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# Neuroimaging In Wernicke's Encephalopathy: A Case Report And Review Of Current Diagnostic Approaches

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***Abstract***
*Wernicke's encephalopathy (WE) remains largely underdiagnosed clinically despite a true prevalence of 0.8-2.8% revealed by autopsy studies, primarily due to clinical presentation variability, with the classic triad present in only 16% of patients. This study presents a case of WE in an 18-year-old adolescent who developed confusion, oculomotor disorders, and ataxia in the context of post-cholecystectomy malnutrition, and examines the contribution of modern neuroimaging. Brain MRI revealed characteristic hyperintensities of the thalami and mammillary bodies on diffusion-weighted and FLAIR sequences, confirming the diagnosis. MRI constitutes the reference diagnostic tool with 93% specificity, with diffusion-weighted sequences offering increased sensitivity for detecting thalamic lesions. Evolution toward Korsakoff's syndrome is accompanied by diffuse brain atrophy and specific metabolic changes on FDG-PET. Optimal treatment requires high-dose thiamine (500 mg three times daily), as conventional doses are insufficient. With 17% mortality and progression to Korsakoff's syndrome in 80% of survivors, modern neuroimaging significantly improves early diagnosis and optimizes therapeutic management.*

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## I. Introduction

Wernicke's encephalopathy is an acute neuropsychiatric syndrome resulting from thiamine deficiency, characterized by mental status changes, ocular abnormalities, and ataxia. Despite being a recognized neurological disorder, Wernicke's encephalopathy remains greatly underdiagnosed in clinical practice, with autopsy studies consistently revealing substantially higher prevalence than clinical recognition suggests. This dramatic underrecognition is largely attributed to the considerable variability of clinical presentation, as the classic symptomatic triad is present in only a minority of patients.

The high rate of misdiagnosis carries significant clinical implications, as untreated or inadequately treated Wernicke's encephalopathy frequently progresses to Korsakoff's syndrome, resulting in permanent memory impairment. The associated mortality rate further underscores the critical importance of early recognition and appropriate thiamine treatment.

Recent advances in neuroimaging, particularly magnetic resonance imaging, have provided valuable diagnostic tools and enhanced understanding of the pathophysiology of both Wernicke's encephalopathy and Korsakoff's syndrome. Given the persistent challenges in clinical recognition despite the availability of effective treatment, a comprehensive review of current neuroimaging findings and their clinical implications is warranted to improve diagnostic accuracy and optimize patient outcomes.

## II. Case Report

This involves an 18-year-old adolescent, brought to the emergency department by his parents for balance disorders, fatigue, and acute confusion evolving over 48 hours, in an afebrile context.

Our patient has a history of chronic lithiasic cholecystitis known for several months, with recurrent abdominal pain and episodes of nausea, recently treated by cholecystectomy on 05/12/2025.
He reports significant weight loss in recent months (quantified at 12 kg) probably related to post-prandial pain.
He otherwise mentions no alcohol consumption or other substance use and no regular medication treatment.
On general clinical examination, he is afebrile at 36.4°C and his blood pressure is 95/60 mmHg.

On neurological examination, his consciousness is fluctuating with temporal-spatial disorientation. He presents bilateral horizontal nystagmus, incomplete horizontal gaze palsy, static and kinetic ataxia with unstable gait.

Regarding neurocognitive assessment, examination reveals anterograde amnesia, moderate confabulation, and anosognosia.

Given this clinical presentation combining confusion, oculomotor disorders, and ataxia, a brain MRI with paramagnetic contrast agent injection (Gadolinium) was performed, using 3D FLAIR, Diffusion, T1 pre- and post-injection sequences, to search for lesions suggestive of Wernicke encephalopathy.

