

Crohn's Disease with Wernicke's Encephalopathy: A Case Report and Literature Review

Fang L, Zhao Y, Tang M, Sun X and Liu Z*

Department of Gastroenterology, Center for IBD Research, Shanghai Tenth People's Hospital of Tongji University, Shanghai 200072, China

*Corresponding author:

Zhanju Liu,
Center for IBD Research, The Shanghai Tenth
People's Hospital of Tongji University, No.
301 Yanchang Road, Shanghai 200072,
China, E-mail: liuzhanju88@126.com

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*Author Contribution:

Fang L, Zhao Y, Tang M, Sun X, Liu Z and these authors are contributed equally to this work.

1. Abstract

Wernicke's Encephalopathy (WE) is an acute and potentially life-threatening neurological disorder due to thiamine deficiency. The classical signs and symptoms of the disorder include ophthalmoplegia, ataxia, and mental confusion. Although WE is known to occur frequently in alcoholics, it has also been reported in a number of non-alcoholic causes. Here, we reported a rare case of a severely malnourished patient with Crohn's Disease (CD) who presented WE after prolonged total parenteral nutrition without thiamine supplementation. This case revealed that it is of importance to give thiamine supplementation for malnourished patients even though they are not alcoholics. This article also reviews cases of CD and WE to discuss the diagnostic evaluation and clinical treatment of WE.

2. Introduction

Metabolic encephalopathy refers to a group of diseases characterized by brain dysfunction due to changes of biochemical metabolism in the body, which cause disorders in brain tissue. As a kind of metabolic encephalopathy, Wernicke's Encephalopathy (WE) is an acute metabolic encephalopathy caused by thiamine deficiency. It is known that chronic alcoholism is the key reason of WE because ethanol can reduce the absorption and utilization of thiamine in small intestine. However, there are also some non-alcoholic causes of WE in clinic, such as severe malnutrition, gastrointestinal diseases, anorexia nervosa, uremia, hemodialysis and pregnancy vomiting [1, 2]. As WE is quite difficult to be distinguished from certain other neurological

diseases to some extent, it is often misdiagnosed, resulting in a bad prognosis of the disease [3].

Crohn's Disease (CD) is a chronic inflammatory disease occurring mainly in the gastrointestinal tract. CD patients with long-term history tend to have malnutrition, especially trace element deficiency. The deficiency of trace elements further influences the process of nutrition absorption and metabolism, and, in turn, aggravates malnutrition. As we all know, Total Parenteral Nutrition (TPN) is one of important therapeutic approaches for severely active CD patients. However, according to previous reports, more than half cases of CD patients complicated with WE are caused by fasting, prolonged TPN without additional trace elements including thiamine. Thus, the long-term TPN without additional trace elements including thiamine may be an important reason of CD complicated with WE in clinic [4-7].

Here we reported a case of CD patient who was demonstrated to be severely malnourished, received several gastrointestinal operations, and developed severe complications including intestinal obstruction and abdominal abscess. After two weeks of TPN, this patient developed WE eventually. As metabolic encephalopathy can be cured with early recognition and timely treatment, we treated this patient with intravenous supplementation of thiamine and observed that her symptoms of WE were alleviated immediately. This case emphasizes the importance of nutritional support in the treatment of CD, and indicates that it may be more frequent than reported epidemiological statistics about the incidence of WE. Physicians should be cognizant of malnutrition in clinical practice of CD treatment.

3. Case Presentation

A 36-year-old non-drinking female with a 9-year history of recurrent Crohn's disease (CD) presented because of 1-week history of belly-ache and fever. She had undergone several gastrointestinal operations including ileostomy, enterolysis and jejunostomy resection. She used to have received methylprednisolone intravenous drip, prednisone oral administration, intravenous administration of anti-TNF (infliximab) and oral medication of azathioprine. In the past 4 years she refused to take any routine tests for evaluating the disease status and any drugs for maintaining the remission of CD.

