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Wernicke's Encephalopathy Masquerading as Hepatic Encephalopathy in Severe Cholestatic Drug-Induced Liver Injury: A Case Report

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Case Report

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Abstract

Background

Wernicke's encephalopathy (WE) is a life-threatening neurological emergency caused by thiamine (vitamin B1) deficiency, classically associated with chronic alcohol use. However, in non-alcoholic patients, it is often precipitated by prolonged periods of malnutrition or chronic illness, where it remains frequently underdiagnosed.

Case presentation:

A 59-year-old lifelong non-alcoholic male presented with a three-month history of progressive cholestatic drug-induced liver injury (DILI) following a course of oral co-amoxiclav therapy. His clinical course was complicated by severe anorexia, weight loss, and severe biochemical hypothyroidism. Despite improving liver enzymes and normalisation of thyroid function following levothyroxine replacement, the patient developed acute confusion, agitation, and truncal ataxia. Initial clinical suspicion was directed toward hepatic encephalopathy (HE) due to persistent jaundice (bilirubin 230 μmol/L); however, the absence of asterixis and the presence of atypical neurological signs prompted neuroimaging. Magnetic resonance imaging (MRI) of the brain revealed symmetrical T2/FLAIR hyperintensities in the mammillary bodies, thalami, and periventricular region of the third ventricle, confirming a diagnosis of WE. Prompt administration of high-dose intravenous thiamine resulted in a full neurological recovery.

Conclusions

This case highlights the "diagnostic trap" of anchoring bias in hepatology, where neurological symptoms are reflexively attributed to HE in the presence of biochemical liver injury. In patients with chronic DILI and protracted anorexia, clinicians must maintain a high index of suspicion for WE to prevent permanent neurological damage.

Background

WE is an acute neuropsychiatric syndrome resulting from the depletion of thiamine pyrophosphate, a critical co-factor in cerebral energy metabolism [1]. While traditionally viewed through the lens of alcohol use disorder, WE in the non-alcoholic population is increasingly recognised as a complication of prolonged malnutrition, hyperemesis, or chronic systemic illness [2, 3].

In the context of severe liver disease, diagnosing WE presents a unique clinical challenge. Neurological deterioration in a jaundiced patient is frequently, and often exclusively, attributed to hepatic encephalopathy (HE). This report describes an instructive case of WE masquerading as HE in a patient

with protracted cholestatic DILI, underscoring the critical need for broad differential diagnoses in hepatology.

Case presentation

A 59-year-old male with no history of alcohol consumption presented with a three-month history of progressive jaundice, severe anorexia, and significant weight loss—a protracted course of systemic illness initiated by a recent course of oral co-amoxiclav. Structural causes of jaundice were excluded by abdominal ultrasonography, magnetic resonance cholangiopancreatography, and contrast-enhanced computed tomography of the abdomen, which demonstrated mild intrahepatic bile duct prominence without extrahepatic biliary obstruction. Initial investigations also revealed an incidental finding of profound biochemical hypothyroidism.

Extensive aetiological screening for viral hepatitis and autoimmune liver disease was negative. Percutaneous liver biopsy confirmed drug-induced cholestatic liver injury, demonstrating portal tract expansion, mixed inflammatory infiltrate, prominent canalicular and hepatocellular cholestasis, and eosinophilic infiltration, without steatohepatitis, fibrosis, or features of autoimmune or viral aetiology.

The patient was managed supportively for DILI, and his hypothyroidism was corrected with levothyroxine replacement therapy. Despite a gradual improvement in his transaminases and normalisation of his thyroid function, his clinical condition deteriorated. He developed acute-onset confusion, psychomotor agitation, and truncal ataxia. Given his persistent jaundice (serum bilirubin plateaued at 230 µmol/L), and a marginally elevated INR (1.6–1.8), the initial working diagnosis was HE.

However, several features argued against this: asterixis (flapping tremor), a sign classically associated with HE, was notably absent on neurological examination; there were no identifiable precipitants such as sepsis, gastrointestinal bleeding, or constipation; and the encephalopathy failed to improve with standard ammonia-lowering therapy. Neurological examination instead demonstrated a wide-based gait and truncal ataxia. The presence of ataxia and agitation in the context of prolonged malnutrition raised the suspicion of a nutritional aetiology.

An urgent MRI of the brain was performed, which demonstrated characteristic symmetrical T2/FLAIR hyperintensities in the periventricular region of the third ventricle (Fig. 1), mammillary bodies (Fig. 2), and medial thalami (Fig. 3) respectively. These radiological findings, combined with his clinical presentation and history of prolonged anorexia, definitively established the diagnosis of WE. The patient was immediately started on high-dose intravenous thiamine therapy (500mg TDS), leading to a rapid and complete resolution of his neurological deficits.

