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HIGH ANION GAP METABOLIC ACIDOSIS (HAGMA), HYPERAMMONEMIA, AND PANCYTOPENIA SECONDARY TO NUTRITIONAL THIAMINE DEFICIENCY: A CASE REPORT.

Emergency Medicine

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ABSTRACT

Background: Wernicke's Encephalopathy (WE) is a life-threatening neuropsychiatric emergency caused by thiamine (vitamin B1) deficiency. While typically associated with chronic alcohol abuse, it can manifest in non-alcoholic patients with severe nutritional deficits. The presentation of concurrent high anion gap metabolic acidosis (HAGMA) due to lactic acidosis, severe iron-deficiency anaemia, and hyperammonemia mimicking hepatic encephalopathy is extremely rare and poses a significant diagnostic challenge.**Case** Description: A 29-year-old non-alcoholic, non-diabetic, non-hypertensive female presented to the Emergency Department with a 3-month history of progressive weakness, neck pain, headache, and bilateral lower limb paraesthesia, culminating in drowsiness and acute confusion over 48 hours. Clinical examination revealed pallor, altered sensorium, diplopia, slurred speech, and disorientation. Investigational workup demonstrated pancytopenia with microcytic indices (MCV: 66.7 fl), high anion gap metabolic acidosis (HAGMA: Anion Gap 25 mmol/L, Delta Ratio 1.7), hypophosphatemia (1.6 mg/dl), and marked hyperammonemia (158 µg/dl). Brain MRI and cerebrospinal fluid analysis were inconclusive, and infectious and toxicological screens were negative.**Management & Outcome:** A primary diagnosis of nutritional Wernicke's encephalopathy compounded by severe iron-deficiency anaemia and secondary hyperammonemia was established. The patient was aggressively treated with intravenous Thiamine (200 mg twice daily), intravenous ferrous sucrose, packed red blood cell transfusions, phosphate supplementation, and oral lactulose. Clinical and biochemical trends showed rapid reversal: sensorium normalized, metabolic acidosis resolved, and serum ammonia decreased to 70 µg/dl by day 5. The patient was discharged asymptomatic on day 6 with corrected haematological parameters.**Conclusion:**This case highlights that thiamine deficiency must be considered in any patient presenting with unexplained HAGMA, lactic acidosis, and altered sensorium, even in the absence of alcoholism. Crucially, it demonstrates that severe nutritional depletion can cause secondary hyperammonemia, which can lead to a misdiagnosis of primary hepatic encephalopathy.

KEYWORDS

Wernicke's Encephalopathy; Thiamine Deficiency; Hyperammonemia; High Anion Gap Metabolic Acidosis; Iron Deficiency Anaemia.

INTRODUCTION:

Wernicke's encephalopathy (WE) is an acute, life-threatening neurological syndrome resulting from a deficiency in thiamine (vitamin B1), a critical cofactor in carbohydrate metabolism[1]. Classically characterized by the triad of ophthalmoplegia, ataxia, and altered mental status[3], the complete triad is missing in up to 84% of cases, frequently leading to underdiagnosis or delayed treatment in non-alcoholic populations[2].

Thiamine pyrophosphate is essential for the pyruvate dehydrogenase complex. Deficiency shifts cellular metabolism toward anaerobic pathways, accumulating pyruvate and causing severe lactic acidosis, typically manifesting as a high anion gap metabolic acidosis (HAGMA). Concurrently, severe iron-deficiency anaemia can exacerbate tissue hypoxia, further driving anaerobic glycolysis and lactic acid production[4].

While hyperammonemia[5] is traditionally viewed as a hallmark of hepatic failure, non-hepatic causes including severe metabolic stress, nutritional deficiencies, and altered cellular enzymatic function are increasingly recognized. This case report outlines a rare clinical convergence: a young, non-alcoholic female who developed reversible hyperammonemic encephalopathy and profound HAGMA driven by severe, concurrent thiamine and iron deficiencies.