On presentation, her temperature was 39°C and she was severely malnourished with a body mass index (BMI) of 12.48 kg/m². Abdominal Computed Tomography (CT) revealed massive hydrops abdominis and free gas. Laboratory results were as follows: C-reactive

protein (CRP) > 200 mg/L (N: < 8.2), white blood cell count 9.02 G/L (N: 3.5-9.5), red blood cell count 2.94 G/L (N: 3.8-5.1), hemoglobin level 80 g/L (N: 115-130), platelets 151 G/L (N: 125-350), N 93% (N: 40-75), serum albumin 2.1 g/dL (N: < 3.5). TPN therapy (Kabiven TM PI 1440 ml; Fresenius Kabi AB; Sweden) was given to her with antibiotic (Biapenem). No any vitamins or trace element substitution were administered in the gastroenterology unit. Meanwhile, abdominal puncture catheter drainage and abdominal lavage with metronidazole (100 ml) were performed daily for two weeks. After abdominal puncture and drainage, the patient's body temperature decreased and stabilized at about 37°C. WBC and CRP gradually decreased to normal levels, while nutritional indicators such as ALB gradually increased (Figure 1). The Nutrition Support Team (NST) was not invited to participate in the patient's care at this stage.

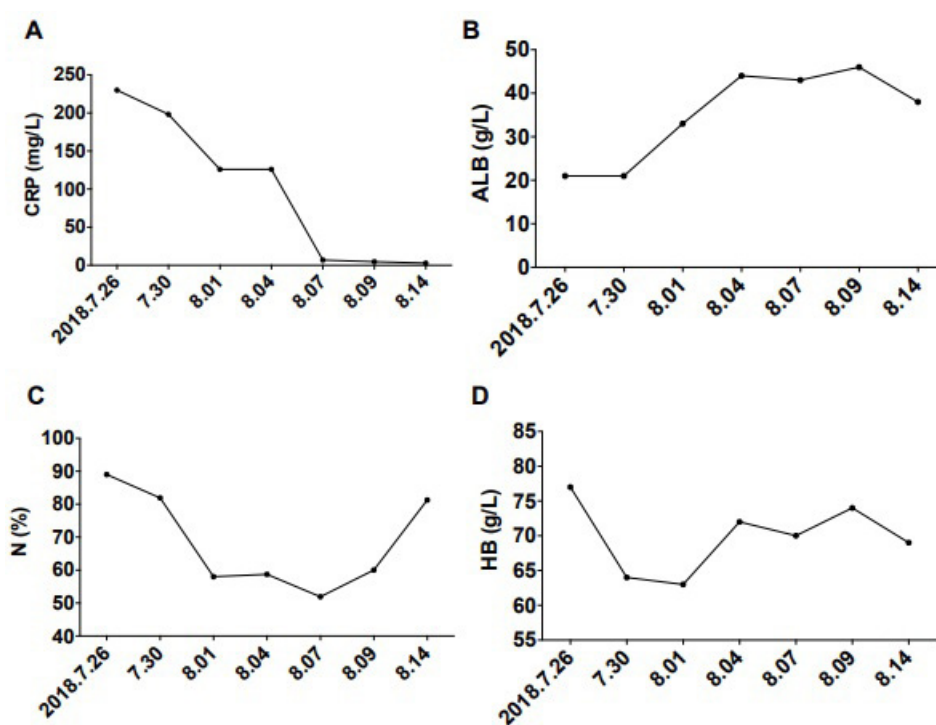


Figure 1: Tendency of inflammatory markers and nutritional indicators. As inflammatory markers, CRP and N% ebbed slowly (A and C), while ALB and HB as nutritional indicators eased up slightly (B and D). CRP, C reactive protein; N%, the percentage of neutrophils; ALB, albumin; HB, hemoglobin.