Discussion

This case illustrates that in the clinical setting of chronic liver injury, encephalopathy is not a monolithic diagnosis. The presence of jaundice should not preclude a rigorous nutritional assessment [3].

Cholestatic DILI frequently precipitates prolonged anorexia, nausea, and vomiting, which can rapidly deplete hepatic thiamine stores and unmask WE [4, 5, 6].

MRI is essential for confirming WE, although imaging patterns vary by aetiology. Alcoholic WE typically demonstrates symmetrical T2/FLAIR hyperintensities in the mammillary bodies, medial thalami, and periaqueductal grey matter, whereas non-alcoholic WE more frequently involves atypical cortical, subcortical, cerebellar, and cranial nerve regions [7, 8] Despite the absence of alcohol use, our case demonstrated a classical radiological pattern. Mammillary body involvement, while highly specific, may be absent. These observations highlight that imaging phenotypes are not strictly dichotomous and must be interpreted in the context of clinical suspicion. Given MRI's limited sensitivity (~ 53%), normal findings do not exclude WE, and empirical thiamine treatment should be guided by clinical suspicion [1, 4].

A significant challenge in this scenario is overcoming "anchoring bias," a cognitive diagnostic trap where clinicians reflexively attribute altered mental status to HE simply due to the presence of biochemical liver injury [6]. Recognition relies on actively seeking atypical clinical features—such as the absence of asterixis or the presence of ocular and cerebellar signs—and utilising sensitive diagnostic frameworks like the Caine criteria alongside neuroimaging [9]. The Caine criteria require at least two of the following for a diagnosis: (i) dietary deficiency, (ii) oculomotor abnormalities, (iii) cerebellar dysfunction, and (iv) altered mental status or memory impairment.

The necessity of early, empirical intervention cannot be overstated. Current European Federation of Neurological Societies (EFNS) guidelines recommend the administration of high-dose intravenous thiamine in any patient with suspected WE [1]. The risk of thiamine toxicity is virtually non-existent, particularly when weighed against the catastrophic risk of progression to permanent Korsakoff syndrome or death if the diagnosis is delayed [1, 10].

Conclusions

This case highlights a critical and underappreciated diagnostic pitfall: in the context of jaundice and biochemical liver injury, neuropsychiatric deterioration must not be reflexively attributed to hepatic encephalopathy. Cholestatic DILI can precipitate prolonged thiamine depletion that manifests as WE, a treatable nutritional emergency that carries irreversible consequences if missed. The key to diagnosis lies in recognising atypical clinical features, applying the Caine criteria, and proceeding to MRI when the clinical picture is not fully explained by hepatic failure. High-dose intravenous thiamine is safe, rapidly effective, and should be administered empirically in any malnourished patient with liver disease in whom WE cannot be excluded.

Abbreviations

- **DILI**

Drug-induced liver injury

- **EFNS**

European Federation of Neurological Societies

- **FLAIR**

Fluid-attenuated inversion recovery

- **HE**

Hepatic encephalopathy

- **INR**

International normalized ratio

- **MRI**

Magnetic resonance imaging

- **TDS**

Ter die sumendum (three times a day)

- **WE**

Wernicke's encephalopathy

Declarations

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Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

UBD was the gastroenterologist looking after the patient. TCU drafted the first manuscript which was revised and supervised by AP. VLA was the neuroradiologist who reported the MRI brain images. All four authors read and approved the final manuscript.

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Availability of data and materials

All data generated or analysed during this study are included in this published article.

References

1. Galvin R, Bråthen G, Ivashynka A, Hillbom M, Tanasescu R, Leone MA, et al. EFNS guidelines for diagnosis, therapy and prevention of Wernicke encephalopathy. Eur J Neurol. 2010;17(12):1408–18.
2. Sechi G, Serra A. Wernicke's encephalopathy: new clinical settings and recent advances in diagnosis and management. Lancet Neurol. 2007;6(5):442–55.
3. Yin H, Xu Q, Cao Y, Qi Y, Yu T, Lu W. Nonalcoholic Wernicke’s encephalopathy: a retrospective study of 17 cases. J Int Med Res. 2019;47(10):4886–94.
4. Zhao P, Zhao Y, Wei Z, Chen J, Yan L. Wernicke encephalopathy in a patient with liver failure: Clinical case report. Med (Baltim). 2016;95(27):e3651.
5. Soulaidopoulos S, Ioannidou M, Chalevas P, Cholongitas E. Wernicke Encephalopathy: A Complication of Acute Liver Failure. Nutr Clin Pract. 2015;30(6):847–8.
6. Ondhia M, Berra G, Bouras E, Schvartsman S, Cohen J. Wernicke’s Encephalopathy: A Diagnostic Challenge in the Setting of Liver Disease. Case Rep Gastrointest Med. 2019;2019:8105671.
7. Elefante A, Puoti G, Senese R, Brunetti A. Non-alcoholic acute Wernicke's encephalopathy: Role of MRI in non typical cases. Eur J Radiol. 2012;81(12):4099–104.
8. Ha ND, Weon YC, Jang JC, Kang BS, Choi SH. Spectrum of MR imaging findings in Wernicke encephalopathy: are atypical areas of involvement only present in nonalcoholic patients? AJNR Am J Neuroradiol. 2012;33(7):1398–402.
9. Caine D, Halliday GM, Kril JJ, Harper CG. Operational criteria for the classification of chronic alcoholics: identification of Wernicke's encephalopathy. J Neurol Neurosurg Psychiatry. 1997;62(1):51–60.

