Nutrition 86 (2021) 111182

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Review

# Wernicke's encephalopathy in Crohn's disease and ulcerative colitis

Erik Oudman [a,b,*], Jan W. Wijnia [a,b], Misha J. Oey [a,b], Mirjam van Dam [a,b], Albert Postma [a,b]

[a] Experimental Psychology, Helmholtz Institute, Utrecht University, the Netherlands
[b] Slingedael Korsakoff Center, Lelie Care Group, Rotterdam, the Netherlands

ARTICLE INFO

*Article History:*
Received 21 March 2020
Received in revised form 31 December 2020
Accepted 19 January 2021

*Keywords:*
Clinical nutrition
Dietary
Crohn's disease
Ulcerative colitis
Inflammation
Gastrointestinal
Wernicke's encephalopathy
Thiamine

ABSTRACT

Crohn's disease (CD) and ulcerative colitis (UC) are chronic and debilitating inflammatory conditions of the gastrointestinal tract. Thiamine can deplete rapidly in CD and UC, which can lead to Wernicke's encephalopathy (WE), is an acute neurologic disorder. Our objective was to systematically review the presentation of WE in CD and UC. We conducted our search from inception using the MeSH terms "Crohn's disease," "ulcerative colitis," and "Wernicke's encephalopathy." Our search yielded 28 case studies reporting on 31 cases. CD was diagnosed in 21 cases, and UC in 10. The first signs of WE were nausea and vomiting (13 cases), double vision (10), blurred vision (10), and hearing loss (4). In 12 cases, partial or complete bowel resection was one of the etiologies of thiamine depletion. In nine cases, thiamine was not supplemented intramuscularly or intravenously while parenteral nutrition or glucose was given to the patient. In 10 cases, detailed descriptions of thiamine treatment were given. Thiamine treatment at suboptimal levels (7 of 10 cases) turned out to lead to residual cognitive deficits in three cases. In three cases with optimal treatment (1500 mg/d intravenously), complete remission of WE symptoms was achieved. Rapid treatment with high doses (500 mg, 3 times/d) of thiamine saves lives, and treats WE in its core symptomatology.



## Introduction

In the 21st century, the prevalence of inflammatory bowel disease (IBD) exceeded 0.3% of the total population in Western societies [1]. During the latter half of the 20th century a significant increase of IBD was reported in North America and Europe [2]. Prominent forms of IBD are Crohn's disease (CD) and ulcerative colitis (UC).

Nutritional care and therapy forms an integral part of the management of CD and UC [3]. Nutritional deficiencies in IBD result from reduced intake, malabsorption, side effects of medication, and systemic inflammation due to active disease [3,4]. Thiamine (vitamin $B_1$) deficiency is relatively common in IBD, resulting in fatigue, irritability, poor memory, sleep disturbances, nausea and vomiting, and abdominal pain, as well as severe neurologic deficits such as Wernicke's encephalopathy [5,6].

Wernicke's encephalopathy (WE) is the result of vitamin $B_1$ depletion, and is an adverse complication of IBD. Three symptoms have become known as the WE triad: ataxia, eye-movement disorders, and mental-status change. The prevalence rate of WE is 0.6–2% of the population, but many cases are detected postmortem based on atrophy of the mammillary bodies, periaqueductal gray matter, or medial thalamic area [6].

Because it is relatively unknown that nutritional health in CD and UC is necessary for prevention of WE, the aim of this article is to review the presentation of WE in CD and UC. We want to help clinicians working with people with CD and UC in properly managing the possibility of malnutrition.

### Methods

#### *Study design*

A systematic review of the literature was performed. Case reports and cases series were included. We did not find any group study on WE in CD, and therefore did not include group studies. We excluded cases where data on the presentation of symptoms was not reported.

#### *Wernicke's encephalopathy*

WE can be diagnosed based on Caine's operational criteria [7]: the classic triad described by Wernicke, evidence on autopsy, or a fast response to thiamine treatment. Critical symptomatology of WE is oculomotor issues (nystagmus or ophthalmoplegia), dietary issues, cerebellar dysfunction (ataxia and balance problems), and a form of delirium or otherwise altered mental status.

All authors contributed to writing up the first draft of the manuscript. E.O. contributed to all sections of the manuscript. J.W.W., M.J.O., M.v.D., and A.P. contributed to the Methods and Results sections of the manuscript.

There is no funding for this research project. The authors declare that they have no conflicts of interest.

*Corresponding author. Tel.: +31(0)102931555
*E-mail address:* e.oudman@leliezorggroep.nl (E. Oudman).

https://doi.org/10.1016/j.nut.2021.111182

*CD and UC*

Reports also had to contain chronic inflammation of the gastrointestinal tract and diagnosis of CD or UC.

