Acta Biomed 2023; Vol. 94, Supplement 1: e2023111 DOI: 10.23750/abm.v94iS1.13879

Case report

Non-alcoholic Wernicke's Encephalopathy mimicking neuromyelitis optica spectrum disorder in a young woman: a case report and literature review

Alessandro Zilioli[1], *Francesco Misirocchi*[1], *Carlotta Mutti*[1,2], *Sonia Romano*[1], *Matteo Minetti*[1], *Elisabetta Chierici*[1], *Irene Florindo*[1], *Marco Spallazzi*[1], *Lucia Zinno*[1]

[1]Department of Medicine and Surgery, Unit of Neurology, University Hospital of Parma, Parma, Italy; [2]Sleep Disorders Center, Department of Medicine and Surgery, University Hospital of Parma, Parma, Italy

Abstract. Wernicke's encephalopathy is an under-recognized life-threatening disease caused by thiamine (vitamin B1) deficiency. It has historically been related to chronic alcoholic intake but other causes of malnutrition, such as invasive gastric surgery and hyperemesis, have been linked to the onset of this illness over the years, often presenting with atypical clinical manifestations. Herein we report a case of a young obese woman affected by non-alcoholic Wernicke's Encephalopathy following a minimally invasive gastrointestinal surgery. She showed an unusual clinical profile characterized by prominent subacute neuro-ophthalmological involvement which combined to her juvenile age, overweight condition and brain lesions, have made diagnosis challenging due to similarities with Neuromyelitis Optica Spectrum Disorder. Our case underscores the relevance of prompt diagnosis in order to prevent the development of irreversible neuropathological changes and to avoid the use of a long-term immunosuppressive treatment. (www.actabiomedica.it)

Key words: Non-alcoholic Wernicke's Encephalopathy, neuromyelitis optica spectrum disorders, malnutrition, thiamine, obesity

Introduction

Wernicke's encephalopathy (WE) is a severe and underestimated disease caused by thiamine (vitamin B1) deficiency, first recognized by Carl Wernicke in 1881 (1).

Historically, it has been primarily associated with alcoholism, but recent studies have identified several other causes (e.g., gastric surgery, hyperemesis and malnutrition), accounting for 23% of WE cases in one autopsy study (2).

The classic clinical presentation characterized by ataxia, mental status changes and ophthalmoplegia is observed in only a small number of patients, with relevant differences between the alcoholic and non-alcoholic subtypes (3) (4).

The non-alcoholic variant exhibits more frequent ocular signs rather than cerebellar involvement, as highlighted by a recent multicenter observational study (5). In addition, rare manifestations such as mild peripheral neuropathy, decreased deep tendon reflexes, and papilledema have been reported(1).

The dissimilarities between these two variants extend beyond clinical features and involve neuroradiological findings. Alcoholic WE predominantly affects brain regions that are highly dependent on thiamine levels for maintaining osmotic gradient levels, such as the periaqueductal areas, thalami and mammillary bodies, which show bilateral and symmetrical involvement. On the other hand, non-alcoholic WE may exhibit atypical MRI findings, including alterations in the dorsal medulla, pons,

cerebellum, corpus callosum and fronto-parietal cortex (6).

The involvement of the periaqueductal and periventricular areas is not exclusive to WE but it is also observed in certain neuroinflammatory disorders such as Neuromyelitis Optica Spectrum Disorder (NMOSD) (7).

NMOSD is an autoimmune disorder affecting the central nervous system, particularly the optic nerves and spinal cord with variable involvement of the brain parenchyma (8). Due to the different locations of brain lesions caused by NMOSD, the clinical presentation may overlap with WE. Indeed, NMOSD is typically characterized by neuro-ophthalmological alterations that may resemble non-alcoholic WE, but it can also rarely exhibit the classical triad of ataxia, ophthalmoplegia and mental status changes (9).

Case presentation

A 20 years-old woman started suffering from subacute progressive bilateral loss of eyesight, blurred vision and diplopia.