10. Nishimoto A, Usery J, Winton JC, Twilla J. High-dose Parenteral Thiamine in Treatment of Wernicke's Encephalopathy: Case Series and Review of the Literature. In Vivo. 2017 Jan-Feb;31(1):121–124.

Figures

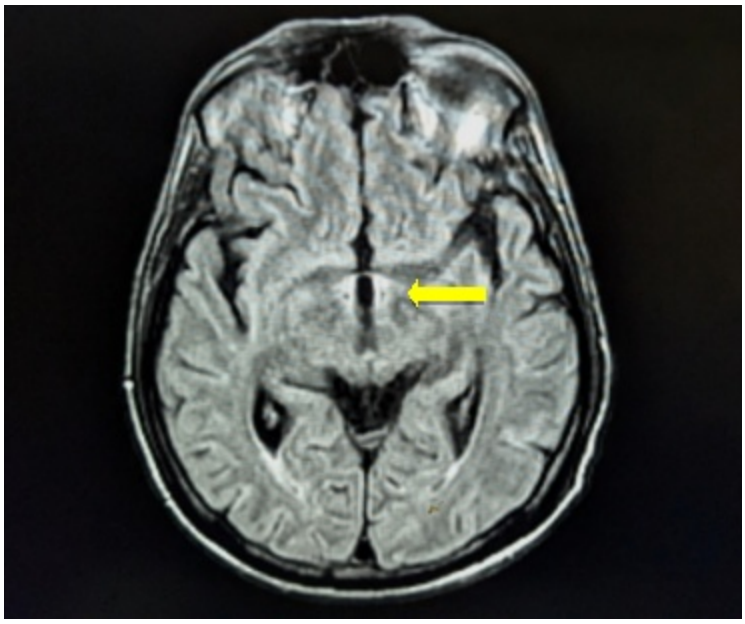


Figure 1

Periventricular FLAIR Hyperintensities Axial fluid-attenuated inversion recovery (FLAIR) image demonstrates symmetrical high signal intensity lesions in the periventricular region of the third ventricle. (Yellow arrow)

