**CLINICAL VIGNETTE**

# Beer and Bread, the Unfortunate Precipitants of Wernicke Encephalopathy

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## *Introduction*

Wernicke encephalopathy (WE) is commonly associated with excessive alcohol use, resulting in thiamine deficiency. However, many other conditions, including anorexia, celiac disease, hyperemesis, malignancy, can also cause WE. Internists encountering patients with vitamin deficiencies, especially in the absence of significant alcohol use, should consider alternate etiologies on the differential. We describe a case of WE triggered by a combination of alcohol use and previously undiagnosed celiac disease.

## *Case Description*

A 51-year-old African American female, with history of eczema, presented to the Emergency Department after 3 months of progressive confusion, 14 kg weight loss, rash, poor appetite, and difficulty with ambulation. Seven months earlier, she started drinking more alcohol than usual (1-3 glasses of wine per day). According to her family, she had been hiding her alcohol use, and they were unsure how much alcohol she was drinking. One week prior to presentation, her family noted she was confused, confabulating, and could not ambulate. Per her family, she answered simple questions incorrectly. For example, when asked "What did you eat for breakfast?" the patient answered "potatoes," but her family clarified that she had eaten eggs. She was confused and distractable during the interview. She had difficulty with balance and walking in a straight line and used a wall to support herself while walking. Although she denied any dizziness or falls, her family reported that she complained of dizziness. She had a long history of eczema and had increased thickening and pruritus on the dorsal surface of her hands and legs for several months.

Her past medical history was notable only for eczema. She had no prior surgeries, no known drug allergies, and was not taking any medications. Her family history was non-contributory. She had worked as a computer programmer for 20 years, but started working from home 7 months prior, due to her worsening rash. She stopped working in the past week due to her progressive confusion and dizziness.

On admission, her heart rate was 120 beats per minute, blood pressure was 134/98 mmHg, temperature was 36.8°C, respiratory rate was 18/bpm, and room air oxygen saturation was 97%. Physical exam was notable for cachexia, patchy and scattered hair-thinning, bilateral horizontal nystagmus on lateral gaze, and cervical lymphadenopathy. Her heart was tachycardic with regular rhythm, no jugular venous distension, and no peripheral edema. Her lungs were clear to auscultation bilaterally in all lung fields. Neurologic exam was notable for a wide-based, ataxic gait with decreased sensation in the bilateral lower extremities at the feet and shins. She was oriented to name, but did not correctly identify the hospital, year, month, or date. Her dermatologic exam showed hyperpigmented, thickened patches on both hands and legs (Figures 1-2). Initial laboratory studies included: WBC 4.36/uL, hemoglobin 13.9 g/dL, MCV 112 fL, RDW 55.9 fL, platelets 255/uL, sodium 142 mmol/L, potassium 5.5 mmol/L, chloride 105 mmol/L, CO2 16 mmol/L, glucose 117 mg/dL, creatinine 0.35 mg/dL, urea nitrogen 5 mg/dL, calcium 10.3 mg/dL, AST 169 U/L, and ALT 55 U/L. She underwent an extensive testing for her altered mental status, including MRI/A Brain, EEG, LP, and CT chest, abdomen, and pelvis.

She was admitted for altered mental status and failure to thrive and was started empirically on high dose IV thiamine, given concern for Wernicke Encephalopathy (WE). CIWA protocol was initiated, but she did not require any benzodiazepines for alcohol withdrawal, and admission alcohol level was undetectable. She received a brief course of high dose steroids (methylprednisolone 1 gram for 1 dose) for possible autoimmune encephalitis with little improvement. Brain MRI/MRA findings included non-specific scattered periventricular, deep and subcortical FLAIR hyperintensities, and were not supportive of stroke, vasculopathy, or intracranial mass. Negative electroencephalography, made protein seizures and seizure-like activity unlikely. CSF studies did not reveal pleocytosis or elevation, making meningeal infections less likely. CSF panels for autoimmune encephalitis and paraneoplastic syndromes also returned negative. CT scans of the chest, abdomen, and pelvis had no findings suggestive of malignancy. Seven days into her hospitalization, her admission thiamine level resulted at 32 nmol/L (reference range: 70-180 nmol/L).