CASE DESCRIPTION:

Patient Presentation:

A 29-year-old non-hypertensive, non-diabetic female presented to the emergency department with a three-month history of progressive generalized weakness, muscle aches, headache, neck pain, and bilateral lower limb tingling and numbness. Over the preceding 48 hours, she developed progressive drowsiness and acute confusion, necessitating admission to the Emergency Medicine Department Critical Care Unit (EMD-CCU). There was no history of fever, jaundice, seizures, vomiting, abdominal pain, chest pain, head trauma, or substance abuse. She was a non-vegetarian, non-smoker, and non-alcoholic.

Clinical Examination:

Upon presentation, the patient was drowsy and restless. Physical examination revealed profound pallor(fig.1). There was no icterus, cyanosis, pedal edema, or lymphadenopathy. Abdominal examination revealed a soft, non-distended abdomen without hepatosplenomegaly, ascites, or dilated superficial veins; bowel sounds were normal.

Neurological evaluation revealed an altered sensorium, disorientation to time and place, slurred speech, and diplopia. Motor examination showed symmetrically reduced power in all four limbs with preserved, normal deep tendon reflexes and bilateral flexor plantar responses. Meningeal signs, including neck rigidity, were absent. Cranial nerve assessment confirmed bilateral pupils were equal in size and reactive to light, with subjective diplopia but no gross nystagmus. Respiratory and cardiovascular examinations were unremarkable.

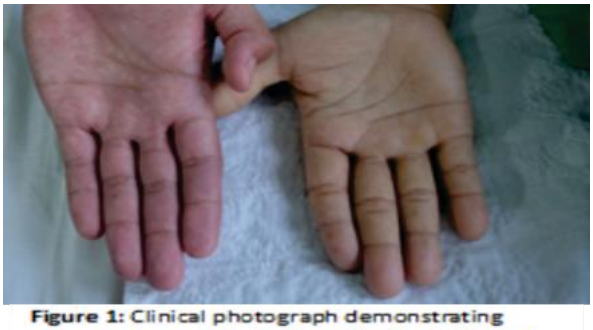

Figure 1: Clinical photograph demonstrating severe palmar pallor in the patient's right hand (right) compared alongside a healthy normal control (left).

Diagnostic Workup:

Initial laboratory investigations revealed pancytopenia with

microcytic indices(fig.2) and signs of severe iron deficiency. The biochemical profile was highly remarkable for high anion gap metabolic acidosis and hyper-ammonemia, while hepatic, renal, and neuro-imaging assessments were normal.

Parameter	Patient Value	Reference Range
Haemoglobin	7.5 → 10.3 (Day 3) → 11.4 (Day 6)	12.0–15.0 g/dl
Total Leukocyte Count	4,400 → 7,800 (Day 6)	4,000–11,000 cells/cumm
Platelet Count	1.30 Lakhs → 3.70 Lakhs (Day 6)	1.50–4.50 lakhs/cumm
Mean Corpuscular Volume (MCV)	66.7	80.0–100.0 fl
Peripheral Smear	Microcytes, tear-drop cells(fig.2)	Normocytic, normochromic
Serum Iron / Ferritin	Decreased	Variable (Deficiency confirmed)
Total Iron Binding Capacity (TIBC)	Increased	240–450 µg/dl
Arterial Blood Gas (ABG)	pH: 7.28, HCO_3^-: 12 mmol/L	pH: 7.35–7.45
Anion Gap / Delta Ratio	AG: 25 mmol/L / Delta: 1.7 mmol/L	AG: 8–16 mmol/L / Delta: 1.0–2.0
Serum Lactate	2.8	< 2.0 mmol/L
Serum Ammonia	158 → 70 (Day 5)	25–95 µg/dl
Serum Phosphate	1.6	2.5–4.5 mg/dl
Coagulation Profile (INR)	1.48	0.8–1.2
Serum Electrolytes (Ca, Mg)	Normal	Within standard limits
TSH / Urine Ketones	Normal / Negative	Variable
CSF Analysis / Brain MRI	Inconclusive / Normal	Normal
Viral Screen (HIV, HBV, HCV)	Negative	Negative
Blood Culture	Sterile	Sterile

Therapeutic Intervention and Clinical Course:

The clinical presentation of HAGMA (lactic acidosis), diplopia, encephalopathy, and paraesthesia strongly supported an acute presentation of Wernicke's encephalopathy superimposed on severe iron deficiency anaemia.

