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CASE REPORT

Thiamine-deficient optic neuropathy associated with Wernicke's encephalopathy in patients with chronic diarrhea

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The deficiency of thiamine manifesting as Wernicke's encephalopathy (WE) and concurrent optic neuropathy is rare. Herein, we report the case of a 29-year-old patient who suffered from bilateral sudden blindness and a disturbance of consciousness after 2 months of chronic diarrhea and minimal food intake. In addition, bilateral abducens nerve palsy with multidirectional nystagmus and no light perception in both eyes were noted. An ophthalmoscopic examination revealed bilateral disc edema with peripapillary flame-shaped hemorrhages. Although the results of analyzing the composition of cerebrospinal fluid showed that they are within normal limits, magnetic resonance imaging (MRI) revealed bilateral hyperintensity over the mammillary body, dorsal medial thalamus, and periaqueductal gray matter. As we suspected thiamine deficiency-induced WE, a high dose of intravenous thiamine was prescribed. After the administration of thiamine, both visual acuity and visual field rapidly improved with the simultaneous recovery of consciousness. This case indicates that, although rare, thiamine deficiency with WE may still occur in patients with chronic diarrhea in Taiwan. Thiamine deficiency should be considered in the differential diagnosis for patients who encounter sudden visual loss after prolonged periods of poor food intake and poor vitamin supplementation.

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Introduction

Although thiamine deficiency may cause various disorders, such as high output heart failure (wet beriberi), lactic acidosis, and gastrointestinal beriberi, the most important neurological disorder is Wernicke's encephalopathy (WE),[1,2] which is clinically characterized by the classical triad of ocular abnormalities, ataxia, and disturbances of consciousness.[3] All of these conditions carry a high rate of morbidity and mortality when unrecognized.

Ocular manifestations of WE are nystagmus, ophthalmoplegia, and optic neuropathy.[4] However, optic neuropathy is not a common presentation of WE and has only been reported in a few anecdotal case reports.[5–11] In a case series of 245 patients with WE, optic neuropathy was reported to be present in only 2.6% of the patients.[4] To the best of our knowledge, WE with optic neuropathy has never been documented in Taiwan. Herein, we report a case of optic neuropathy presenting as optic disc edema with peripapillary flame-shaped hemorrhages and severe visual impairment in a nonalcoholic male patient with thiamine deficiency and WE.

Case report

A 29-year-old male patient without systemic diseases or associated family history presented with sudden bilateral blindness, ataxia, disturbance of consciousness, and body weight loss (20 kg) after 2 months of chronic diarrhea at a frequency of approximately one to two bowel movements a day and poor food intake. The patient's family reported that he did not use drugs, neither drank alcohol nor smoked tobacco. A few weeks before admission, his food intake decreased and consisted mainly of carbohydrates, because of frequent nausea, vomiting, and intermittent epigastric cramping pains immediately after eating. General weakness had rapidly progressed and he had become more dependent on manual assistance in the last 20 days. He experienced blurred vision (oculus unitas) about 7 days before being admitted in our hospital. As the condition rapidly deteriorated, he ultimately became confined to bed and developed mental changes with total blindness within 3 days. On presentation, he exhibited severe truncal ataxia, a state of total confusion, bilateral abducens nerve palsy (Fig. 1A) with multidirectional nystagmus and no light perception (NLP) in both eyes. The patient showed signs of apathy, inattentiveness, and an indifference to his surroundings. Spontaneous speech was minimal, and provoked speech indicated general disorientation to time, place, and purpose. Results of a physical examination revealed a blood pressure level of 87/64 mmHg, pulse rate of 158 beats/minute, respiratory rate of 20 breaths/minute, and body temperature of 35.6°C. Bilateral disc edema with peripapillary flame-shaped hemorrhages was observed (Fig. 2) after ophthalmoscopic examination, and a slit-lamp examination showed an otherwise unremarkable anterior segment except for an absence of light reflex in both eyes. A computed tomography of the head showed normal findings. An analysis of the cerebrospinal fluid and sepsis workup including cytomegalovirus, syphilis, and human immunodeficiency virus revealed negative results. The intracranial pressure had not increased. Toxin profiles and tumor markers were analyzed, but no abnormal findings were evident. Biological chemicals and blood profile were all within normal limits except for lactic acidosis (lactate: 61 mg/dL; normal range: about 4.5—19.8 mg/dL). Liver functioning was also normal. A subsequent magnetic resonance imaging (MRI) of the brain revealed abnormal hyperintensity over the mammillary body, dorsal medial thalamus, and periaqueductal gray matter in the axial fluid-attenuated inversion recovery (FLAIR) images, with corresponding sites on diffusion-weighted images (DWIs) (Fig. 3). Although the facilities for examining the serum thiamine levels were not available in our hospital, thiamine deficiency was suspected because his nutritional intake had been insufficient for approximately 2 months. Associated WE was suspected based on the clinical history, symptoms, and MRI findings. Therefore, high doses of intravenous thiamine (300 mg/day) were given immediately after the initial evaluation. Visual acuity improved dramatically from NLP to counting fingers after 12 hours. Rapid recovery of