*Search strategy and study selection*

We searched the Cochrane Database of Systematic Reviews, PubMed, and Scopus, using MeSH terms ("Wernicke's encephalopathy," "Crohn's disease," "ulcerative colitis"), from inception, and removed all duplicates. Papers in all languages could be included. One of us (E.O.) screened all abstracts for eligibility and extracted information from full-text descriptions for this review. The others of us checked the selection of papers. The last systematic literature search was on November 22, 2020.

*Outcomes*

We extracted and indexed the following data: year of publication, age, gender, etiology of WE, WE symptoms, and magnetic resonance imaging (MRI) findings.

*Treatment*

Proper treatment of WE consists of 500 mg of parenteral thiamine three times/d until symptoms resolve, according to European guidelines [8]. Active treatment can save lives and reverse this acute neurologic disorder. Suboptimal treatment of WE is defined as <500 mg of thiamine as the initial dose.

## Results

*General overview*

We identified 31 case descriptions in the published literature (see Fig. 1 for a flowchart and Table 1 for case descriptions), published in 29 manuscripts [9–37], suggesting that WE is not frequently reported in CD and UC, based on a prevalence rate of 0.3%. Twenty-one of the cases of WE were diagnosed in people with CD, and 10 in people with UC.

Importantly, new cases of WE have continuously been published, with three case studies from the 1980s, five from the 1990s, five from the 2000s, and 18 from the 2010s. The tripling of cases in the last 10 years suggests that it is still relevant to consider this differential diagnosis. We reviewed reports of 16 cases in women and girls and 15 in men and boys. The average age was 36.3 y, with a range of 5–64 y.

*Etiology of WE in CD and UC*

In all cases, WE developed as a consequence of multiple factors contributing to thiamine depletion in CD and UC. In all cases, weakening of health status was evident as a direct consequence of CD or UC before the onset of WE. Thirteen cases developed after nausea and vomiting, and 12 after partial or total bowel resection. In eight cases, the individuals received total parenteral nutrition without thiamine. Malnourishment before onset of WE was evident in seven cases, and diarrhea in six. In one case, WE developed after acute glucose infusion without thiamine supplementation. Some patients had a combination of these factors leading to WE.

*Wernicke's encephalopathy: Presenting characteristics*

In 19 cases, altered sight (diplopia in 10, loss of vision in 10, both in 3) was a presenting sign of WE. Unexpectedly, in four cases altered hearing (hearing loss in three, acoustic hallucinations in one) was a presenting sign.

The most profound characteristic of WE in the case descriptions reviewed was altered mental status (26 cases), presenting itself as delirium, confusion, or problems in alertness, drowsiness or cognition. Eye-movement disorders were present in 25 cases, presenting as nystagmus (19) and ophthalmoplegia (9), resulting from extraocular muscle weakness. In 15 cases, ataxia was present, ranging from gait abnormalities to full inability to walk or move. The full triad was present in 13 cases, a larger proportion than the 16% reported in postmortem case descriptions of WE in people with alcoholism [38].

*Imaging*

In 21 of the 22 case descriptions where an MRI was performed, the procedure revealed radiologic alterations. Alterations in the thalamic area of the brain were common.

*Treatment: Too little, too late*

In 12 cases, there was a detailed report on the treatment of WE symptoms. Of interest, two patients did not survive [10,17], and were diagnosed postmortem. One male patient received a total colectomy in UC and was subsequently left in a comatose state [10]. A female patient with CD died after receiving a glucose infusion, causing a malnourished state with diarrhea and vomiting [17].

In seven case studies, the parenteral doses of thiamine given were lower than the recommended 1500 mg/d [12,14,18,20,32,33,37], leading to residual cognitive damage (mild amnesia or cognitive disorders) in three cases [12,18,33]. This is in contrast to cases in which the optimal thiamine doses were given, resulting in a complete remission of WE symptoms in all cases [24,26,29].

Of interest, in one case study, hyperbaric oxygen therapy (HBOT) was combined with thiamine therapy to treat WE following hemicolectomy in CD [37].

## Discussion

Because of chronic inflammation and vomiting, people with CD and UC are particularly at risk for developing WE as a consequence of thiamine deficiency [39,40]. Substantial vitamin $B_1$ treatment in all people at risk for malnourishment in IBD is necessary to prevent the development of WE. In our review, treatment was often not preventive, but also the core symptoms of WE were not actively treated, because of suboptimal doses of thiamine. These issues lead to adverse outcomes, such as chronic cognitive disorders.

In the majority of the reported cases, WE was caused by nausea and vomiting in CD and UC. Vomiting is a primary cause of WE, specifically if people become malnourished due to prolonged vomiting. Parenteral thiamine supplementation is therefore necessary in all people who show signs of prolonged vomiting in CD or UC, to prevent them from developing WE. Oral supplements are not absorbed in significant enough amounts in people who vomit, leading to insufficient prophylaxis of WE [5]. One of the most remarkable findings in our review is that WE in CD and UC was frequently diagnosed after progressive deterioration of symptoms. For example, ileostomy was applied to alleviate chronic intestinal infections, leading to diminished capacity to absorb thiamine. Also, total parenteral nutrition and glucose were given to bypass the severely compromised capacity of the gastrointestinal tract, but this inadvertently led to increased thiamine consumption. We suggest that limited capacity to absorb thiamine, increased consumption of thiamine in IBD, and loss of thiamine due to vomiting all can lead to symptoms of WE.