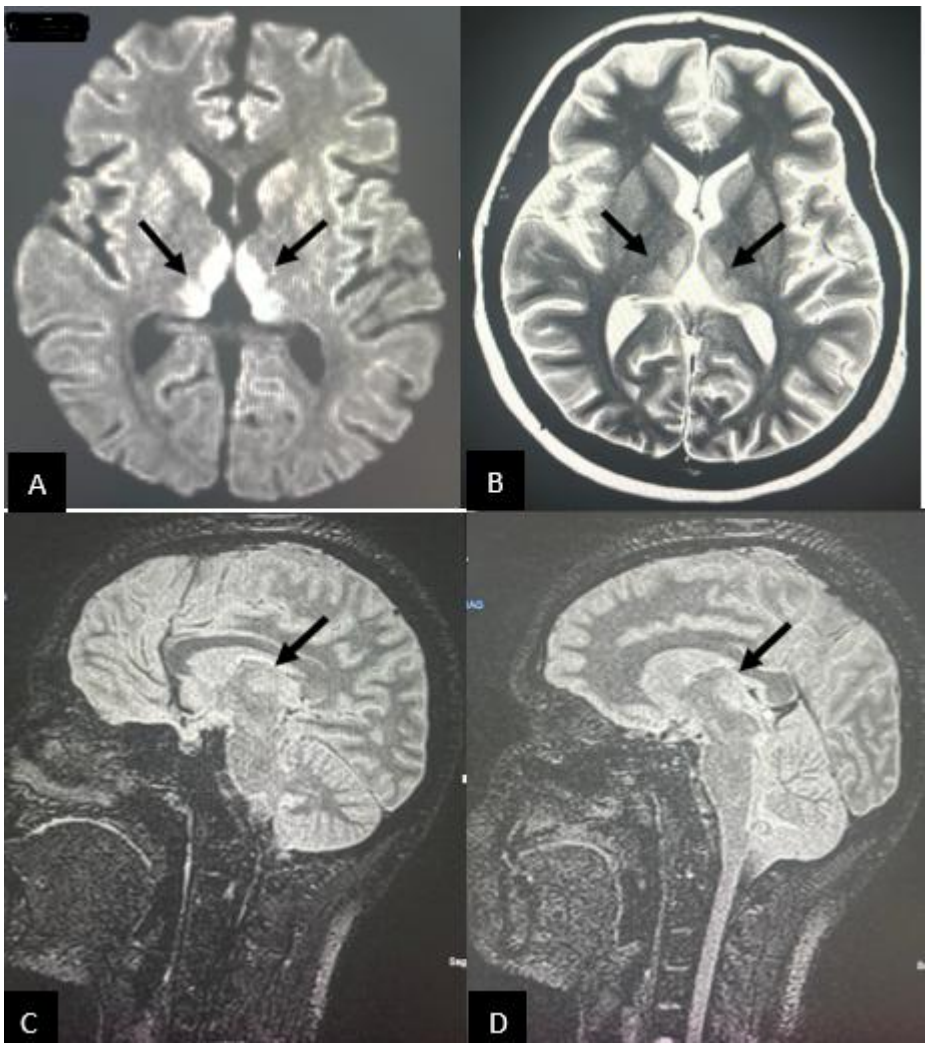


*Figure 1: Diffusion sequence of a brain MRI in an 18-year-old patient showing hyperintensity of the thalami (A). T2 sequences in axial section (B) and sagittal 3D FLAIR (C and D) showing moderate hyperintensity of the thalami.*

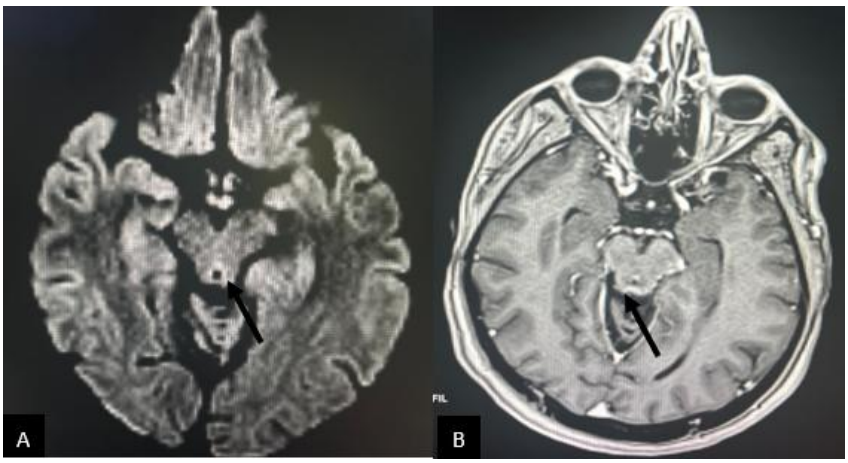


*Figure 2:Diffusion sequence of a brain MRI in an 18-year-old child showing a hyperintensity of the tectal plate (A), and axial 3D T1 sequence after Gadolinium injection (B) showing moderate contrast enhancement at this level.*