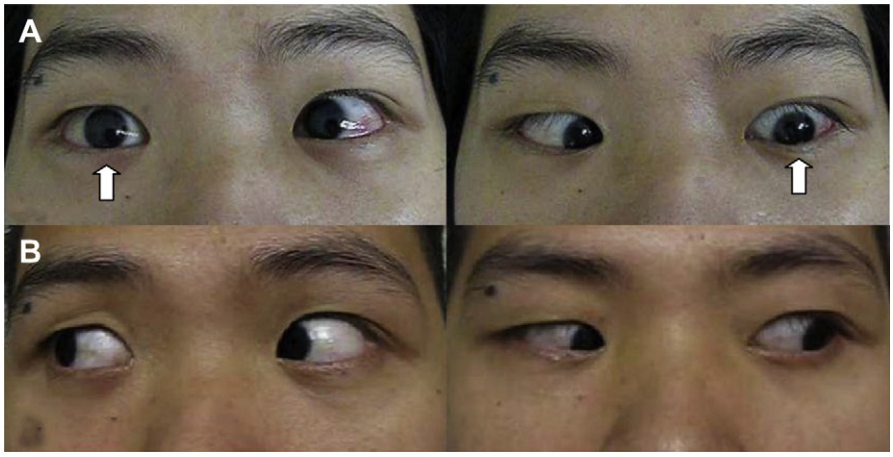

Figure 1 A 29-year-old male with chronic diarrhea and poor nutritional intake presented to our hospital with ataxia, multidirectional nystagmus, and sudden blindness. (A) Bilateral abducens palsy (arrow) was noted at the initial presentation. (B) Dramatic disappearance of bilateral abducens palsy after administering intravenous thiamine supplements for 1 week.