She was continued on high dose thiamine intravenously, followed by oral supplementation. Given minimal evidence for excessive alcohol use, she was evaluated for alternate causes of thiamine deficiency. Celiac disease testing showed elevated transglutaminase IgA (20.9, reference range: <20.0 CU) and

gliadin Ab IgA (110.9, reference range: <20.0 CU). She was diagnosed with WE and completed five days of IV thiamine supplementation, followed by ongoing oral supplementation, with improvement in her mental status. She was evaluated by gastroenterology and reported improvement in her symptoms with a gluten-free diet. Biopsies obtained during post discharge esophagogastroduodenoscopy found villous flattening and intraepithelial lymphocytes, confirming the diagnosis of Celiac disease (Figures 3-4).

***Discussion***

Wernicke encephalopathy and thiamine deficiency are established consequences of alcoholism. Although alcoholism is the most common association for thiamine deficiency (roughly 25%), other associated conditions include celiac disease, anorexia nervosa, hyperemesis of pregnancy, malignancy, thyrotoxicosis, bariatric surgery, hemodialysis, and AIDS,[1] each with unique pathophysiology. In alcoholism, pathophysiology is multifactorial, including diminished hepatic storage and utilization, increased renal wasting, and reduced intake and absorption.[1] In this case, celiac disease in combination with mild alcohol use likely accelerated severe WE.

This patient presented with three classic signs of WE: ataxia, nystagmus, and confusion. However, thiamine deficiency as a presenting symptom of celiac disease is markedly atypical. Her WE was likely accelerated by alcohol use. Celiac disease causes blunting of jejunal villi, the primary site of thiamine absorption, resulting in malabsorption. Ataxia and peripheral neuropathy are additional neurologic complications of celiac disease with associated cerebellar and grey matter MRI abnormalities, which are not improved by vitamin supplementation.[2,3] Our patient had significant peripheral neuropathy, which could have been a manifestation of celiac disease, dry beri beri (another disorder caused by thiamine deficiency), other nutritional deficiencies (B12, folate), or alcoholic peripheral neuropathy.

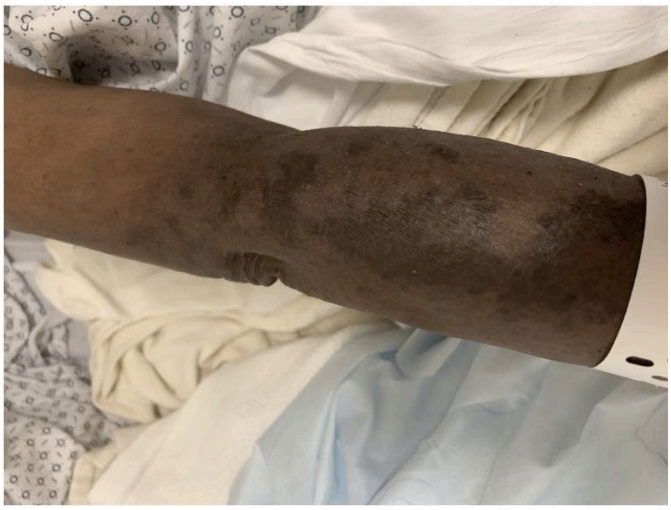
She also had patchy areas of hair thinning, and a rash with skin thickening and hyperpigmentation. Celiac disease is classically associated with dermatitis herpetiformis, but is also associated with alopecia areata, and alopecia areata may be the only presenting feature of celiac disease.[4,5] In one study by Corazza et al, the association between the two conditions was statistically significant, and suggests serum antibodies associated with celiac disease should be a part of the evaluation for alopecia areata.[5] Our patient had developed alopecia areata, as well as prominent skin findings consistent with atopic dermatitis, both of which are associated with celiac disease.[4] Atopic dermatitis is associated with sensitization to various food allergens, and celiac disease is found more frequently in patients with atopic dermatitis compared to the general population.[4,6]