Hearing loss is an uncommon presenting sign of WE, with only eight reported cases up until 2014 [26]. In this review, three cases presented with hearing loss and tinnitus, possibly reflecting a specific presentation of WE in CD and UC. Walker et al. [26] suggest that only a subgroup of young female patients are at particular risk

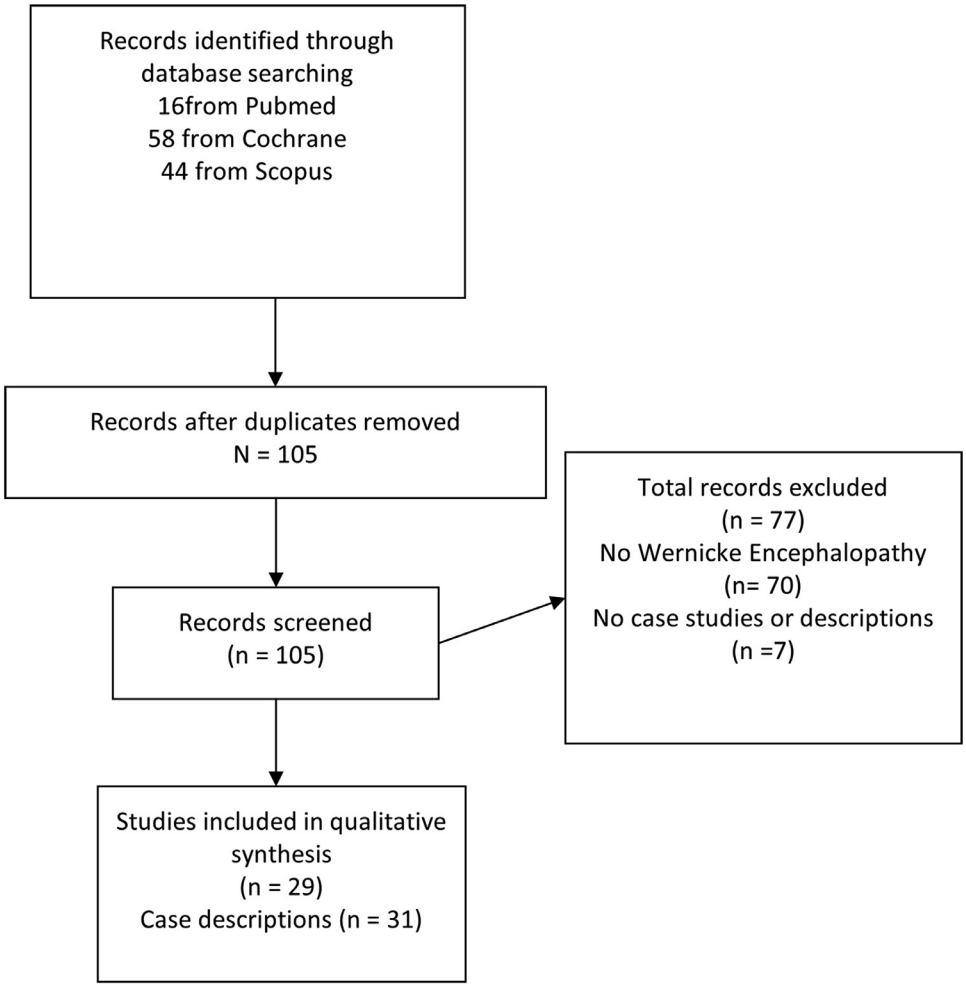


**Fig. 1.** Flowchart of case-study inclusion, illustrating the number of articles identified in the literature search and reasons for exclusion. Thirty-one cases in 28 studies met the inclusion and exclusion criteria.

for this WE symptom, but our review showed that in one case an older female patient had hearing loss as a presenting sign of WE. Recently, Fousekis et al. (2018) [41] have suggested that because of systemic disease, all people with IB have an increased risk for developing hearing issues. Moreover, it is possible that a lack of thiamine will result in neuropathy of the nervus cochlearis, leading to hearing issues because of a thiamine deficiency [8].

In 19 cases, WE presented with altered vision. In 10, vision was blurred or fully absent, and in 10, diplopia was present. Importantly, in all 19 cases, the individuals complained of altered vision, making this symptom of particular value for early diagnosis of WE in CD and UC. In the majority of reported cases, altered vision was not reviewed as a serious neurologic condition, leading to relatively late treatment of WE.