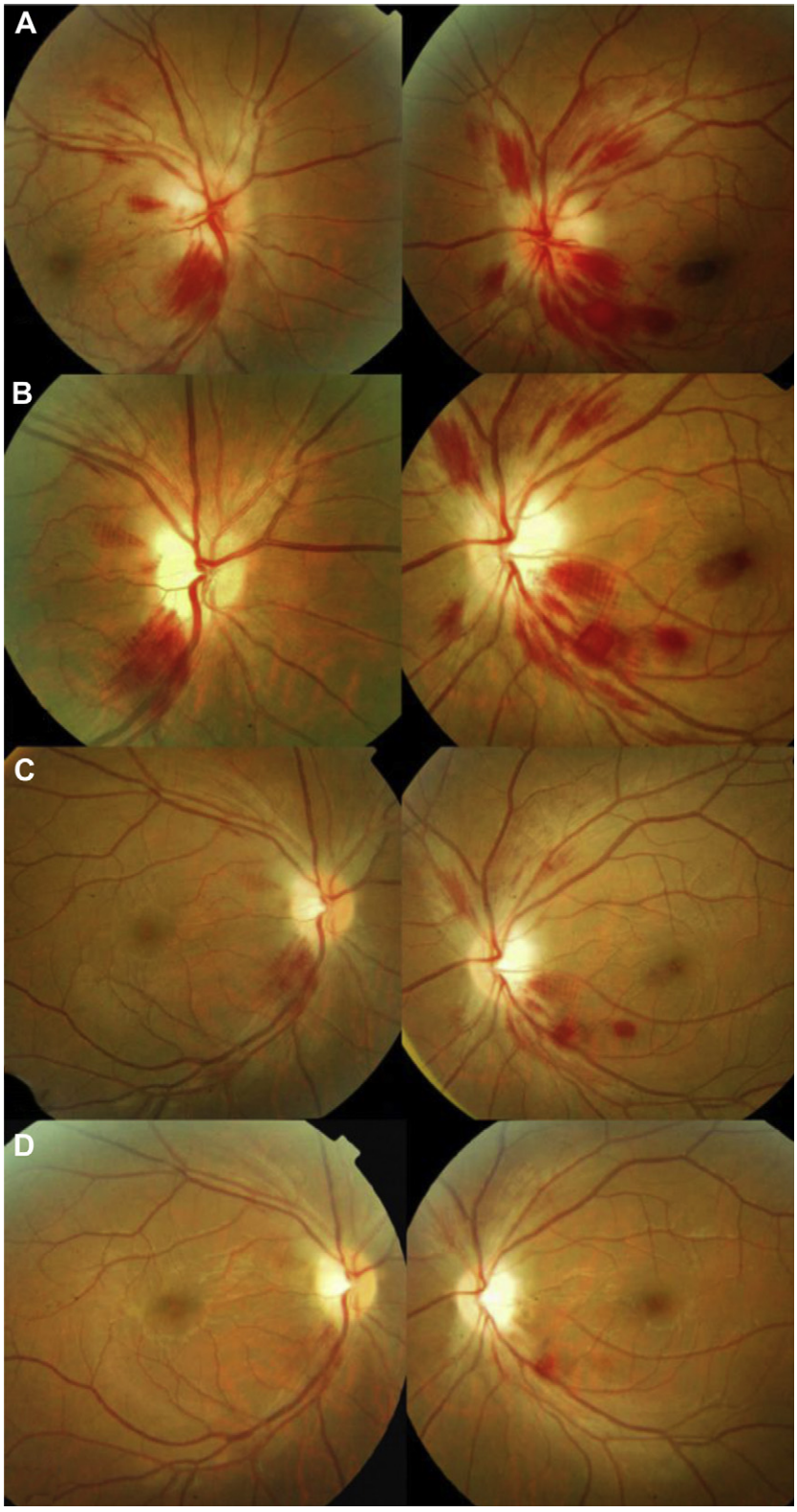

Figure 2 (A) Bilateral disc edema with flame-shaped hemorrhages was found at the initial presentation. The best-corrected visual acuity (BCVA) was no light perception (NLP) in both eyes. (B) One week after treatment, a slight decrease of bilateral nasal disc edema was observed. Bilateral BCVA improved from NLP to 2/60. (C) Near disappearance of disc edema and regressed flame-shaped hemorrhages were found on ophthalmoscopic examination after 2 weeks of treatment. Bilateral BCVA were still 2/60. (D) Three weeks after treatment, disc edema subsided completely; however, pallor of both optic discs began to appear. The bilateral BCVA remained the same (2/60).