On admission day 20, this patient had sudden-onset epileptic manifestations and then recovered spontaneously in 2-3 minutes. Then she became cognitive dysfunction, intermittent confused speech, and dizziness. Her symptoms worsened on the next day. Arterial blood gases were analyzed, and no significant pH or base excess alterations were found. Brain MRI was performed and revealed a high signal-intensity lesion in bilateral frontotemporal cortex, ventromedial thalamus, papillary body, periaqueductal area of midbrain, pons and dorsal medulla oblongata. which was compatible with WE (Figure 2). Since electroencephalogram and lumbar puncture cerebrospinal fluid examination were both negative, the patient was diagnosed as CD accompanied by Wernicke's encephalopathy finally. The NST

was immediately involved. Oliclinomel N7 750 mL (Baxter S.A., Lessines, Belgium), comprising 1020 kcal/d or 30 kcal/kg/d, with 5.6 g nitrogen, 136 g glucose, 34 g lipid, 27.2 mmol sodium, 20.4 mmol potassium, 1.7 mmol calcium, 1.9 mmol magnesium, and 8.5 mmol phosphate, was used with an infusion rate of 50 mL/h. The 5% glucose solution was discontinued. Enteral formula (short chain polypeptide) was recommended as oral nutritional supplement that provided an additional 500 kcal. Immediate empirical therapy was started using thiamine 100 mg twice a day. The neurologic symptoms and signs resolved within a week. Although the patient still had problem in speaking, her normal cognitive function was almost restored. Before the patient was discharged from the hospital, the NST devel-

oped a personalized continuing nutrition plan of oral diet adjusted to 1000 kcal/d. Enteral formula was recommended as oral nutritional supplement that provided an additional 1000 kcal. A month after discharge, on the first visit to the outpatient clinic, her BMI was 16.88 kg/m² and cranial MRI revealed these organic lesions mentioned

above disappeared (Figure 3). Regular intravenous injection of anti-TNF (infliximab) was given as a maintenance treatment for the Crohn's disease. Since then the patient was followed-up in outpatient clinic every 2 months. She is currently in full clinical remission.

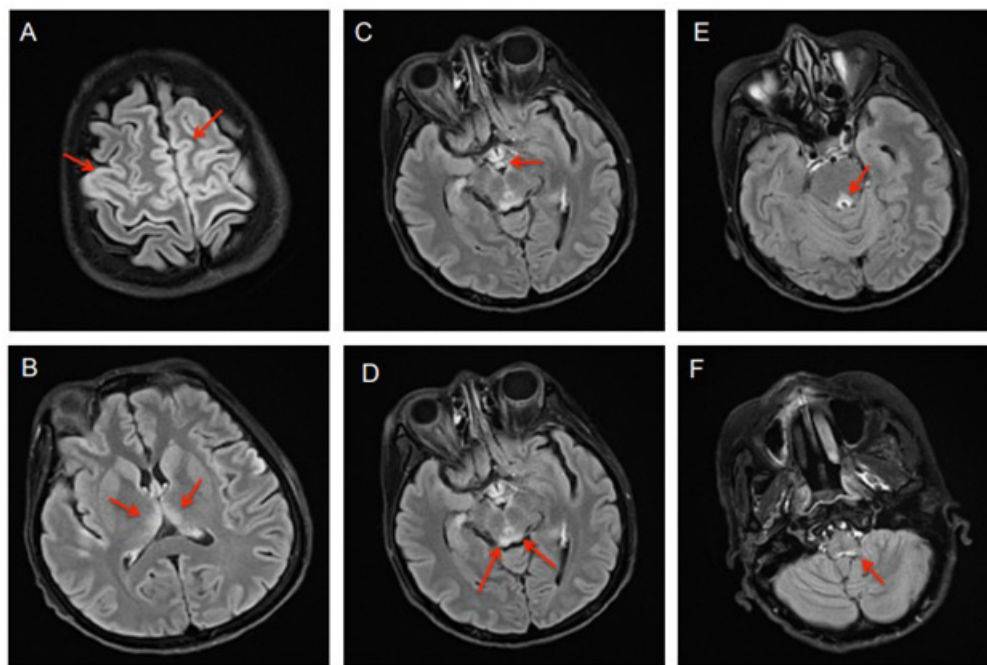


Figure 2: Cranial MRI indicated WE. Images of cranial MRI displayed multiple abnormal signal foci in bilateral frontotemporal cortex (A), ventromedial thalamus (B), papillary body (C), periaqueductal area of midbrain (E), pons (C) and dorsal medulla oblongata (F), which indicate Wernicke's encephalopathy.