Eye-movement disorders such as nystagmus and ophthalmoplegia were relatively common in the presentations of WE in CD and UC. Earlier research suggests that it is likely that eye-movement disorders represent the most severe form of thiamine depletion, since this symptom is most common in WE following anorexia nervosa [42] and least common in WE following obesity surgery [43].

Radiologic imaging can be used to support the diagnosis of WE, but it is not always sensitive to WE symptomatology. Often, hyperintensities are visible in the thalamic region, in line with previous research on WE [8]. In almost all reported CD and UC cases, MRI was sensitive for detecting WE. In people with alcoholism, MRI was only sensitive in 53% of the cases. This finding possibly reflects a delayed recognition of WE in CD and UC cases, but also could reflect a more detrimental outcome in CD and UC. Since thiamine supplementation is most effective when given as early as possible, it is not necessary to include additional diagnostic tools before providing thiamine.

When WE is suspected, it is important to give high doses of thiamine to treat the underlying thiamine deficiency. A dose of 500 mg of thiamine three times/d is effective in resolving thiamine issues and actively treating WE. Originally, a treatment duration of 3–5 d was suggested, but according to recent literature a high-dose treatment of parenteral thiamine should be continued for at least 2 mo [8,44]. Magnesium levels are sometimes low in IBD, and therefore also require supplementation [8]. In this review, three patients received high doses of thiamine, leading to full recovery of WE. In four cases, suboptimal treatment resulted in residual cognitive disorders following WE. These results suggest that higher doses of thiamine given parenterally have the potential to reverse WE.

In one case study, thiamine supplementation was accompanied by HBOT, leading to complete resolution of WE symptoms [37]. To our knowledge, this is the first study applying HBOT in WE. HBOT has been successfully applied in radiation tissue injury following radiotherapy for cancer [45]. Recently, studies have reported improvement of cognitive functions in Alzheimer's disease [46,47] and stroke [48,49] following HBOT, suggesting treatment potential

**Table 1**
Demographic and clinical characteristics

| Reference | CD/UC | Gender | Age, y | Reason | Ataxia | Eye-movement disorder | Mental- and sensory-status change | Visual/auditory problem | MRI | Thiamine treatment/ outcome |
|---|---|---|---|---|---|---|---|---|---|---|
| Van Noort et al. [9] | UC | M | 35 | Glucose administration without thiamine | – | + (ophthalmoplegia) | – | Blindness | NA | |
| Mattioli et al. [10] | UC | M | 22 | Vomiting and diarrhea, total colectomy, TPN without thiamine | – | + (nystagmus and ophthalmoplegia) | + (drowsiness) | Loss of vision, diplopia | NA | IV/total recovery |
| Mattioli et al. [10] | UC | M | 47 | Total colectomy | – | + (nystagmus) | + (coma) | – | NA | No treatment/deceased |
| Parkin et al. [11] | CD | F | 44 | TPN without thiamine and ileum resection | – | + (nystagmus) | + (memory dysfunction) | – | Subcortical white matter lesions | No treatment/Korsakoff's syndrome |
| Shiozawa et al. [12] | UC | F | 61 | Subtotal colectomy, diarrhea, WE after TPN stopped | + | + (ophthalmoplegia) | + (semi-coma) | – | Hyperintense periventricular areas of the third and fourth ventricles and periaqueductal area | IV 50 mg/d/some recovery |
| Arakawa et al. [13] | CD | M | 23 | TPN without thiamine after ileus | + | + (nystagmus) | + (memory dysfunction, dizziness) | | Hyperintense periventricular areas | IV/slight cognitive impairment |
| Hahn et al. [14] | CD | F | 20 | Chronic TPN with oral multivitamin | + (shuffling gait) | + (nystagmus, and later ophthalmoplegia) | + (confusion) | Diplopia | Hyperintense upper medulla, midbrain, and thalamus | IV 50 mg/d/no Korsakoff's syndrome |
| Bamber [15] | CD | F | 60 | Malnourishment and glucose administration without thiamine | + | + (nystagmus) | + (loss of consciousness) | – | NA | No treatment/ deterioration |
| Ziping et al. [16] | CD | M | 30 | Progressive weight loss, diarrhea, nausea and vomiting | + | – | + (loud speech) | Diplopia | NA | Unknown |
| Larnaout et al. [17] | CD | F | 50 | Vomiting, diarrhea, malnourishment | ? (not testable) | ? (not testable) | + (coma) | – | NA | No treatment/deceased after glucose infusion |
| Eggspühler et al. [18] | CD | F | 42 | Inactive CD after resection of the small intestine and the duodenum and pyloroplasty | + | + | + (forgetfulness) | Diplopia | Hyperintense mammillary bodies, fornix, tractus mammillothalamicus, and floor of the fourth ventricle | IV 100 mg/d/mild amnesia |
| Flabeau et al. [19] | CD | F | 31 | Partial colectomy and TPN without thiamine | – | + (nystagmus) | + (apathy, headache) | Blurred vision, hearing loss, tinnitus | Inferior colliculus | IV/symptoms resolved |
| Borlot et al. [20] | CD | M | 5 | TPN after pancreatitis without thiamine | – | + (upbeat nystagmus) | + (drowsiness, meaningless speech) | – | Hypersignal in the thalamus, predominating in the mesial region and discrete hypersignal in the periaqueductal gray | IV 100 mg/d/no Korsakoff's syndrome |
| Santos Andrade et al. [21] | UC | F | 37 | Total colectomy, pancreatitis, vomiting | – | + | – | | Hyperintense mammillary bodies | NA |
| Pereira et al. [22] | CD | M | 27 | TPN after total colectomy | + | + (nystagmus) | + (aphasia, seizures, confusion) | Diplopia | Bilateral frontal cortical high signal intensity | IV/tetraparesis, spasms, aphasia |
| Željko et al. [23] | CD | F | 18 | TPN after ileostomy with oral thiamine supplementation after 18-kg weight loss over 6 mo | – | + (nystagmus) | + (nausea) | Diplopia | Symmetrical bilateral hyperintensity in the hypothalamus and on the floors of the third and fourth ventricles | IV/no Korsakoff's syndrome |