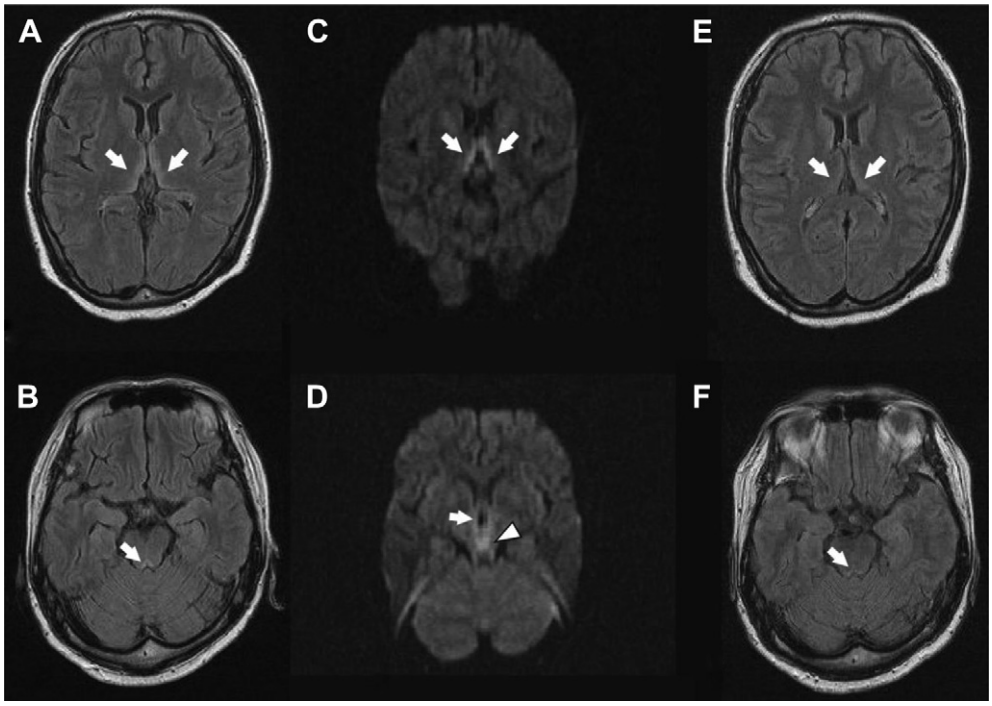

Figure 3 (A, B) Axial fluid-attenuated inversion recovery (FLAIR) images show abnormal hyperintensity within the medial thalami area surrounding the third ventricle (arrows in A) and pontine tegmentum (arrow in B). (C, D) Diffusion-weighted images (DWIs) show highly hyperintense areas within the bilateral thalami (arrows in C), periaqueductal area (arrow in D) and mammillary bodies (arrowhead in D) but no abnormal signal intensity in the other brain regions. These lesions on DWIs are more clearly visible than on the conventional T2-weighted image. (E, F) Post-treatment axial FLAIR images show that the area of previous abnormal hyperintense areas including bilateral medial thalami (arrows in E) and pontine tegmentum (arrow in F) decreased after 3 weeks.

consciousness and alertness and a decrease in serum lactate (from 61 to 28.7 mg/dL) were also found. A mini-mental state examination (MMSE) revealed a decrease in memory, multiple higher cognitive function, and visuospatial ability.

Parenteral administration of high dosages of thiamine for 1 week showed marked improvements in confusion, orientation, memory loss, slurred speech, and extraocular movements (Fig. 1B). Visual acuity and visual field (Fig. 4) also improved. However, visual evoked potential (VEP) arranged 1 week after treatment still showed poor waveform and prolonged latencies of P100 in both eyes with pattern and goggle-flash VEP, suggesting persistent optic nerve impairment in both eyes. Although both disc edema and peripapillary flame-shaped hemorrhages subsided gradually during hospitalization (Fig. 2B—2D), the best-corrected visual acuity only reached 2/60. Persistent nystagmus was noted despite total recovery of consciousness and ataxia after 3 weeks. Upon admission, an endoscopic gastro-duodenoscopy, colonoscopy, and biopsy of the duodenum were performed, which showed negative results. Gastric stasis was also not found. A follow-up MRI of the brain 3 weeks after treatment demonstrated the normalization of previously high signal intensities over the areas of the pontine tegmentum and bilateral medial thalami (Fig. 3E and 3F) compatible with the marked improvement in MMSE. He was then discharged to a rehabilitation center for continued physical rehabilitation and thiamine supplementations. At the time of the last phone contact (about 2 months after initial treatment), the patient had normal consciousness and slightly improved visual acuity.