She underwent an ophthalmologic evaluation which revealed severe bilateral visual loss (< 2/10) and concomitant bilateral optic neuropathy with papilledema and flame hemorrhages. Consequently, she was admitted to our Neurology Department for observation.

Her medical history was unremarkable, except for obesity and a recent laparoscopic cholecystectomy due to gallstones, which had caused relapsing biliary colic disease with reduced caloric intake, weight loss and nausea/vomiting. The initial clinical examination showed bilateral sixth nerve palsy with slight deficit in adduction, mild cognitive slowing, numbness in the legs, and an ataxic gait.

CT head and CT angiography of cerebral arteries were normal, and blood tests revealed only abnormal liver function enzyme levels. Due to the complex clinical presentation and the severity of visual loss, we initiated intravenous supplementation of thiamine (500 mg three times per day for two days, following by 250 mg per day), in suspicion of non-alcoholic WE, and high doses of intravenous methylprednisolone (1gr for 5 days), since an inflammatory CNS disease such as NMOSD could not be ruled out.

A brain MRI performed the day after the admission showed hyperintense bilateral periaqueductal, thalamic and diencephalic FLAIR-T2 signal, without gadolinium enhancement or decrease in ADC values (Fig. 1); CSF analysis displayed normal values of cell and protein counts with negative intrathecal oligoclonal bands synthesis and negative results in the viral-bacterial screen.

We observed a significant improvement in visual acuity and oculomotor disturbances as soon as the treatments were initiated, with the appearance of bi-directional gaze-evoked nystagmus. Concurrently, the cognitive slowing disappeared.

Ophthalmologic follow-up performed one-week after the admission showed normal visual acuity with improvement in flame hemorrhages and reduction in papilledema. At the one-month follow-up, her neurological examination was unremarkable, except for persistence of bilateral nystagmus. Additionally, the serum samples tested for anti-aquaporin-4 (AQP-4) antibodies and anti-myelin oligodendrocyte glycoprotein yielded negative results, and the brain MRI showed complete resolution of aforementioned alterations (see Fig.1).

Discussion

Herein we have reported the case of a young obese woman affected by non-alcoholic WE.

Our patient showed a prominent subacute neuro-ophthalmological involvement which, combined with her juvenile age, overweight condition, and neuroradiological similarities to NMOSD, made the diagnosis challenging.

Initially, we focused on ocular manifestations. As reported in a recent literature review (10), several causes may underlie bilateral optic neuropathy.

The severe visual loss, combined with bilateral optic neuropathy presenting with papilledema and flame hemorrhages could have been one of the typical onsets of a CNS inflammatory disorder. However, bilateral optic neuropathy with optic disc swelling is rarely observed in WE, although thiamine deficiency is mainly related to cranial nerve disorders, conjugate gaze palsy