(*continued on next page*)

**Table 1** (*Continued*)

| Reference | CD/UC | Gender | Age, y | Reason | Ataxia | Eye-movement disorder | Mental- and sensory-status change | Visual/auditory problem | MRI | Thiamine treatment/ outcome |
|---|---|---|---|---|---|---|---|---|---|---|
| Davies et al. [24] | UC | F | 64 | Pneumonia, malnourishment | ? | – | + (drowsiness) | – | High signal in the periaqueductal area, superior colliculi, and posterior medial thalami | IV 500 mg 3 time/d/ dramatic improvement |
| Delgado et al. [25] | CD | F | 42 | Ileocolic resection, presacral abscess, vomiting, sepsis, *Acinetobacter* infection | – | + (nystagmus) | + (mutism, delirium) | – | Minimal cortical hyperintensity in the left temporal and right frontal lobes | IV/normal |
| Walker et al. [26] | UC | F | 61 | 18-kg weight loss in 1 mo, nausea, vomiting, *Clostridium difficile* infection | + | + (nystagmus, ophthalmoplegia) | + (poor mental status) | Visual disturbance, hearing loss | Hyperintensity in periaqueductal gray, quadrigeminal plate, bilateral superior colliculi, bilateral mammillary bodies, bilateral fornices, hypothalamic region, both medial thalami | IV 500 mg 3 times/d/ complete recovery |
| Delavar Kasmaei et al. [27] | CD | M | 41 | Nausea and vomiting in untreated CD | + (progressive ataxia, dysphagia) | + (nystagmus, ophthalmoplegia) | + (confusion, apathy, disorientation) | Diplopia | Hyperintense mammillary bodies | IV/mild ataxia |
| Machado et al. [28] | CD | M | 40 | Malnourishment, esophageal candidiasis, TPN with oral thiamine | + (weakness and paresthesia, dysphagia) | + (ophthalmoplegia) | + | Visual impairment, diplopia | NA | IV 200 mg 3 times/d/no Korsakoff's syndrome |
| Guler et al. [29] | UC | F | 36 | Nausea, vomiting, diarrhea | + | + (ophthalmoplegia) | + (dizziness, slurred speech, delusions) | Diplopia | Bilateral frontal, temporal, and parietooccipital cortico-subcortical hyperintensities | IV 1500 mg/d/complete remission |
| Miller [30] | CD | F | 17 | Pancreatitis, nausea, vomiting | + | – | + (confusion, coma) | Diplopia, blurred vision, hearing loss | Hyperintensities in the bilateral thalami, periaqueductal gray matter and frontal cortex | IV/no Korsakoff's syndrome |
| Shin et al. [31] | CD | M | 22 | Malnourishment, TPN without thiamine after perianal abscess | – | + (nystagmus) | + (confused speech, dizziness, seizures) | Blurred vision | High-signal-intensity lesion at both right and left sides of the mammillary body and tectum, and the periaqueductal space | IV/no Korsakoff's syndrome |
| Shin et al. [31] | CD | F | 34 | Malnourishment, TPN without thiamine, abscess, vomiting | + | – | – | Blurred vision | High-signal-intensity lesion at the inferior colliculus of the midbrain and pontomedullary junction | IV/no Korsakoff's syndrome |
| Barnes and Kerner [32] | UC | M | 16 | TPN without thiamine, total colectomy, pancreatitis, ileus | + | – | – | Acoustic hallucination | NA | IV 400 mg/no Korsakoff's syndrome |
| Vogrig et al. [33] | CD | M | 47 | Colectomy, vomiting, fistula surgery | – | + (upbeat nystagmus) | + (memory problems, burning pain in distal limbs) | Loss of sight | Bilateral medial thalamic hyperintensity | IV 200 mg 3 times/d/ mild amnesia |
| Welsh et al. [34] | CD | M | 22 | Malnourishment | + | + (nystagmus) | + (seizures, fatigue, dysarthria, vertigo) | Diplopia | NA | |