Discussion

Our case suffered very severe visual impairment and neurological deficits after prolonged diarrhea and poor nutritional intake. Although the facilities for examining the serum thiamine levels (such as erythrocyte transketolase activity, urinary thiamine, and serum thiamine measured with high-performance liquid chromatography analysis) were not available in our hospital, the diagnosis of thiamine deficiency-related WE and associated optic neuropathy in our patient was based on his clinical history of long-term diarrhea and poor nutritional intake, characteristic ocular and neurological manifestations, characteristic MRI findings, and a dramatic improvement in both clinical manifestations and lactic acidosis after thiamine administration. A thorough investigation of his gastrointestinal condition with a gastroduodenal endoscopy, duodenal biopsy, and colonoscopy also excluded other differential diagnoses such as Whipple's disease or celiac disease.

Our patient had all the characteristic clinical signs of WE, including a disturbance of consciousness, ataxia, bilateral abducens palsy, nystagmus, and optic neuropathy. The fundus changes (Fig. 2) in our patient are typical of thiamine-deficient optic neuropathy, which is mainly

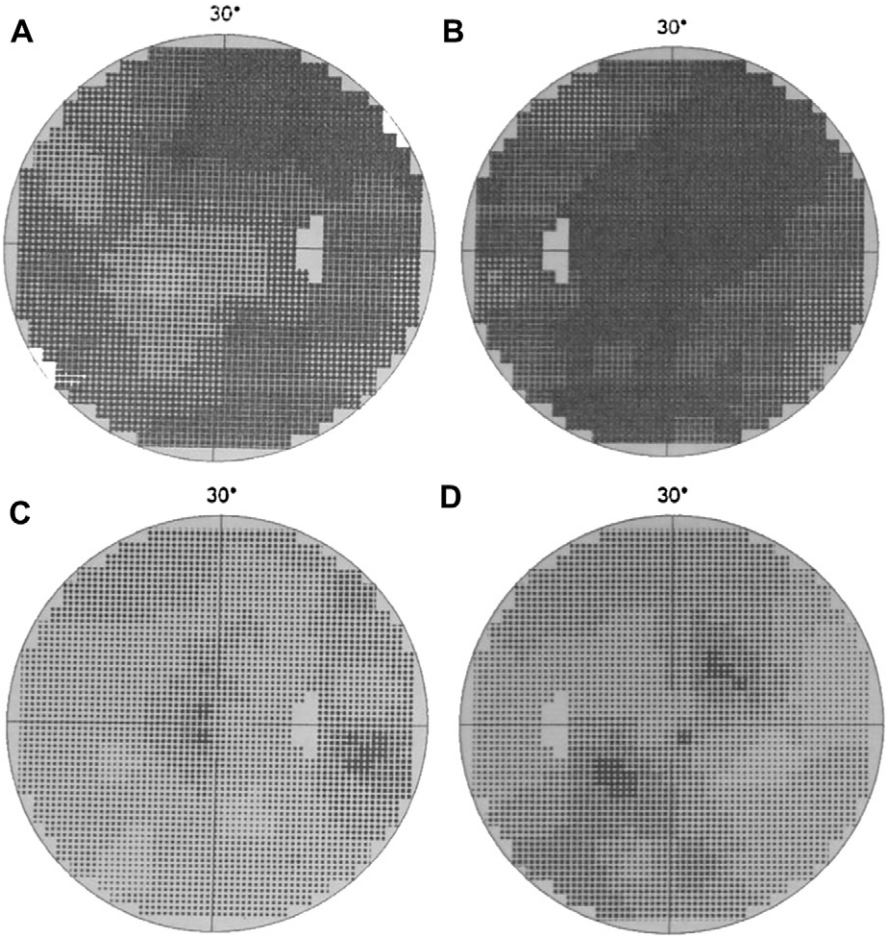

Figure 4 (A, B) Twelve hours after administering intravascular thiamine supplement, the best-corrected visual acuity (BCVA) improved from no light perception to counting fingers over 80 cm (oculus dexter) and 60 cm (oculus sinister). The mean visual field defect was 23.0 dB in the right eye and 26.8 dB in the left eye. (C, D) After 1 week of treatment with thiamine, the mean visual field defect decreased to 8.3 dB in the right eye and 9.6 dB in the left eye. The BCVA improved to 2/60 (oculus unitas) from counting fingers.