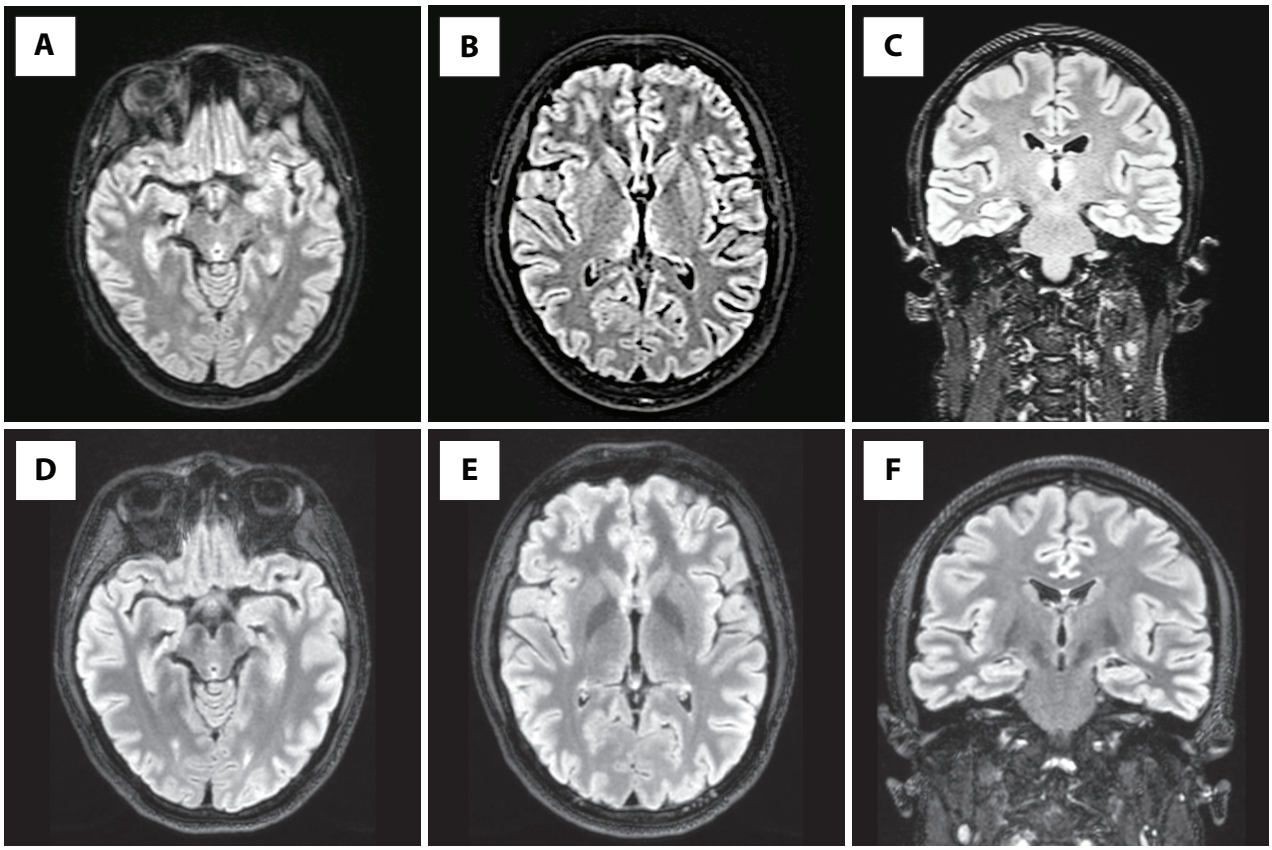

Figure 1. On top, axial (A - B) and coronal (C) CUBE Fluid Attenuated Inversion Recovery (FLAIR) showing hyperintense bilateral periaqueductal, thalamic and diencephalic signal at the disease onset. On bottom, axial (D - E) and coronal (F) MRI showing a complete resolution of the alterations.

and nystagmus. (11). The mechanisms behind the development of such ocular manifestations in WE are not yet understood.

Additionally, the overweight condition could have been considered a protective element against the development of WE. Nevertheless, thiamine has a half-life range between 10-20 days (12) and WE is increasingly diagnosed after short periods of poor vitamins intake, as highlighted by a systematic review of obese patients undergoing bariatric surgery (13), although it is rarely related to minimally invasive surgery (14). Referring back to our patient, her obesity state did not constitute a safeguarding factor, considering how the high caloric intake typical of obese patients is not usually matched with appropriate thiamine intake, as shown by low thiamine values in obese patients' serum (15,16).

The neuroradiological features consisting of hyperintense bilateral periaqueductal, thalamic and diencephalic FLAIR-T2 signal resemble the typical aspects of NMOSD with regard to the affected anatomical regions. Both diseases, although with different pathogenetic mechanisms, involve the peri-ependymal areas where there is a high thiamine metabolism rate (4) and a high AQP4 expression (7) leading to astrocytic cell damage. Therefore, the neuroradiological differences between these two conditions are subtle. As previously described (9), the involvement of the mammillary bodies could be an element supporting the diagnosis of thiamine deficiency, while parenchymal lesions support a neuroinflammatory etiology.

Taking into account these diagnostic challenges, in our case, the in-depth medical history analysis was crucial in establishing the correct diagnosis before the result of AQP-4 analysis. One month before admission, the patient started to suffer from relapsing biliary colic disease and then she underwent laparoscopic

cholecystectomy; both these factors led to several vomiting episodes, resulting in reduced caloric intake and weight loss. All these findings contributed to the development of thiamine deficiency and its subsequent clinical abnormalities.