(*continued on next page*)

**Table 1** (*Continued*)

| Reference | CD/UC | Gender | Age, y | Reason | Ataxia | Eye-movement disorder | Mental- and sensory-status change | Visual/auditory problem | MRI | Thiamine treatment/ outcome |
|---|---|---|---|---|---|---|---|---|---|---|
| Battista et al. [35] | CD | M | 53 | Nausea, vomiting | + | + (nystagmus, ophthalmoplegia) | + (confusion) | Diplopia | Hyperintensity of periaqueductal gray, mammillary bodies, hypothalamus, and medial thalamus | IV/clear improvement |
| Doğan et al. [36] | UC | M | 36 | 35-kg weight loss, diarrhea, vomiting, colectomy | + | + (nystagmus) | + (disorientation, slowness) | | Hyperintense medial thalami | IV/mild amnesia |
| Abdelwali et al. [37] | CD | F | 43 | Hemicolectomy, epigastric pain | + | + (nystagmus) | + (memory problems, drowsiness, headache) | | Hyperintense posteromedial thalamus and bilateral mammillary bodies | IV 500 mg + HBOT/ complete remission |

CD, Crohn's disease; HBOT, hyperbaric oxygen therapy; MRI, magnetic resonance imaging; NA, not available; TPN, total parenteral nutrition; UC, ulcerative colitis; WE, Wernicke's encephalopathy.

for WE. Of importance, in one recent case study, the combination of antibiotic treatment with metronidazole and HBOT resulted in acute encephalopathy [50], suggesting a potential risk of applying HBOT in combination with antibiotic treatment for cognitive functioning.

Although the treatment guidelines for IBD include diagnostics and treatment of nutritional deficiency of several vitamins, and multivitamin deficiency is common in IBD, thiamine is not one of the described deficiencies [5,39]. Based on our review, it is likely that specifically people who lose weight, have complications of IBD, or receive total parenteral nutrition without thiamine are at risk for the development of WE. A fourth mechanism possibly putting people with IBD at risk for WE is bacterial dysbiosis leading to less biosynthesis of vitamin $B_1$ [51]. It is therefore possible that the thiamine deficiency seen in IBD is relatively indirect to the disease, and therefore not incorporated in current treatment standards [5,39]. Earlier research has pointed out that individuals with CD (in remission) do have lower dietary intake, also putting them at more risk for the development of WE [52]. Also, in a small-scale study, individuals with CD had lower thiamine levels than individuals without [53]. In people with IBD, subclinical thiamine deficiency can lead to fatigue in up to 40% of cases [54]. It is currently unknown how many people with IBD are thiamine deficient, and WE seems to be relatively uncommon in this patient group. Possible underlying mechanisms leading to thiamine deficiency should be investigated in future research.

A limitation of the present review is that we reviewed only case descriptions. Therefore, predictive information regarding prevalence rates and incidence rates is limited. Despite this limitation, the level of detail in the case studies reviewed leads to new insights on WE after CD and UC.

## Conclusion

In conclusion, there is a growing number of people worldwide with UC and CD. Malnourishment-related WE is rare, but can be fully prevented by prophylactic thiamine supplementation. Specifically in people with vomiting or diarrhea, thiamine supplementation is necessary. Mental confusion, eye-movement disorders, and ataxia are often missed as crucial symptoms of WE. After the initial onset of symptoms, rapid treatment with high doses of thiamine is still a lifesaving measure, ameliorating WE.

## References


[1] Ng SC, Shi HY, Hamidi N, Underwood FE, Tang W, Benchimol EI, et al. Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review or population-based studies. Lancet 2017;390:2769–78.

[2] Molodecky NA, Soon IS, Rabi DM, Ghali WA, Ferris M, Chernoff G, et al. Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. Gastroenterology 2012;142:46–54.

[3] Donnellan CF, Yann LH, Lal S. Nutritional management of Crohn's disease. Therap Adv Gastroenterol 2013;6:231–42.

[4] Owczarek D, Rodacki T, Domagala-Rodacka R, Cibor D, Mach T. Diet and nutritional factors in inflammatory bowel diseases. World J Gastroenterol 2016;22:895–905.

[5] Ghishan FK, Kiela PR. Vitamins and minerals in IBD. Gastroenterol Clin North Am 2019;46:797–808.

[6] Sechi G, Serra A. Wernicke's encephalopathy: new clinical settings and recent advances in diagnosis and management. Lancet Neurol 2007;6:442–55.

[7] 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;62:51–60.

[8] Thomson AD, Cook CH, Touquet R, Henry JA. The Royal College of Physicians report on alcohol: guidelines for managing Wernicke's encephalopathy in the accident and emergency department. Alcohol Alcohol 2002;37:513–21.

