevent, reduce, and control seizures. However, the use of antiepileptic drugs remains controversial. Available case reports have found that most patients are poorly treated with antiepileptic drugs alone and that antiepileptic drugs, such as phenytoin sodium, cause insulin resistance and elevated blood glucose levels, leading to decreased antiepileptic effects and NKH-associated exacerbation of epilepsy[11]. The disease has a favourable prognosis; poor glycaemic control is the main cause of its recurrence. NKH seizures are difficult to recognize and can be misdiagnosed in the emergency medical setting due to a lack of awareness, making early and accurate recognition and appropriate treatment important.

CONCLUSION

We have reported a case of NHK-related seizures, focusing on detailed characteristics derived from various MRI sequences. This case study provides valuable insights into the pathogenesis, diagnostic processes, and potential treatment strategies for this rare condition. Our findings underscore the importance of comprehensive MRI analysis in managing complex neurological presentations associated with metabolic disorders, paving the way for future research in this field.

ACKNOWLEDGEMENTS

We are grateful to the patient and his family for their collaboration.

FOOTNOTES

Co-corresponding authors: Kefeng Li and Ting Li.

Author contributions: Wu J, Feng H, Zhao Y, and Li K conceived the article and wrote the manuscript draft; Wu J, Li J, and Li T were involved in the clinical care of the patient. Both Li T and Li K have played important and indispensable roles in the experimental design, data interpretation and manuscript preparation as the co-corresponding authors. Li T conceptualized, designed, and supervised the whole process of the project. Li K was instrumental and responsible for data re-analysis and re-interpretation, figure plotting, comprehensive literature search, preparation and submission of the current version of the manuscript. This collaboration between Li K and Li T is crucial for the publication of this manuscript and other manuscripts still in preparation. All authors critically reviewed the manuscript for intellectual content and edited the article.

Supported by Four "Batches" Innovation Project of Invigorating Medical Through Science and Technology of Shanxi Province, No. 2023XM016.

Informed consent statement: Informed consent for publication was obtained from the patient's guardian.

Conflict-of-interest statement: All the authors declare that they have no conflict of interest.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

Country/Territory of origin: China

ORCID number: Ting Li 0009-0004-7713-3319; Kefeng Li 0000-0002-7233-4347.

S-Editor: Liu JH
L-Editor: A
P-Editor: Yu HG

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