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TREATMENT

Refractory Hypotension in a Patient with Wernicke's Encephalopathy

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Abstract — A 57-year-old male patient with gastric carcinoma underwent radical distal gastrectomy type II + Braun anastomosis, and received total parenteral nutrition for 10 days after surgery, followed by small amounts of semi-liquid nutrition for 3 days and liquid nutrition for 2 days. The patient developed refractory hypotension for more than 1 week in the early course of disease, and on Day 15 after surgery presented with characteristic signs of Wernicke's encephalopathy, including diplopia and mental confusion. The hypotension did not improve despite appropriate fluid replacement soon after admission. Treatment with moderate dose of thiamine for 3 months partly relieved ophthalmoplegia and confusion, but not Korsakoff syndrome. This extraordinary presentation with refractory hypotension and the unusual course of the disease encouraged us to present this case.

INTRODUCTION

Wernicke's encephalopathy is a syndrome characterized by an acute or subacute onset of ataxia, ophthalmoplegia and mental status changes. It was first described by Karl Wernicke in 1881 in three patients who had a sudden onset of paralysis of eye movement, ataxic gait and mental confusion. He designated it as 'polioencephalitis haemorrhagica superioris', an inflammatory process of the grey matter around the third and fourth ventricles and aqueduct of the Sylvius, which was subsequently termed as Wernicke's encephalopathy. Russian psychiatrist Sergei Sergeievich Korsakoff detailed an amnesic disorder seen in patients with Wernicke's encephalopathy in 1887 and gave the first comprehensive account of this disorder. He called the condition 'psychosis polyneuritica', which was renamed as Korsakoff's syndrome by Friedrich Jolly in 1897. It is of interest that the relationship between Wernicke's disease and Korsakoff's syndrome was appreciated neither by Wernicke nor by Korsakoff. In 1897, Murawieff first postulated that a common causal relationship was responsible for both (Victor and Ropper, 2001). The exact cause was elicited in the 1930s, when avitaminosis was first considered by Bender and Schilder and linked to thiamine deficiency by Prickett in 1934 and Alexander in 1940 (Victor *et al.*, 1989; Peters *et al.*, 2007). This led to the first study on the therapeutic effects of thiamine (vitamin B1) for Korsakoff psychosis by Bowman *et al.* (1939). As Wernicke's encephalopathy and Korsakoff's psychosis share a common aetiology, they are now viewed as a clinical spectrum known as Wernicke-Korsakoff syndrome (Peters *et al.*, 2007).

Wernicke's encephalopathy is most frequently associated with alcoholism, but non-alcoholic Wernicke's encephalopathy has been increasingly described in conditions that cause nutritional insufficiency, such as in hyperemesis gravidarum (Chaturachinda and McGregor, 1968), bariatric surgery, Crohn's disease, prolonged parenteral feeding or even in a hunger strike (Sechi and Serra, 2007).

A postoperative gastric cancer patient who presented with refractory hypotension was later confirmed as having Wernicke's encephalopathy by magnetic resonance imaging (MRI) studies. The unusual course of the disease prompted us to present his interesting case history for discussion.

CASE HISTORY

A 57-year-old male patient with gastric carcinoma underwent radical distal gastrectomy type II + Braun anastomosis, and received total parenteral nutrition (3.1 mg thiamine daily was included) for 10 days after surgery, followed by small amounts of semi-liquid nutrition for 3 days and liquid nutrition for 2 days. The patient presented with somnolence, blunted affect and diplopia on Day 5 after surgery. On Day 18 after surgery, he developed mental confusion, was unable to get up and answer any question. The patient was then admitted to Changhai Hospital of the Second Military Medical University (Shanghai, China). The family reported that the patient had a habit of drinking ~100 ml 40% alcohol per day for 30 years.

Physical examination revealed heart rate (HR) 113 bpm, temperature 36.8, blood pressure (BP) 90/70 mmHg. The patient was somnolent with an indifferent facial expression, and uncooperative in examination. Neurological examination showed a beating vertical nystagmus. The left eye was laterally deviated. The diameter of the left and right pupil was about 3 and 2.5 mm, respectively. Direct and consensual response to light was normal. Laboratory examination indicated plasma total bilirubin 19.0 μmol/l (normal range: 2–18.0 μmol/l), alanine aminotransferase (ALT) 360 U/l (normal level :< 64.0 U/l), amylase 141 U/l (normal range: 8–64 U/l), blood urea nitrogen 24.5 mmol/l (normal range: 2.5–6.5 mmol/l) and creatinine 117 mmol/l (normal range: 96–106 mmol/l). Blood routine was normal: white blood cell (WBC) 8.55×10^9/l, GRAN 63.6%, red blood cell 5.08 × 1012/l, HGB 147.0 g/l and platelet 223×10^9/l. Electrolytes were within the normal range: sodium 145 mmol/l, chlorine 103 mmol/l and potassium 5.2 mmol/l.