characterized by bilateral optic disc swelling (papilledema) and peripapillary flame-shaped hemorrhages. Although the mechanism of the development of disc swelling and peripapillary flame-shaped hemorrhages in this condition are not yet fully understood, it is possible that optic neuropathy may cause a rapid and severe deterioration of both visual acuity and visual field. In our patient, vision in the acute stage was impaired to the level of NLP. Although the optic disc swelling and the peripapillary hemorrhages gradually subsided after treatment, the optic disc was rendered atrophic and pale (Fig. 2C and 2D), indicating permanent damage. The vision of our patient only recovered to 2/60 with persistent VEP abnormality and visual field defect (Fig. 4) after treatment.

The symptoms of ophthalmoplegia (abducens palsy) and nystagmus are related to the involvement of the pontine tegmentum and the change in mental status is related to the involvement of the thalamic or mammillary bodies. Pathological studies have confirmed that neural and vascular damage may occur in the mammillary bodies, periaqueductal areas, and medial nucleus of the thalamus and cause the characteristic brain lesions of WE.[12,13] These changes are compatible with the abnormal findings in MRI (Fig. 3). The characteristic findings of MRI are symmetrical areas of increased signal intensity on T2-weighted images, FLAIR, and DWIs around the third ventricle in the dorsomedial parts of the thalami and in the periaqueductal regions of the midbrain.[14–16] The DWI is particularly sensitive to intracellular edema and can more distinctly demonstrate the symmetrical hyperintense signals of the thalamus and midbrain in WE.[5] The same findings were also observed in our case (Fig. 3C and 3D).

Many situations, such as chronic alcoholic intoxication, long-term starvation, hyperemesis gravidarum, anorexia nervosa, gastric bypass surgery, total parenteral nutrition without thiamine supplementation, chronic renal dialysis, and some antimetabolites such as amprolium, oxythiamine, and pyrithiamine may induce thiamine deficiency.[17,18] An analysis of thiamine deficiency should be considered in all patients with a history of alcoholism, malnutrition, malabsorption, tumors, inflammation, other severe debilitating diseases, and in parenteral hyperalimentation. Thiamine is a water-soluble vitamin that is absorbed in the jejunum and the ileum. Its biological half-life is approximately 10—20 days. Because the human body has limited tissue storage of

thiamine, it must be continuously supplied in food. Deficiency of thiamine can occur after 3 weeks of total dietary abstinence. Our patient had chronic diarrhea and vomiting for 2 months with limited food intake, which was much longer than the half-life of stored thiamine in the body.

Early recognition and therapy with intravenous thiamine can rapidly reverse these potentially life-threatening conditions. However, recognition of any of these entities is difficult in clinical practice, with reports of only up to 20% of WE cases being diagnosed clinically compared with postmortem necropsy studies.[19] Because the morbidity from WE can be reversed by timely administration of parenteral thiamine supplements and large doses of thiamine can be given without documented toxic effects, Lindberg and Oyler[20] recommended that all comatose patients of unknown cause should be given parenteral thiamine before definite confirmation of thiamine deficiency. Usually, rapid recovery of consciousness could be ensured after thiamine administration in patients with WE. However, some permanent neurological sequelae and visual impairment frequently remained after treatment, as noted in our patient. These results further emphasized the importance of early diagnosis and treatment.

Conclusion

This case indicated that, although rare, thiamine deficiency with WE and associated optic neuropathy may still occur in patients with chronic diarrhea even in the absence of alcoholism. It is also important to highlight the fact that the classical triad is not always typical in a clinical environment. Therefore, we conclude that thiamine deficiency should be considered in patients who encounter sudden visual loss and optic neuropathy after a prolonged period of poor food intake and poor vitamin supplementation.

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