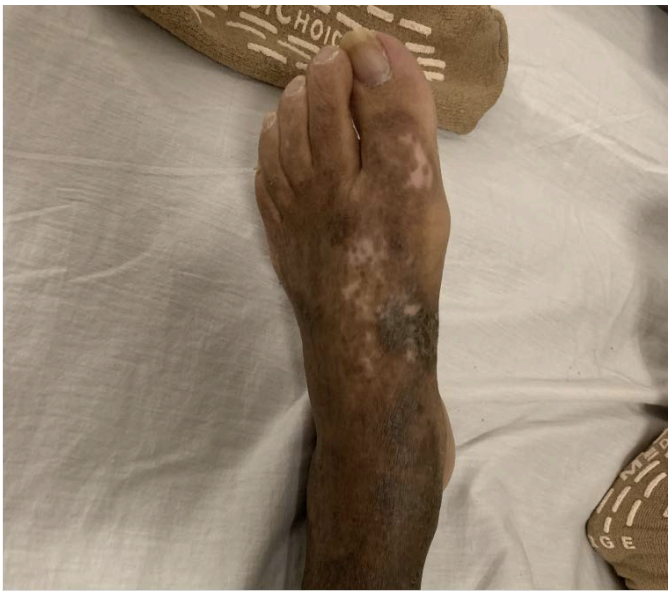
Additionally, her antibody profile featured only mild elevation in the classic antibody anti-transglutaminase-2. Recent studies identified additional autoantibodies present in celiac disease, including gliadin, transglutaminase-3, actin, ganglioside, collagen, calreticulin, and zonulin.[7] There is a wide spectrum of autoantibody reactivity in celiac disease, and further characterization of these antibodies may aid in identifying subtypes of the disease and development of therapeutics.

Celiac disease was not suspected earlier given her lack of diarrhea, although this is not uncommon in African American patients.[8] Celiac disease is underdiagnosed in African Americans, likely due to differences in presentation, with nutritional deficiencies rather than the classic diarrhea symptoms.[8] In a cohort of African American patients with celiac disease, only 22% presented with diarrhea, whereas 44% of patients presented with some type of nutritional deficiency.[8]

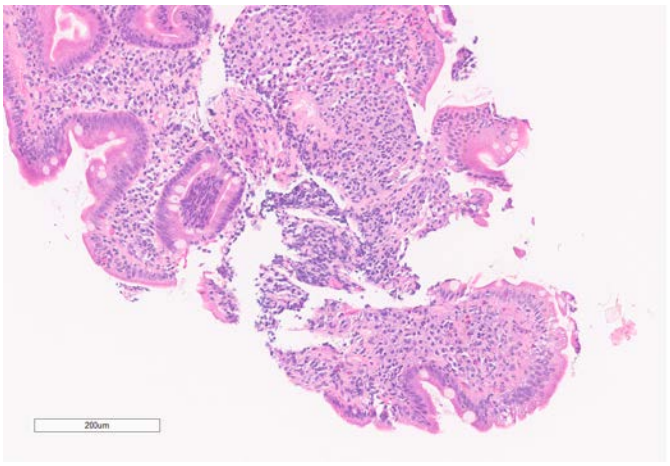
Although the clinical presentation of WE was clear, the underlying etiology was likely two-fold, relating to concomitant Celiac disease and alcohol use. The complexity of this case highlights the importance of a thorough assessment of patients presenting with WE. Although alcohol abuse is most common, patients with an unclear alcohol use history should be screened for other underlying drivers of thiamine deficiency.