Lumbar puncture showed that intracranial pressure was slightly increased (185 mmH_2O) and cerebral spinal fluid was stained with blood, with protein 0.39 g/l, sugar 2.7 mmol/l, chloride 129 mmol/l, WBC 0/l and a moderate

increase of the total cell count ($12{,}400 \times 10^6$/l). EEG mainly showed diffuse low-amplitude theta waves and rare alpha wave in all brain regions. Axial diffusion-weighted cranial magnetic resonance scans displayed hyperintensity (arrowheads) in both middle thalami (A), mammillary bodies (B) and periaqueductal grey (C) (Fig. 1), which were consistent with Wernicke's encephalopathy.

Hypotension (90/60 mmHg) remained unchanged despite appropriate fluid replacement soon after admission. However, hypotension (90/60 mmHg) and the mental status of the patient did not improve significantly. The patient developed a fever (39°C) and fell into coma on Day 2 of hospitalization, when the lowest BP was 70/58 mmHg, HR was 130 beats/min and SaO_2 was 88%. Chest X-ray and blood routine (WBC 15.5×10^9/l and GRAN 68.8%) showed the evidence of pulmonary infection. Dopamine, hydrocortisone and epinephrine were administered urgently, in addition to antibiotics (ceftazidime and levofloxacin). With undisrupted use of sufficient dopamine, BP was maintained at 85–95/50–60 mmHg. On Day 3 of hospitalization, the patient received 100 mg intravenous thiamine per day for 2 weeks and then he was placed on oral thiamine tablet (100 mg daily).

Bp remained unstable and it needed to use vasopressors for more than 1 week. Severe pulmonary infection was brought under control 1 month after hospitalization. Ophthalmoplegia was entirely relieved on Day 7 of hospitalization, while mild vertical nystagmus still existed 1 month after admission. Confusion was relieved on Day 10 of hospitalization, and the patient was cooperative in physical examination. On Day 20 of hospitalization, cranial MRI (Fig. 2) showed left thalamic haemorrhage, and abnormal signals around the periaqueduct and in the mammillary body disappeared. A persistent deficiency of memory was noted for 3 months after admission.

DISCUSSION

In our patient, the ocular muscle palsy was attributable to impairment to the third nerve nuclei, and the nystagmus was attributable to impairment to the vestibular region. The amnesic psychosis remained prominent 3 months after his admission likely due to severe lesions of the bilateral thalami. It is known that lesions responsible for memory loss are those of the thalami, predominantly of the medial dorsal nuclei (and their connections with the temporal lobes and amygdaloid nuclei). Fewer than 20% patients recovered (Victor and Ropper, 2001).

The condition of hypotension lasted about 1 week in our patient despite appropriate fluid replacement soon after admission. Severe hypothalamic lesions and/or a coexistent cardiovascular beriberi may account for it. In addition, small postoperative food intake and severe lung infection after the disease onset were also partly responsible. On Day 10 after surgery, the patient was conscious, could intake semi-liquid nutrition and walked by himself, and then was discharged. There were no signs of peritoneal irritation and abdominal bleeding on Day 18 after surgery when he was readmitted. Therefore, there were no available evidence supporting that hypotension was a direct result of surgery. The patient developed significant hypotension and confusion on the first day of admission (routine blood test and temperature were normal) while infection signs (fever and leukocytes) occurred on the second day of admission, suggesting that the hypotension was not the result of infection-induced

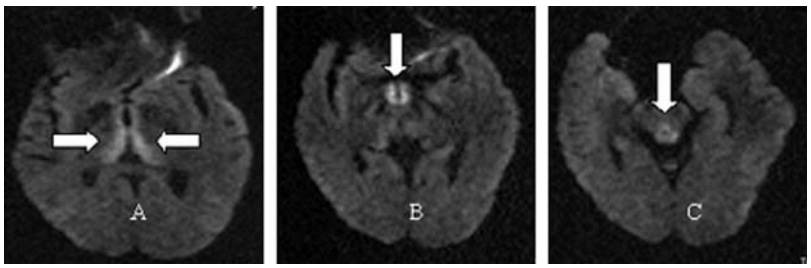

Fig. 1. Axial diffusion-weighted cranial magnetic resonance scan displays hyperintensity (arrowheads) in both middle thalami (**A**), mammillary body (**B**) and periaqueductal grey (**C**) (on Day 3 of hospitalization).

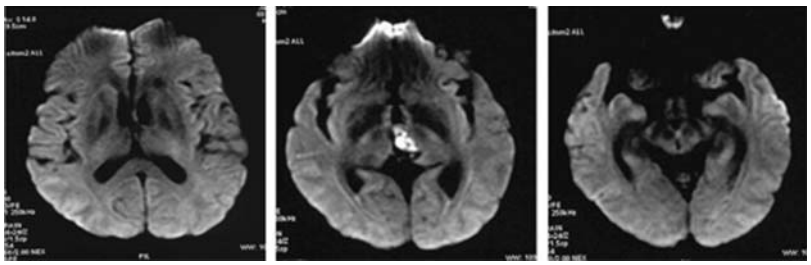

Fig. 2. Flair axial MR imaging demonstrates left thalamic haemorrhage and abnormal signals around the periaqueduct and in the mammillary body disappears (on Day 20 of hospitalization).

endotoxic shock. On the other hand, the emergence of septic shock often takes some time.