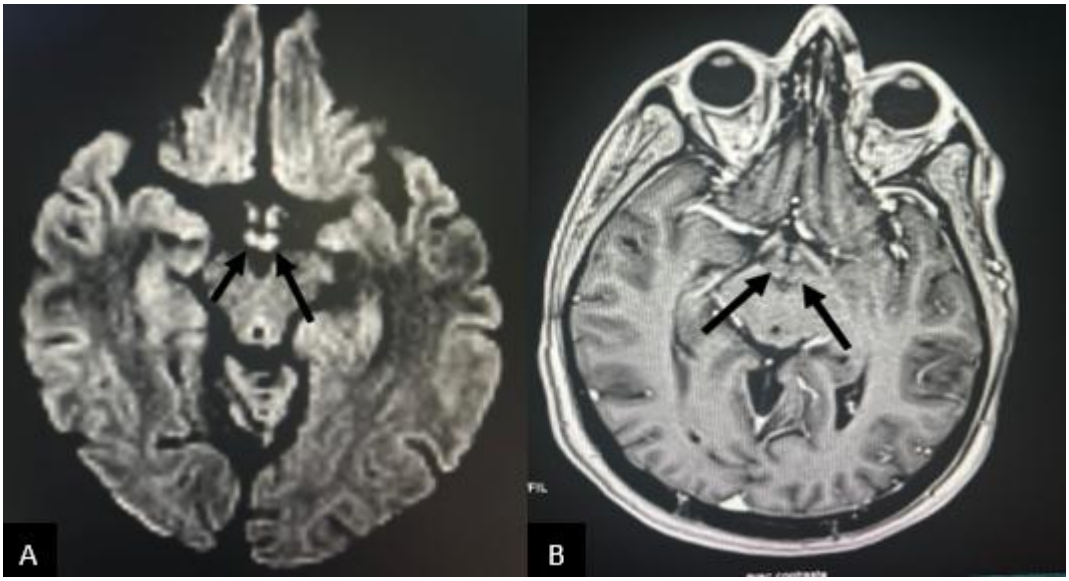


*Figure 3: Diffusion sequence of a brain MRI in an 18-year-old patient showing hyperintensity of the mammillary bodies (A) and axial 3D T1 sequence after Gadolinium injection (B) showing moderate contrast enhancement at their level.*

## III. Discussion

**Prevalence and underdiagnosis of Wernicke's encephalopathy**

Wernicke's encephalopathy (WE) remains largely underdiagnosed in clinical practice, as demonstrated by autopsy studies revealing a prevalence of 0.8-2.8% compared to only 0.04-0.13% reported in clinical studies (1). This discordance is particularly marked in alcoholic patients where 75-80% of WE cases confirmed at autopsy had not been diagnosed during routine clinical examination (1). In children, approximately 58% of cases escape initial clinical diagnosis (1).

The clinical underrecognition is primarily explained by the variability of symptomatic presentation. Contrary to popular belief, the classic triad of ataxia, ocular motor abnormalities, and altered consciousness is present in only 16% of patients (1), while 19% present none of the triad symptoms at the acute stage (1). This clinical reality underscores the crucial importance of imaging techniques for improving early diagnosis.

**Pathophysiology and temporal evolution of lesions**

Neuropathological and imaging data reveal a precise temporal sequence of metabolic and morphological alterations. Thiamine deficiency leads to brain lesions within 2-3 weeks, a timeframe corresponding to the time necessary to deplete the body's thiamine stores, which are sufficient for only 18 days (1).

Metabolic impairment follows a characteristic chronological progression: after 4 days of deficiency, decreased α-ketoglutarate dehydrogenase activity is observed in astrocytes, followed after one week by reduced transketolase activity, while no change in pyruvate dehydrogenase activity is observed for up to 10 days (1). This metabolic failure produces a diffuse decrease in cerebral glucose utilization with severe impairment of cellular energy metabolism (1).

At the symptomatic stage of WE, increased lactate production by both neurons and astrocytes is observed, with intracellular lactate accumulation, pH reductions, and focal acidosis (1). DNA fragmentation in thalamic neurons resulting in apoptotic cell death appears after approximately 2 weeks of thiamine deficiency (1).

**Neuroimaging: diagnostic and prognostic contribution**

**Acute phase imaging**

MRI currently constitutes the most valuable method for confirming WE diagnosis, with a sensitivity of 53% but high specificity of 93% (4). In direct comparison, computed tomography identifies density abnormalities in paraventricular thalamic regions in only 13% of WE patients, whereas MRI identifies T2 hyperintensities in the same region in 47% of patients (4). MRI can also detect hyperintensities in periaqueductal gray matter in 40% of WE patients (4).

FLAIR sequences prove particularly sensitive for detecting periventricular edematous lesions by eliminating cerebrospinal fluid signal (5). Diffusion-weighted imaging (DWI) offers additional diagnostic advantage, showing more marked thalamic hyperintensities than conventional T2 and FLAIR sequences in certain cases (3,4).

The most frequently affected regions include the medial thalamus and periventricular region of the third ventricle (80-85%), periaqueductal area (59-65%), mammillary bodies (38-45%), and mesencephalic tectum (36-38%) (4). These areas are proposed to be more sensitive to thiamine deficiency due to their high thiamine-dependent glucose metabolism rate (4).