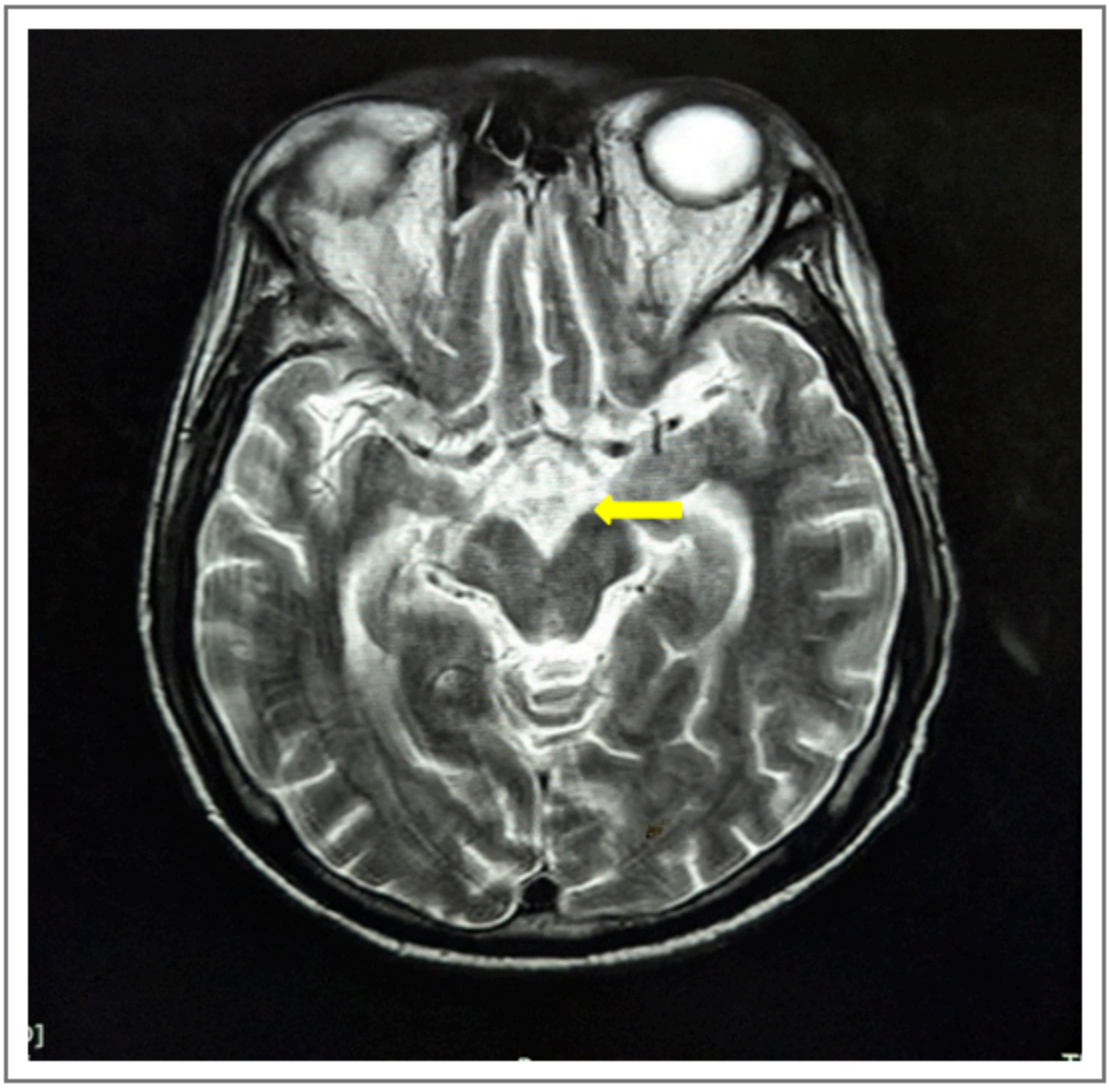


Figure 2

Mammillary Body Involvement. Axial T2-weighted image demonstrates slightly altered symmetrical high signal intensity lesions within the mammillary bodies. (Yellow Arrow)

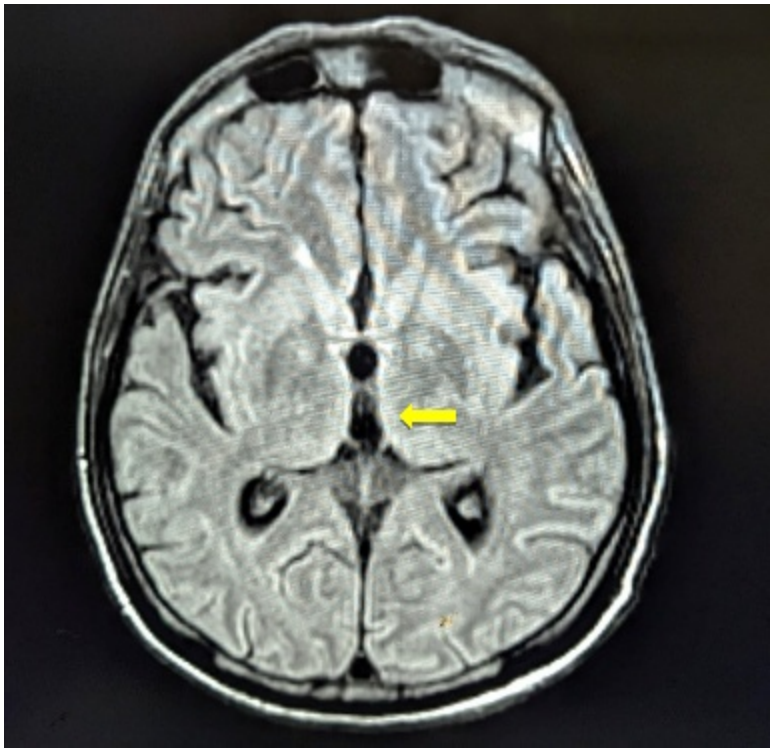


Figure 3

Medial Thalamic Hyperintensities. Axial fluid-attenuated inversion recovery (FLAIR) image demonstrates symmetrical high signal intensity lesions in the medial thalami. (Yellow Arrow)