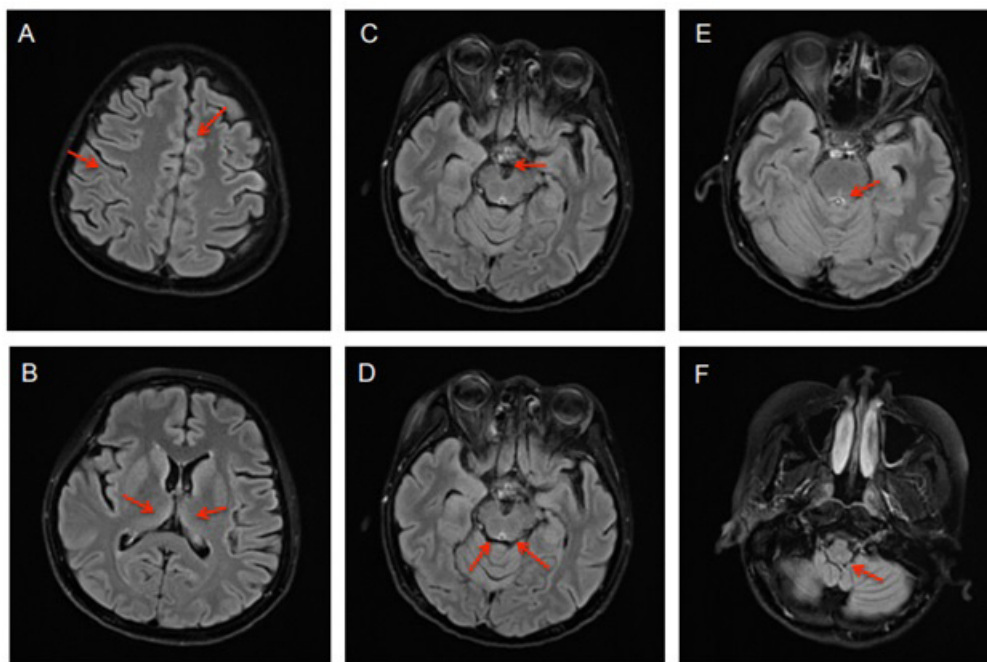


Figure 3: Reexamined cranial MRI showed no abnormalities areas (A-F). Brain MRI revealed a high signal-intensity lesion in bilateral frontotemporal cortex, ventromedial thalamus, papillary body, periaqueductal area of midbrain, pons and dorsal medulla oblongata. which was compatible with WE.

4. Discussion

Thiamine is a water-soluble vitamin and mainly absorbed in the duodenum and jejunum, which is one of important coenzymes in the process of carbohydrate metabolism, especially in the brain, like assistance in the oxidation of pyruvate⁸. Thiamine deficiency leads to metabolic imbalance, resulting in neuronal death-related diseases like WE. WE is a clinical manifestation of thiamine deficiency. The main symptoms include oculomotor nerve dysfunction, ataxia, and mental state changes [9]. Although WE is known to occur frequently in alcoholics, it has also been reported in a number of non-alcoholic causes, for example, chronic recurrent diseases such as CD and long-term TPN after gastrointestinal surgery [10].

According to literature review in Pubmed (<https://www.ncbi.nlm.nih.gov/pubmed>), only 7 cases of CD with WE have been reported (Table 1): 5 of them were CD patients who had received long-term TPN [4, 5, 7]; 1 case was a patient with partial small bowel resection, duodenectomy and pylorotomy [11]; and another 1 case experienced long-term chronic diarrhea and vomiting, and received treatment with TPN during hospitalization without additional trace element support, but finally died unfortunately [11]. Among these 5 TPN-related cases, 1 received TPN intermittently for a long time (about 11 years) [7], 2 received short-term TPN (about two weeks) after surgical intervention due to abdominal abscess and perforation [4, 5], and the remaining 2 cases had received TPN for 3 months and 17 days, respectively [4, 6].