**Evolution toward Korsakoff's syndrome**

Longitudinal imaging reveals that focal signal intensity abnormalities of WE lesions normalize with time, but this radiological resolution does not directly correlate with clinical improvement (3). In follow-up studies, thalamic and periaqueductal hyperintensities observed on T2-weighted, FLAIR, and diffusion-weighted images disappear, but patients retain balance problems and cognitive deficits (3).

Brain atrophy and diffuse white matter signal intensity changes may constitute chronic stage imaging characteristics (3,5). Volume loss is predominantly diffuse rather than focal, possibly related to cachexia-induced brain atrophy (3).

Quantitative studies demonstrate graded volumetric deficits, from uncomplicated alcoholics to Korsakoff's syndrome (KS) patients, in mammillary bodies, hippocampus, thalamus, cerebellum, and pons (5). These deficits follow a continuum, with uncomplicated alcoholics showing deficits of approximately 0.5 standard deviations below healthy controls, while KS patients show deficits of 1.0-2.0 standard deviations (5).

**Neuroanatomical substrates of memory deficits**

FDG-PET functional neuroimaging studies reveal relative white matter hypermetabolism and subcortical gray matter hypometabolism in KS patients (2). When occipital metabolism is used as reference, KS patients show significant hypometabolism only in retrosplenial cortex according to region-of-interest analysis, but significant bilateral white matter hypermetabolism according to statistical parametric mapping analysis (2).

When white matter metabolism is used as reference, KS patients show hypometabolism in diencephalic gray matter, consistent with known underlying neuropathology, as well as medial temporal and retrosplenial hypometabolism, interpreted as secondary metabolic effects within diencephalic-limbic memory circuits (2).

Structure-function correlations support the critical role of interactions between thalamus, mammillary bodies, hippocampus, frontal lobes, and cerebellum for memory formation and executive functions (4). Disruption of these circuits by WE and chronic alcoholism substantially contributes to KS neuropsychological deficits (4,5).

**Genetic and individual factors**

Data suggest variable genetic susceptibility to WE. Transketolase variants with decreased affinity for thiamine pyrophosphate have been identified in fibroblasts from Wernicke-Korsakoff syndrome patients, with this abnormality persisting through several culture generations in the presence of excess thiamine and absence of ethanol (1). These genetic variants may predispose certain individuals to WE during marginal or thiamine-deficient diets (1).

Other potentially implicated genetic variants include modifications in the SLC19A2 gene encoding the high-affinity thiamine transporter, with three novel genetic variants identified in the 3' untranslated region in 25 individuals with alcoholism and Wernicke-Korsakoff syndrome (1). APOE ε4 allele polymorphisms are also associated with intellectual decline severity in KS patients, with ε4 allele frequency being significantly higher in KS patients with global intellectual deficit compared to those with preserved intellectual function apart from amnesia (1).

**Clinical and therapeutic implications**

Pharmacokinetic studies indicate that empirical minimum treatment of 500 mg thiamine hydrochloride (dissolved in 100 ml normal saline), administered by infusion over 30 minutes, three times daily for 2-3 days, is recommended for patients showing WE signs (1). In case of effective response, 250 mg thiamine intravenously or intramuscularly daily for 3-5 days or until clinical improvement ceases should be continued (1).

Thiamine doses between 100-250 mg per day may not restore vitamin status, improve clinical signs, or prevent death (1). When WE patients are inappropriately treated with low thiamine doses, biochemical abnormalities caused by deficiency can lead to irreversible brain damage (1).

Estimated WE mortality is 17% (1), and approximately 80% of surviving patients develop KS (1). Prophylactic treatment (intramuscular administration of 250 mg thiamine once daily for 3-5 consecutive days) is recommended for all patients with severe alcohol withdrawal, malnourished patients, and individuals with poor diet and malnutrition signs (1).

**Future perspectives and challenges**

Longitudinal animal models confirm progression and resolution of thiamine deficiency-induced brain lesions, validating imaging utility for therapeutic monitoring (5). These studies also reveal synergistic interaction

between alcohol exposure and thiamine deficiency on brain damage, with thiamine-deficient rats with prior alcohol exposure being particularly susceptible to developing brain lesions and showing attenuated thalamic recovery (5).

Future challenges include identifying patients genetically predisposed to WE for optimizing prophylaxis, and developing effective therapies for KS (1). The search for randomized controlled trials remains necessary to define optimal dose and duration of thiamine treatment for both prophylaxis and treatment of WE and KS prevention in individuals with chronic alcoholism and those without alcoholism (1).

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