Only few reports have been published about such misdiagnosis, which was overlooked during the past years (9,17-20).

In a case reported by Ye et al (9), a woman presenting the classic clinical triad and periventricular lesion on brain MRI was misdiagnosed as being affected by WE. Only the lack of a clinical response to thiamine supplementation and the positive result of AQP-4 analysis made the diagnosis of NMOSD possible.

Interestingly, as reported by Zhang et al. (19) NMOSD may follow WE. In their case, a woman showing ocular manifestations and unstable walking improved after B1 vitamin replacement, and brain MRI showed resolutions. However, six months after discharge, she experienced urinary incontinence and numbness in her limbs and trunk. Through a blood sample to detect the presence of antibodies, NMOSD was recognized.

Conclusions

We attempted to shed light on some atypical features of non-alcoholic WE, aiming to enhance its prompt recognition, even in the young-adult population affected by optic neuropathy. An early WE diagnosis is crucial to initiate life-saving supplementation as soon as possible, preventing the onset of irreversible neuropathological changes and avoiding the use of long-term immunosuppressive treatments, which may be considered in the case of misdiagnosis with NMOSD.

In situations where the distinction between these two entities is not clear, we recommend timely thiamine replacement while awaiting the result of AQP-4 analysis.

Acknowledgements: None.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical Standard Statement: The patient gave an informed consent in the use of his personal data for research and teaching purpose.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Authors Contribution: Conceptualization AZ, FM and LZ; Writing – Original Draft Preparation AZ, FM and LZ; Writing – Review & Editing CM, SR, MM, EC, IF, MS and LZ.

References

1. Zubaran C, Fernandes JG, Rodnight R. Wernicke-Korsakoff syndrome. Postgrad Med J. 1997 Jan;73(855):27-31. doi: 10.1136/pgmj.73.855.27. PMID: 9039406; PMCID: PMC2431190.
2. Lindboe CF, Løberg EM. Wernicke's encephalopathy in non-alcoholics. An autopsy study. J Neurol Sci. 1989 Apr;90(2):125-9. doi: 10.1016/0022-510x(89)90095-6. PMID: 2723677.
3. 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.
4. Zuccoli G, Gallucci M, Capellades J, et al. Wernicke encephalopathy: MR findings at clinical presentation in twenty-six alcoholic and nonalcoholic patients. AJNR Am J Neuroradiol. 2007 Aug;28(7):1328-31. doi: 10.3174/ajnr.A0544. PMID: 17698536; PMCID: PMC7977668.
5. Chamorro AJ, Rosón-Hernández B, Medina-García JA, et al. 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.
6. Manzo G, De Gennaro A, Cozzolino A, Serino A, Fenza G, Manto A. MR imaging findings in alcoholic and nonalcoholic acute Wernicke's encephalopathy: a review. Biomed Res Int. 2014;2014:503596. doi: 10.1155/2014/503596. Epub 2014 Jun 24. PMID: 25050351; PMCID: PMC4094710.
7. Wingerchuk DM, Lennon VA, Lucchinetti CF, Pittock SJ, Weinshenker BG. The spectrum of neuromyelitis optica. Lancet Neurol. 2007 Sep;6(9):805-15. doi: 10.1016/S1474-4422(07)70216-8. PMID: 17706564.
8. Wingerchuk DM, Banwell B, Bennett JL et al, International Panel for NMO Diagnosis. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015 Jul 14;85(2):177-89. doi: 10.1212/WNL.0000000000001729. Epub 2015 Jun 19. PMID: 26092914; PMCID: PMC4515040.