Table 1: Cases summary of CD with WE

Case	Gender	Age	Drinking	Behavior of disease	Duration (years)	Surgery	Time of TPN	Symptom	Treatment	Outcome	Reference
1	F	20	N/A	N/A	11	N/A	long term	Dizziness and memory difficulty	Intravenous vitamin B1 and vitamins compound	Cured	Ref.4
2	F	50	No	A3,L1,B1	4	No	No	Progressive disturbance of consciousness and coma	None	Death	Ref.12
3	F	42	No	A2,L1+L4,B1	22	Partial resection of jejunum, No duodenum and pylorus	No	Memory disorders, muscle paralysis, horizontal nystagmus and ataxia.	Intravenous vitamin B1	Recovery, short-term memory impairment	Ref.11
4	M	20	No	N/A	5	N/A	3 months	Dizziness, ataxia and vision loss.	Intravenous vitamin B1	Cured	Ref.5
5	M	22	No	A2,L3,B3	4	Partial ileectomy and colectomy	14 days	Confusion, progressive nystagmus, diplopia, nausea and hypotension.	Intravenous vitamin B1	Cured	Ref.6
6	M	22	No	A2,L3,B3	N/A	Incision and drainage of perianal abscess	3 weeks	Progressive blurred vision, cognitive impairment, language impairment	Intravenous vitamin B1	Cured	Ref.7
7	F	34	No	A2,L1,B3	N/A	No	17 days	Sudden vertigo and ataxia	Intravenous vitamin B1	Cured	Ref.7

The diagnosis of WE is quite difficult in clinical practice as no useful means can be applied to distinguish it from other neurological diseases. According to previous studies, only about 16–38% of WE patients have typical WE clinical manifestations, and most were diagnosed dependent on cranial MRI [13, 14]. This case revealed that cranial MRI is of importance in unknown disorders of head diseases.

There were a lot of risk factors in this case, covering almost all factors reported in the previous cases of CD with WE. This patient had a 9-year history of recurrent CD before admission and had undergone several gastrointestinal surgeries, leading to the malnourished state. Despite relatively short period of fasting compared with previous cases [2, 7], active inflammation in intestinal mucosa might lead to an increase of thiamine requirement and contribute to the development of WE.

There is no uniform standard for the specific treatment of the disease. Hahn et al. described an intravenous administration of thiamine (50 mg daily) to treat WE patient's mental status and neurologic status had recovered completely in 2 months [7]. European Federation of Neurological Societies (EFNS) recommended either intramuscular injection or intravenous supplementation of thiamine (200 mg thrice-daily) before glucose supplement [3]. Recent studies recommended high dose supplementation of thiamine at least 500 mg per day for more than three days [15, 16], suggesting higher doses of thiamine given parenterally have the potential to reverse WE. The dose in this case was "100 mg twice-daily" by intramuscular injection in the first four days, then "200 mg twice-daily" by intravenous administration for another 2 days, and finally turned to "200 mg twice-daily" by intramuscular injection under the guidance of physicians from the Department of Nutriology. But the patient still had problems in speaking after high dose of thiamine supplement. There might be ascribed to several reasons as follows: First, thiamine supplement was given at the time when the patient was still treated with parenteral glucose support which consumed a large amount of thiamine; Second, the electrolyte disorders were not corrected timely, since various electrolytes, like serum magnesium and potassium, are important cofactors of energy metabolism [17, 18]; Finally, in addition to thiamine, other vitamins and trace elements also play important roles in energy metabolism [17, 19]. Indeed supplement of other B vitamins was not conducted in the early stage of the disease.

In summary, this case reveals the importance of nutritional monitoring and nutritional supplement for CD patients in clinical practice, especially those recurrent cases or those with history of gastrointestinal surgeries. In addition to routine nutritional risk assessment, electrolytes and trace element supplementation are also important factors to alert physicians about possible nutritional risks.

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