Acute Wernicke's encephalopathy complicating chronic gallstone ileus

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An autopsy performed on a 53-year-old man who had unrelieved obstruction of the small bowel due to gallstone ileus revealed morphological features that were typical of acute Wernicke's encephalopathy. The likely sequence of disease in this patient was the development of thiamine deficiency owing to the unrelieved intestinal obstruction, which resulted in the development of acute Wernicke's encephalopathy. A high clinical awareness is required for the diagnosis of acute Wernicke's encephalopathy in patients with malnutrition from any cause.

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Introduction

Acute Wernicke's encephalopathy (WE) is a neurological disease that is caused by thiamine deficiency. It is historically associated with chronic alcoholism but also occurs due to other causes of malnutrition. The occurrence of acute WE due to gallstone ileus, as described in this case report, has not been documented in the *Medline* literature database between 1966 and the end of 1997.

Case report

A 53-year-old male retired textile worker who had an unremarkable past history was admitted to the surgical department at the Caritas Medical Centre on 26 August 1993, following a slip and fall. The patient was a chronic smoker; it was noted that he was also a social drinker, but no further details about this were documented. Physical examination showed a smell of alcohol in the patient's breath, a minor abrasion on his forehead and cheek, sinus tachycardia of 130 beats per minute, and blood pressure of 110/60 mm Hg. There were no stigmata indicating chronic liver disease. The skull and chest X-rays were normal. The patient was placed under neurological observation during which he developed yellowish faeculent vomitus; his blood pressure was 90/60 mm Hg 1 hour later. Further enquiry revealed that he had taken a herbal medicine for abdominal discomfort and that he had had constipation for the past 2 days. He was given nasogastric suction. Intravenous fluid was administered and oral intake of food and fluid was not permitted.

Subsequent investigations showed impaired renal function (serum urea 36.5 mmol/L [normal range, 4.2-7.5 mmol/L], serum creatinine 410 μmol/L [normal range, 50-110 μmol/L], sodium 135 mmol/L [normal range, 135-155 mmol/L], potassium 3.5 mmol/L [normal range, 3.5-5.5 mmol/L]), leucocytosis with neutrophilia (white cell count 17.9×10^9 /L), and metabolic alkalosis. The liver function test gave normal results, except for a low serum albumin level (30 g/L [normal range, 35-55 g/L]). During the next 12 hours, the patient's condition deteriorated: he became feverish, had basal chest crepitations, needed copious nasogastric aspiration, was in shock (blood pressure 70/50 mm Hg, pulse rate 90 beats per minute), and had oliguria. Septicaemic shock was diagnosed. He was given copious fluid, potassium replacement, and intravenous antibiotics (penicillin G and cefoperazone), and his central venous pressure was closely monitored. His condition improved over the next few days; there was diuresis, normalisation of blood pressure, pulse and temperature, and an improvement of renal function (urea 7.0 μmol/L, creatinine 79 μmol/L). The liver function test showed slight impairment of liver function (serum total bilirubin 37 μmol/L [normal range, 3-21 μmol/L], serum total protein 57 g/L [normal range,

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65-78 g/L], albumin 29 g/L; normal transaminase and alkaline phosphatase levels). Blood cultures were negative.

A diagnosis of intestinal obstruction was suspected and an X-ray of the abdomen showed fluid levels in the dilated loops of the small bowel. Ultrasonography did not show the presence of any gallstones. Barium meal and follow-through showed leakage of contrast medium in the second part of duodenum, with reflux of contrast medium into the biliary tree and a grossly dilated upper small bowel. Gallstone ileus was diagnosed; however, the patient refused surgery and discharged himself against medical advice 2 weeks after admission.

The patient was readmitted 3 weeks later in a very poor state. His mental state was dull, and he was pyrexic, markedly dehydrated, hypotensive (blood pressure 70/30 mm Hg) and had a pulse rate of 130 beats per min. The abdomen was not distended but showed tenderness. X-ray examination showed barium in dilated loops of the small bowel, retained from the barium meal examination of the previous admission. He was again treated with intravenous fluid and antibiotics, and oral intake was not permitted. Tests showed hypernatraemia (sodium 161 mmol/L), hypokalaemia (potassium 3.1 mmol/L), raised urea (14.6 mmol/L) and pancytopenia (haemoglobin 106 g/L [normal range, 135-180 g/L], white cell count 3.4 x 10^9/L, platelet count 23x10^9/L). On the third day after readmission, the patient's condition suddenly deteriorated, with rapid progression into coma, bradycardia, generalised hypotonia, and bilateral pinpoint pupils. Pontine haemorrhage was suspected. He was resuscitated, intubated, and placed on assisted ventilation. He died on the fifth day after readmission—about 6 weeks from initial presentation.