9. Ye L, Xu Z, Deng J, Yang J. Classical Triad and Periventricular Lesions Do Not Necessarily Indicate Wernicke's Encephalopathy: A Case Report and Review of the Literature. Front Neurol. 2020 Jun 10;11:451. doi: 10.3389/fneur.2020.00451. PMID: 32587564; PMCID: PMC7297919.
10. Mun-Wei L, Gayathri G, Kwang Hwee G, Ruban K, Suresh Kumar V, Shatriah I. Optic Discs Swelling Procrastinates Wernicke's Encephalopathy Associated with Hyperemesis Gravidarum: A Case Report and Review of Literature. Cureus. 2018 Jun 12;10(6):e2793. doi: 10.7759 /cureus.2793. PMID: 30112269; PMCID: PMC6089490.
11. Cogan D G, Victor M. Ocular signs of Wernicke's disease. AMA Arch Ophthalmol. 1954 Feb;51(2):204-11. doi: 10.1001/archopht.1954.00920040206007. PMID: 13123606.
12. Teitleman M, Katzka DA. A case of polyneuropathy after gastric bypass surgery. MedGenMed. 2005 Apr 11;7(2):21. PMID: 16369400; PMCID: PMC1681565
13. Singh S, Kumar A. Wernicke encephalopathy after obesity surgery: a systematic review. Neurology. 2007 Mar 13; 68(11):807-11. doi: 10.1212/01.wnl.0000256812.29648.86. PMID: 17353468.
14. Verma V, Donadee C, Gomez L, Zaretskaya M. Nonalcoholic Wernicke's Encephalopathy Associated with Unintentional Weight Loss, Cholecystectomy, and Intractable Vomiting: The Role of Dual Thiamine and Corticosteroid Therapy. Case Rep Neurol Med. 2014;2014:430729. doi: 10.1155/2014/430729. Epub 2014 Jan 19. PMID: 24716018; PMCID: PMC3970253.
15. Gratton SM, Lam BL. Visual loss and optic nerve head swelling in thiamine deficiency without prolonged dietary deficiency. Clin Ophthalmol. 2014 May 22;8:1021-4. doi: 10.2147/OPTH.S64228. PMID: 24899800; PMCID: PMC4039400.
16. Carrodeguas L, Kaidar-Person O, Szomstein S, Antozzi P, Rosenthal R. Preoperative thiamine deficiency in obese population undergoing laparoscopic bariatric surgery. Surg Obes Relat Dis. 2005 Nov-Dec;1(6):517-22; discussion 522. doi: 10.1016/j.soard.2005.08.003. Epub 2005 Sep 28. PMID: 16925281.
17. Karri M, Ramasamy B, Perumal S, Kannan KT. Neuromyelitis optica spectrum disorder mimicking Wernicke's encephalopathy. J R Coll Physicians Edinb. 2020 Sep;50(3):305-306. doi: 10.4997/JRCPE.2020.320. PMID: 32936110.
18. Supahiah P, Thomas BHI, Zhen PC, Aris AM, Abdul-Jalil F, Din NM. Wernicke Encephalopathy as the First Presentation of Neuromyelitis Optica Spectrum Disorder With Horizontal Nerve Palsy. J Neuroophthalmol. 2021 Dec 16. doi: 10.1097/WNO.0000000000001444. Epub ahead of print. PMID: 34924530.
19. Zhang D, Yang X, Zhang Z, Zhao W, Duan P, Du G. Nonalcoholic Wernicke's Encephalopathy Followed by Neuromyelitis Optica Spectrum Disorders: A Case Report. Neurol India. 2019 Nov-Dec;67(6):1562-1564. doi: 10.4103/0028-3886.273629. PMID: 31857564.
20. Shan F, Zhong R, Wu L, Fan Y, Long Y, Gao C. Neuromyelitis optica spectrum disorders may be misdiagnosed as Wernicke's encephalopathy. Int J Neurosci. 2016 Oct;126(10):922-7. doi: 10.3109/00207454.2015.1084619. Epub 2015 Aug 19. PMID: 26287559.

Correspondence:
Received: 31 October 2022
Accepted: 2 March 2023
Alessandro Zilioli MD
Department of Medicine and Surgery, Unit of Neurology
Via Gramsci 14
Parma, 43126, Italy
Phone: +39 -0521-703569
E-mail: alessandro.zilioli@unipr.it