The patient was immediately started on aggressive nutritional and metabolic resuscitation:

1. **Intravenous Thiamine:** 200 mg administered intravenously twice daily.
2. **Haematological Support:** Intravenous ferrous sucrose 100 mg infusion alongside packed red blood cell (PRBC) transfusions.
3. **Metabolic Management:** Intravenous phosphate supplementation and empirical multivitamin therapy.
4. **Hyperammonemia Resuscitation:** Oral lactulose syrup titrated to bowel movements.

Following the initiation of thiamine and iron therapy, the patient showed dramatic clinical improvement by Day 2. The metabolic acidosis resolved, and sensorium fully cleared. By Day 3, the haemoglobin rose to 10.3 g/dl, and serum ammonia consistently declined, reaching a normal value of 70 µg/dl by Day 5. The patient made a full recovery without any residual neurological deficits and was discharged on Day 6.

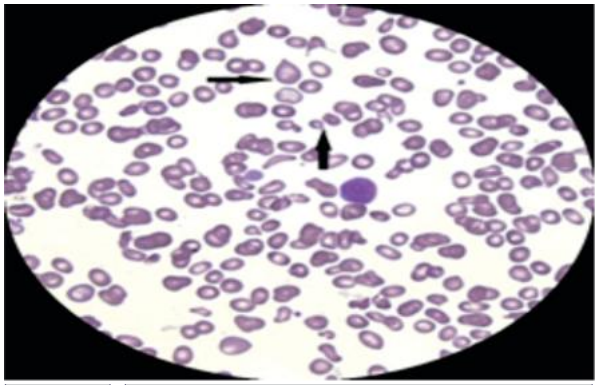

Figure 2: Peripheral smear (×1000) showing microcytic hypochromic anaemia with anisopoikilocytosis. The upper arrow points to a **teardrop cell (dacrocyte)** and the lower arrow highlights a **microcyte**, characteristic of severe iron deficiency.

DISCUSSION:

This case highlights a rare, complex clinical intersection where profound thiamine[6] and iron deficiencies presented simultaneously as HAGMA, lactic acidosis, and hyperammonemic encephalopathy, closely mimicking primary hepatic coma.

Pathophysiology of Thiamine-Induced HAGMA and Lactic Acidosis:

Thiamine pyrophosphate (TPP) serves as an indispensable coenzyme for pyruvate dehydrogenase (PDH) and α-ketoglutarate dehydrogenase, which are critical drivers of the mitochondrial tricarboxylic acid (TCA) cycle[7]. When thiamine stores are depleted, the conversion of pyruvate to acetyl-CoA is blocked. Pyruvate is instead preferentially reduced to lactate by lactate dehydrogenase, resulting in a type B lactic acidosis.

This anaerobic shift explains the patient's presentation with a High Anion Gap Metabolic Acidosis (HAGMA) of 25 mmol/L and an elevated serum lactate of 2.8 mmol/L. This metabolic strain was further worsened by tissue hypoxia from severe iron-deficiency anaemia (haemoglobin 7.5 g/dl, MCV 66.7 fl), which restricted oxygen delivery to tissue and accelerated anaerobic glycolysis.

The Conundrum of Non-Hepatic Hyper-ammonemia:

The most unusual finding in this case was the marked elevation of serum ammonia (158 µg/dl) in a patient with completely normal liver function tests, normal hepatic imaging, and sterile cultures. Hyper-ammonemia is typically caused by primary hepatic failure or urea cycle defects. However, secondary non-hepatic hyper-ammonemia can occur during severe nutritional depletion and metabolic exhaustion.

TTP is also a vital cofactor for erythrocyte transketolase in the pentose phosphate pathway, which generates NADPH necessary for maintaining cellular reducing equivalents. A severe energy crisis within cells, combined with profound hypophosphatemia (1.6 mg/dl)[8]-which reduces substrate availability for adenosine triphosphate (ATP) synthesis-can impair the energy-dependent urea cycle enzymes in the liver, leading to transient hyperammonemia. This metabolic block explains why the patient's encephalopathy and hyperammonemia responded rapidly to thiamine, iron, and phosphate resuscitation, rather than standard anti-hepatic encephalopathy regimens alone.

