Wernicke Encephalopathy: Wet Brain **Twitter/Instagram: @emboardbombs**

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Introduction

Wernicke-Korsakoff syndrome is a neurologic pathology secondary to vitamin B1 (thiamine) deficiency. Wernicke encephalopathy (WE) is an acute condition requiring emergent treatment to prevent death or irreversible progression to Korsakoff syndrome (KS). Wernicke's is difficult to diagnose, and if left untreated, Wernicke's is associated with a 20% mortality. It has often been called "wet brain", due to the devastating changes on memory, and psychological components of the brain. This review serves as a guide to the presentation, diagnosis, and management of Wernicke encephalopathy.

Risk Factors

Upon autopsy, 0.4% to 2.8% of the general population in the Western world had brain lesions consistent with WE.[1] WE is most closely associated with chronic alcoholism, however, it is also seen in settings of poor nutrition. Interestingly, the appearance of WE lesions discovered on autopsy was 12.5% of alcohol abusers in one report, but in those with alcohol-related deaths, this prevalence jumps to 29-59%.[2,3]

WE is closely associated with:

- Chronic alcoholism
- Poor nutrition (anorexia nervosa, hyperemesis of pregnancy, prolonged IV feeding)
- Malabsorption (gastrointestinal disease, bariatric surgery)
- Increased metabolic demand (systemic malignancy)
- Loss of water-soluble thiamine (hemodialysis, peritoneal dialysis)
- Acquired immunodeficiency.

Pathophysiology

Thiamine is a cofactor for multiple enzymes that are important for energy metabolism.[4,5] The absence or decreased levels of thiamine causes a breakdown of the Krebs cycle (we promise you don't have to memorize it again), leading to ATP depletion and end organ damage. Thiamine requirements are directly related to metabolic rate and is crucial for high metabolic demand and high glucose intake. WE can present in at-risk patients if administered IV glucose before thiamine.[6]

Clinical Manifestations

The classic triad of WE include encephalopathy, oculomotor dysfunction, and gait ataxia. *Importantly, all components of this triad are only present in one-third of patients*.[7]

- Encephalopathy: this is extremely variable, and can include subtle things like disorientation, indifference, and inattentiveness early on. It is very uncommon for decreased level of consciousness to present as an early symptom, but in the late stages expect stupor or coma.[4]
- Oculomotor dysfunction: Occurs with nystagmus. Usually, you will see a lateral rectus palsy and conjugate gaze palsies. *Nystagmus is the most common* and is induced by horizontal gaze to both sides.[4]
- Gait ataxia: this can precede other symptoms by a few days or weeks.[4] Another important reason to always walk your patients when performing a neurologic exam!
- Some patients might have hypotension and hypothermia, mimicking sepsis.

Diagnosis

WE is a clinical diagnosis. There is not a single laboratory finding or neuroimaging that can make the diagnosis. WE is typically associated closely with patients who have alcohol use disorder and is easily missed when the patient does not have this present in their history. It is also missed as many clinicians emphasize the presence of all aspects of the triad, which is not seen in two-third of patients.

WE diagnosed in patients that have two of four components of the Caine Criteria:

- Dietary deficiency
- Oculomotor abnormalities
- Cerebellar dysfunction
- Altered mental status or mild memory impairment

In a previously conducted study of 106 autopsied patients with history of alcohol use disorder, the sensitivity for diagnosis of WE was 22% when using classic triad compared to 85% when using the Caine criteria.[8]

Stop with the "banana bags"

Naturally, any clinician wants to avoid this pathology and empirically give thiamine. Banana bags contain 100 mg of thiamine. This has traditionally been stated as the "recommended" daily amount for treatment of Wernicke's. However, this was an arbitrary dose assignment in the 1950s, not based on any scientific research. In fact, current research suggests higher amounts of thiamine need to be

given due to the short parenteral half-life.[9] Currently, many experts state that at-risk patients should be taking 100 mg twice a day orally. If you are concerned about your patient having Wernicke's, a banana bag is not going to solve the problem.