[9] Van Noort BBA, Bos PJM, Klopping C, Wilmink JM. Optic neuropathy from thiamine deficiency in a patient with ulcerative colitis. Doc Ophthalmol 1987;67:45–51.

[10] Mattioli S, Miglioli M, Montagna P, Lerro MF, Pilotti V, Gozzetti G. Wernicke's encephalopathy during total parenteral nutrition: observation in one case. JPEN J Parenter Enteral Nutr 1988;12:626–7.

[11] Parkin AJ, Blunden J, Rees JE, Hunkin NM. Wernicke-Korsakoff syndrome of nonalcoholic origin. Brain Cogn 1991;15:69–82.
[12] Shiozawa T, Shiota H, Shikata E, Kamei S, Mizutani T. Development of Wernicke's encephalopathy during the period of oral food intake after a subtotal colectomy for ulcerative colitis. Rinsho Shinkeigaku 1995;35:169–74. [in Japanese].
[13] Arakawa K, Okada M, Ohta H, Ogasawara M, Baba K. [Two cases of Wernicke's encephalopathy caused by an intravenous solution without vit. B1]. Er Bi Lin Chuang 1996;89:1309–17. [in Japanese].
[14] Hahn JS, Berquist W, Alcorn DM, Chamberlain L, Bass D. Wernicke encephalopathy and beriberi during total parenteral nutrition attributable to multivitamin infusion shortage. Pediatrics 1998;101:E10.
[15] Bamber MG. Wernicke's encephalopathy. Lancet 1998;352:655.
[16] Ziping L, Chunming L, Yuanhang W, Dan W. [Crohn disease with beriberi and Wernicke encephalopathy: one case]. Zhongguo She Qu Yi Shi Yi Xue Zhuan Ye 2004;21:48–9.
[17] Larnaout A, El-Euch G, Kchir N, Filali A, Hamida MB, Hentati F. Wernicke's encephalopathy in a patient with Crohn's disease: a pathological study. J Neurol 2001;248:57–60.
[18] Eggspühler AW, Bauerfeind P, Dorn T, Siegel AM. Wernicke encephalopathy—a severe neurological complication in a clinically inactive Crohn's disease. Eur Neurol 2003;50:184–5.
[19] Flabeau O, Foubert-Samier A, Meissner W, Tison F. Hearing and seeing: unusual early signs of Wernicke encephalopathy. Neurology 2008;71:694.
[20] Borlot F, de Freitas MR, de Araujo LV, Delgado AF, Koda YKL, da Paz JA, et al. [Wernicke encephalopathy in a child with Crohn disease]. Rev Paul Pediatr 2009;27:452–5. [in Portuguese].
[21] Santos Andrade C, Tavares Lucato L, da Graça Morais Martin M, Joaquina Marques-Dias M, Antonio Pezzi Portela L, Scarabôtolo Gattás G, et al. Non-alcoholic Wernicke's encephalopathy: broadening the clinicoradiological spectrum. Br J Radiol 2010;83:437–46.
[22] Pereira DB, Pereira ML, Gasparetto EL. Nonalcoholic Wernicke encephalopathy with extensive cortical involvement: cortical laminar necrosis and hemorrhage demonstrated with susceptibility-weighted MR phase images. AJNR Am J Neuroradiol 2011;32:E37–8.
[23] Željko K, Darija VB, Dina LK, Marko B. Wernicke's encephalopathy during parenteral nutrition in a Crohn's disease patient. Nutrition 2011;27:503–4.
[24] Davies SB, Joshua FF, Zagami AS. Wernicke's encephalopathy in a non-alcoholic patient with a normal blood thiamine level. Med J Aust 2011;194:483–4.
[25] Delgado MG, Vega J, Santamarta E, Caminal L. Complex partial status epilepticus in a patient with Crohn's disease. BMJ Case Rep 2013;6:bcr2013200503.
[26] Walker MA, Zepeda R, Afari HA, Cohen AB. Hearing loss in Wernicke encephalopathy. Neurol Clin Pract 2014;4:511–5.
[27] Delavar Kasmaei H, Baratloo A, Soleymani M, Nasiri Z. Imaging-based diagnosis of Wernicke encephalopathy: a case report. Trauma Mon 2014;19:e17403.
[28] Machado J, Ministro P, Cancela E, Araujo R, Castanheira A, Silva A. Acute neurologic disorder in Crohn's disease: a rare life-threatening complication. GE Port J Gastroenterol 2014;21:31–4.
[29] Guler A, Alpaydin S, Sirin H, Calli C, Celebisoy N. A non-alcoholic Wernicke's encephalopathy case with atypical MRI findings: clinic versus radiology. Neuroradiol J 2015;28:474–7.
[30] Miller D. Blind, deaf and confused: an unusual case of Wernicke's encephalopathy in a young adult (P2.012). Neurology 2016;86:S16.