Diagnostic Framework for Wernicke's Encephalopathy:

Contemporary diagnostic criteria require at least two of the following: (1) dietary deficiencies, (2) oculomotor abnormalities, (3) cerebellar dysfunction, and (4) altered mental status or mild memory impairment. This patient met three criteria: clear dietary and nutritional deficits (severe iron deficiency, hypophosphatemia, and pancytopenia), oculomotor involvement (diplopia), and altered mental status (acute confusion, slurred speech, and progressive drowsiness).

While neuroimaging via MRI can show characteristic symmetric T2/FLAIR hyperintensities in the periaqueductal gray matter, thalami, and mamillary bodies, a normal or inconclusive MRI occurs in up to 50% of acute cases[9]. Thus, a normal MRI does not rule out WE, which remains a primarily clinical diagnosis.

Clinical Management Corollaries:

The standard treatment for suspected WE requires immediate, high-dose intravenous thiamine replacement[10]. Rapid administration is essential because delayed treatment can transition WE into Korsakoff's psychosis—an irreversible amnestic state marked by confabulation and severe cognitive defects.

Additionally, because magnesium is an essential cofactor for TPP-dependent enzymes, any concurrent hypomagnesemia must be corrected to prevent treatment resistance, though this patient had normal baseline magnesium levels. The rapid improvement in this patient's clinical state, resolution of HAGMA, and normalization of serum ammonia within 48 hours of starting intravenous thiamine serves as diagnostic confirmation of this underlying nutritional crisis.

CONCLUSION:

1. **Broaden Diagnostic Considerations:** Wernicke's encephalopathy should be included in the differential diagnosis for any patient presenting with an unexplained altered sensorium

and high anion gap lactic acidosis, even without a history of chronic alcoholism.

2. **Recognize Nutritional Hyperammonemia:** Severe nutritional depletion and metabolic cofactor deficiencies can present with non-hepatic hyperammonemia, mimicking hepatic encephalopathy.
3. **Initiate Treatment Promptly:** Intravenous thiamine replacement must be started immediately based on clinical suspicion. This therapy can completely reverse severe biochemical anomalies and neurological deficits, avoiding permanent neurological injury.

REFERENCES:

1. Sechi G, Serra A. Wernicke's encephalopathy: new clinical settings and recent advances in diagnosis and management. *Lancet Neurol*. 2007;6(5):442-455.
2. Caine D, Halliday JL, 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.
3. Butterworth RF. Effects of thiamine deficiency on brain metabolism: implications for the pathogenesis of Wernicke's encephalopathy. *Neurochem Int*. 1993;22(2):147-154.
4. Osaku FM, de Almeida EA. Lactic acidosis secondary to severe iron deficiency anemia: an overlooked association. *Am J Emerg Med*. 2020;38(4):851-853.
5. Clay AS, Hainline BE. Hyperammonemia in the ICU: medical progress. *Chest*. 2007;132(4):1368-1378.
6. Attaluri P, Castillo A, Edriss H, Nugent K. Thiamine deficiency: an important, fully reversible cause of type B lactic acidosis. *Proc (Bayl Univ Med Cent)*. 2018;31(4):434-436.
7. Singleton CK, Martin PR. Molecular mechanisms of thiamine utilization. *Curr Mol Med*. 2001;1(2):197-207.
8. genchi G, et al. Hypophosphatemia-induced metabolic encephalopathy mimicking neurological crises. *Nutr Clin Pract*. 2019;34(3):399-404.
9. Sullivan EV, Pfefferbaum A. Neuroimaging of the Wernicke-Korsakoff syndrome. *Alcohol Alcohol*. 2009;44(2):155-165.
10. Galvin R, Bråthen G, Ivashynka A, et al. EFNS guidelines for diagnosis, therapy and prevention of Wernicke's encephalopathy. *Eur J Neurol*. 2010;17(12):1408-1418.