Oral "rally packs", or multivitamins, are totally acceptable alternatives in patients who just need vitamin supplementation- not thiamine replacement. Most patients do not have difficulty absorbing vitamins in their gastrointestinal tract. It is reasonable to assume most of our alcoholic patients have an *intake* problem, not a malabsorption one. Oral multivitamins are understandably much cheaper than banana bags. They are also easier to give and take less time.[10]

Management

Patients with suspected WE should receive immediate IV thiamine. The supported regimen is 500mg of IV Thiamine over 30 minutes TID for two consecutive days and 250mg IV or IM QD for an additional five days.[11] Do you really have to give thiamine before glucose? Who knows, but also, who cares. There are many more important things to argue about in medicine. Other electrolytes should be checked and repleted as necessary as many patients have underlying nutritional deficits. Improvement in symptoms can occur as soon as a few hours to within a few days of beginning thiamine treatment.

References

1. Harper C, Fornes P, Duyckaerts C, Lecomte D, Hauw JJ. An international perspective on the prevalence of the Wernicke-Korsakoff syndrome. Metab Brain Dis. 1995 Mar;10(1):17-24. doi: 10.1007/BF01991779. PMID: 7596325.
2. Torvik A, Lindboe CF, Rogde S. Brain lesions in alcoholics. A neuropathological study with clinical correlations. J Neurol Sci 1982; 56:233.
3. Naidoo DP, Bramdev A, Cooper K. Autopsy prevalence of Wernicke's encephalopathy in alcohol-related disease. S Afr Med J 1996; 86:1110.
4. Victor M, Adams RA, Collins GH. The Wernicke-Korsakoff syndrome and related disorders due to alcoholism and malnutrition, FA Davis, Philadelphia 1989.
5. Sinha S, Kataria A, Kolla BP, Thusius N, Loukianova LL. Wernicke Encephalopathy-Clinical Pearls. Mayo Clin Proc. 2019 Jun;94(6):1065-1072. doi: 10.1016/j.mayocp.2019.02.018. PMID: 31171116.
6. Koguchi K, Nakatsuji Y, Abe K, Sakoda S. Wernicke's encephalopathy after glucose infusion. Neurology. 2004 Feb 10;62(3):512. doi: 10.1212/01.wnl.0000099189.56741.a7. PMID: 14872047.
7. Chamorro AJ, Rosón-Hernández B, Medina-García JA, Muga-Bustamante R, Fernández-Solá J, Martín-González MC, Seco-Hernández E, Novo-Veleiro I, Suárez-Cuervo C, Mateos-Díaz AM, Monte-Secades R, Machado-Prieto B, Puerta-Louro R, Prada-González C, Fernández-Rial Á, Sabio-Repiso P, Vázquez-Vigo R, Antolí-Royo AC, Gomila-Grange A, Felipe-Pérez NC, Sanvisens-Bergé A, Antúnez-Jorge E, Fernández-Rodríguez CM, Alvela-Suárez L, Fidalgo-Navarro A, Marcos M; Wernicke-SEMI Group; Alcohol and Alcoholism Group; Spanish Society of Internal Medicine (SEMI). Differences Between Alcoholic and Nonalcoholic Patients With Wernicke Encephalopathy: A Multicenter Observational Study. Mayo Clin Proc. 2017 Jun;92(6):899-907. doi: 10.1016/j.mayocp.2017.02.019. PMID: 28578781.
8. 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 Jan;62(1):51-60. doi: 10.1136/jnnp.62.1.51. PMID: 9010400; PMCID: PMC486695.
9. Donnino MW et al. Myths and misconceptions of Wernicke's encephalopathy: what every emergency physician should know. Ann Emerg Med. 2007;50(6): 715-21.
10. Krishel S et al. Intravenous vitamins for alcoholics in the emergency department: a review. J Emerg Med. 1998 May-Jun;16(3):419-24.
11. Cook CC, Hallwood PM, Thomson AD. B Vitamin deficiency and neuropsychiatric syndromes in alcohol misuse. Alcohol Alcohol. 1998 Jul-Aug;33(4):317-36. doi: 10.1093/oxfordjournals.alcalc.a008400. PMID: 9719389.