In the light of neurological symptoms and signs as well as laboratory examination, differential diagnoses included central pontine myelinolysis, Miller-Fisher's syndrome and basilar artery syndrome.

Central pontine myelinolysis is usually found in alcoholics but also in non-alcoholics with liver disease, malnutrition, cancer, congestive heart failure and adrenal insufficiency. One of the common causes is rapid correction of hyponatremia. The patient usually develops weakness in the extremities, dysphagia, dysarthria, diplopia and confusion (Charness, 1993; Truedsson *et al.,* 2002). Although our patient had a history of cancer and some of these symptoms, this diagnosis could be excluded by the normal plasma sodium concentration (145 mmol/l, normal range 135–148 mmol/l).

Miller-Fisher's syndrome is considered as a variant of Guillain-Barre's syndrome, characterized by ophthalmoplegia, areflexia and ataxia (Fisher, 1956). Weakness and sensory disturbances of the limbs may also occur. The syndrome is associated with upper respiratory tract infection and its incidence appears to be highest in Asia. The nosological position of the symptoms is not clear, and the peripheral and central nervous system are both involved (Truedsson *et al.*, 2002). The prognosis is usually good, and a symptoms-free full recovery is expected in 6 months (Fisher, 1956). Our patient had no infection history. In addition, the mental status, MRI findings and partial recovery after treatment with thiamine ruled out this diagnosis.

Basilar artery syndrome due to basilar thrombosis usually affects the dorsal portion (tegmentum) of the pons, leading to unilateral or bilateral abducens (VI) nerve palsy and impairment of horizontal eye movements. Vertical nystagmus may be present while coma, hemiplegia or quadriplegia is common. Our patient had no motor deficits and extensor plantar response. Cranial MRI showed that the tegmentum of pons was not involved, thus excluding this diagnosis.

Ataxia, ophthalmoplegia and mental confusion are characteristic signs of Wernicke's encephalopathy. Hypothalamic involvement may lead to hypothermia and hypotension. Mild anisocoria and sluggish reaction to light are occasionally seen. The clinical triad of ophthalmoplegia, ataxia and global confusional state, although pathognomonic for Wernicke's encephalopathy is found in 16% affected patients. Additionally, 19% patients did not present any symptoms of the classic triad of Wernicke's encephalopathy (Torvik *et al.*, 1982; Harper *et al.*, 1986), although usually one or more symptoms may appear later in the course of the disease (Sechi *et al.*, 1996; Vasconcelos *et al.,* 1999).

To our knowledge, this is the first documented case of refractory hypotension as a definite sign of Wernicke's encephalopathy at presentation. Postural hypotension and tachycardia are uncommon symptoms or signs at presentation (Sechi and Serra, 2007), probably due to impaired function of the autonomic nerve system, or more specifically to a defect in the sympathetic outflow (Victor and Ropper, 2001). As we know, the three-neuron sympathetic pathway projects from the hypothalamus. There may be mild hypothermia due to hypothalamic involvement.

Patients who die in the acute stages of Wernicke's encephalopathy often show symmetrical lesions in the paraventricular regions of the thalamus and hypothalamus, mammillary bodies, periaqueductal region of the midbrain, floor of the fourth ventricle and superior cerebellar vermis. The lesions are usually found in the mammillary bodies and infrequent in other areas. Microscopic changes are characterized by varying degrees of necrosis of the parenchymal structures. Discrete haemorrhage is found only in 20% cases, and many of them appear to be agonal in nature (Victor and Ropper, 2001). The condition of our patient had been severe since admission and complicated upper gastrointestinal haemorrhage later.

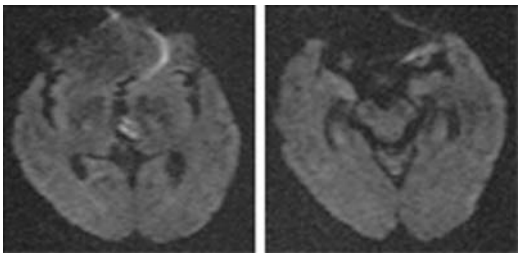

Fig. 3. Axial diffusion-weighted cranial magnetic resonance scan demonstrates that left thalamic haemorrhage is being absorbed and abnormal signals around the periaqueduct and in the mammillary body disappears (on Day 60 of hospitalization).

MRI mammillary body lesions in Wernicke's encephalopathy have also been described in the literature. In our patient, MRI images not only clearly showed the lesions of the mammillary body but completely recorded its dynamic evolution (Fig. 3), which, in our opinion, is very valuable.

In summary, we report a patient who developed refractory hypotension as sign of Wernicke's encephalopathy at presentation. A deficiency of memory remained prominent despite treatment with thiamine for 3 months. Hypotension is an uncommon sign of Wernicke's encephalopathy and severe lesions of the bilateral thalami may have accounted for it. This is a rare finding in Wernicke's encephalopathy, indicating that the susceptibility of different human brain regions to thiamine deficiency varies from individual to individual, causing different symptoms and signs.

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