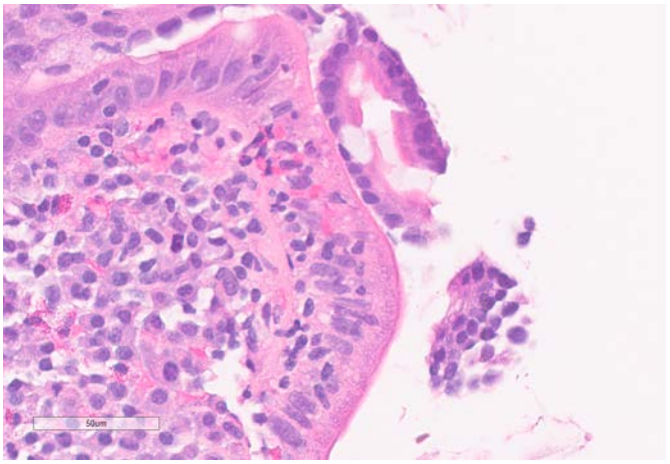
***Figures***





**Figures 1-2:** Images of hyperpigmented rash with areas of excoriation and hypopigmentation, consistent with atopic dermatitis.





**Figures 3-4:** Pathology slides (10x, 40x) from esophagogastro-duodenoscopy showing villous flattening and intraepithelial lymphocytes.

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**REFERENCES**


1. **Isenberg-Grzeda E, Kutner HE, Nicolson SE**. Wernicke-Korsakoff-syndrome: under-recognized and under-treated. *Psychosomatics*. 2012 Nov-Dec;53(6):507-16. doi: 10.1016/j.psym.2012.04.008. PMID: 23157990.
2. **Currie S, Hadjivassiliou M, Clark MJ, Sanders DS, Wilkinson ID, Griffiths PD, Hoggard N**. Should we be 'nervous' about coeliac disease? Brain abnormalities in patients with coeliac disease referred for neurological opinion. *J Neurol Neurosurg Psychiatry*. 2012 Dec;83(12): 1216-21. doi: 10.1136/jnnp-2012-303281. Epub 2012 Aug 20. PMID: 22906616.
3. **Nikpour S**. Neurological manifestations, diagnosis, and treatment of celiac disease: A comprehensive review. *Iran J Neurol*. 2012;11(2):59-64. PMID: 24250863; PMCID: PMC3829244.
4. **Caproni M, Bonciolini V, D'Errico A, Antiga E, Fabbri P**. Celiac disease and dermatologic manifestations: many skin clue to unfold gluten-sensitive enteropathy. *Gastroenterol Res Pract*. 2012;2012:952753. doi: 10.1155/2012/952753. Epub 2012 May 30. PMID: 22693492; PMCID: PMC3369470.
5. **Corazza GR, Andreani ML, Venturo N, Bernardi M, Tosti A, Gasbarrini G**. Celiac disease and alopecia areata: report of a new association. *Gastroenterology*. 1995 Oct;109(4):1333-7. doi: 10.1016/0016-5085(95)90597-9. PMID: 7557104.

6. **Zauli D, Grassi A, Granito A, Foderaro S, De Franceschi L, Ballardini G, Bianchi FB, Volta U**. Prevalence of silent coeliac disease in atopics. *Dig Liver Dis*. 2000 Dec;32(9):775-9. doi: 10.1016/s1590-8658(00)80354-0. PMID: 11215557.
7. **Alaedini A, Green PH**. Autoantibodies in celiac disease. *Autoimmunity*. 2008 Feb;41(1):19-26. doi: 10.1080/08916930701619219. PMID: 18176861.
8. **Brar P, Lee AR, Lewis SK, Bhagat G, Green PH**. Celiac disease in African-Americans. *Dig Dis Sci*. 2006 May;51(5):1012-5. doi: 10.1007/s10620-005-9000-5. Epub 2006 Apr 27. PMID: 16642428.