[31] Shin IS, Seok H, Eun YH, Lee YB, Lee SE, Kim ER, et al. Wernicke's encephalopathy after total parenteral nutrition in patients with Crohn's disease. Intest Res 2016;14:191–6.
[32] Barnes D, Kerner J. Severe lactic acidosis in a parenteral nutrition-dependent teenager with ulcerative colitis. Dig Dis Sci 2016;61:2804–6.
[33] Vogrig A, Zanoni T, Moretto G. Nystagmus and lower extremity hyperalgesia after colectomy. JAMA 2016;316:1488–9.
[34] Welsh A, Rogers P, Clift F. Nonalcoholic Wernicke's encephalopathy. CJEM 2016;18:309–12.
[35] Battista F, Tinella E, Colosimo C. An acute neurological complication of Crohn's disease. Funct Neurol 2018;33:165–6.
[36] Doğan İG, Altiokka GU, Türker F, Saka B, Bilgiç B, Orhan EK. Wernicke's encephalopathy due to non-alcoholic gastrointestinal tract disease. Noro Psikiyatr Ars 2018;55:307–14.
[37] Abdelwali KN, Benelberhdadi I, Rahaoui A, Berhili C, Borahma M, Lagdali N, et al. Role of hyperbaric oxygen therapy and thiamine in Wernicke's encephalopathy secondary to Crohn's disease: "let there be light. Acta Sci Gastrointest Dis 2019;2:26–8.
[38] Harper CG, Giles M, Finlay-Jones R. Clinical signs in the Wernicke-Korsakoff complex: a retrospective analysis of 131 cases diagnosed at necropsy. J Neurol Neurosurg Psychiatry 1986;49:341–5.
[39] Lamb CA, Kennedy NA, Raine T, et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. Gut 2019;68(S3):s1–106.
[40] Harries AD, Rhodes J. Undernutrition in Crohn's disease: an anthropometric assessment. Clin Nutr 1985;4:87–9.
[41] Fousekis FS, Saridi M, Albani E, et al. Ear involvement in Inflammatory Bowel Disease: A Review of the Literature. J Clin Med Res 2018;10:609–14.
[42] Oudman E, Wijnia JW, Oey M, van Dam M, Postma A. Preventing Wernicke's encephalopathy in anorexia nervosa: a systematic review. Psychiatry Clin Neurosci 2018;72:774–9.
[43] Oudman E, Wijnia JW, van Dam M, Biter LU, Postma A. Preventing Wernicke encephalopathy after bariatric surgery. Obes Surg 2018;28:2060–8.
[44] Infante MT, Fancellu R, Murialdo A, Barletta L, Castellan L, Serrati C. Challenges in diagnosis and treatment of Wernicke encephalopathy. Nutr Clin Pract 2016;31:186–90.
[45] Bennett MH, Feldmeier J, Hampson NB, Smee R, Milross C. Hyperbaric oxygen therapy for late radiation tissue injury. Cochrane Database Syst Rev 2016;4:CD005005.
[46] Shapira R, Efrati S, Ashery U. Hyperbaric oxygen therapy as a new treatment approach for Alzheimer's disease. Neural Regen Res 2018;13:817–8.
[47] Harch PG, Fogarty EF. Hyperbaric oxygen therapy for Alzheimer's dementia with positron emission tomography imaging: a case report. Med Gas Res 2018;8:181–4.
[48] Liska GM, Lippert T, Russo E, Nieves N, Borlongan CV. A dual role of hyperbaric oxygen in stroke neuroprotection: preconditioning of the brain and stem cells. Cond Med 2018;1:151–66.
[49] Gonzales-Portillo B, Lippert T, Nguyen H, Lee JY, Borlongan CV. Hyperbaric oxygen therapy: a new look on treating stroke and traumatic brain injury. Brain Circ 2019;5:101–5.
[50] Baldinger E, Sirotkin I, Zeng WM, Rizzo J, Murphy E, Martinez C, et al. Acute encephalopathy following hyperbaric oxygen therapy in a patient on metronidazole. Fed Pract 2019;36:166–9.
[51] Yoon SMY. Micronutrient deficiencies in inflammatory bowel disease: trivial or crucial? Intest Res 2016;14:109–10.
[52] Filippi J, Al-Jaouni R, Wiroth JB, Hébuterne X, Schneider SM. Nutritional deficiencies in patients with Crohn's disease in remission. Inflamm Bowel Dis 2006;12:185–91.
[53] Kuroki F, Lida M, Tominaga M, Matsumoto T, Hirakawa K, Sugiyama S, et al. Multiple vitamin status in Crohn's disease. Dig Dis Sci 1993;38:1614–8.
[54] Contantini A, Pala MI. Thiamine and fatigue in inflammatory bowel diseases: an open-label pilot study. J Altern Complement Med 2013;19:704–8.