Post-mortem examination showed that the gall bladder was contracted; there was a choledochoduodenal fistula of approximately 1.5 cm in diameter. The proximal small bowel was markedly dilated (up to 7 cm in diameter) and contained brownish fluid. A large gallstone (6.5x3.5x3 cm) and two smaller ones (each 1.5 cm across) were impacted in the middle part of the small bowel and caused complete obstruction. The distal small bowel and large bowel were collapsed. Both lungs showed features of aspiration pneumonia. The liver showed mild macrovesicular fatty changes.

The brain was normal in weight and external appearance. Standard sectioning showed multifocal areas of petechial haemorrhage which involved the mammillary bodies (Fig 1), and the periventricular region of the third ventricle and the floor of the fourth ventricle. Other parts of the brain were unremarkable. Microscopy of the haemorrhagic areas showed very prominent capillaries that contained swollen endothelial cells; perivascular haemorrhage and spongiosis were also noted (Fig 2). There was a focal prominence of astrocytes around the lesion but the neurons were largely well preserved. There were no features of ischaemic infarction. The combination of the topographical distribution and the histology of the lesions was characteristic of WE in the acute stage. Other organs were normal. The cause of death was thus gallstone ileus which was complicated by aspiration pneumonia and acute WE.

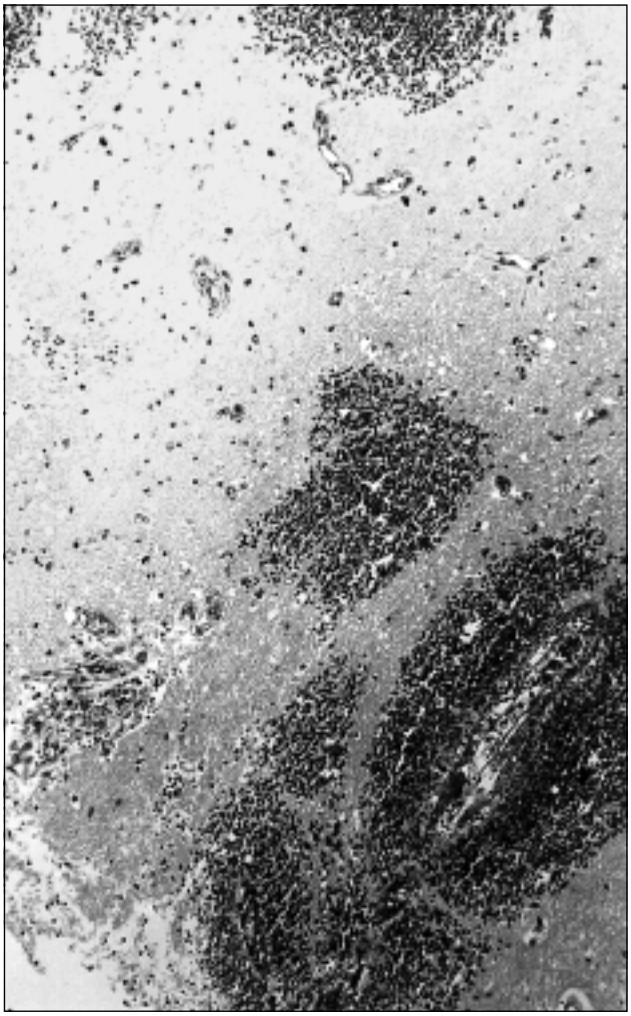

Fig 1. Photomicrograph of one of the mammillary bodies showing haemorrhage and prominent vessels (H&E, x100)

Discussion

Wernicke's encephalopathy consists of the clinical triad of apathy, ataxia, and ocular abnormalities. It usually develops in chronic alcoholics and is due to thiamine (Vitamin B_1) deficiency. Thiamine pyrophosphate is an essential cofactor for a number of enzyme systems

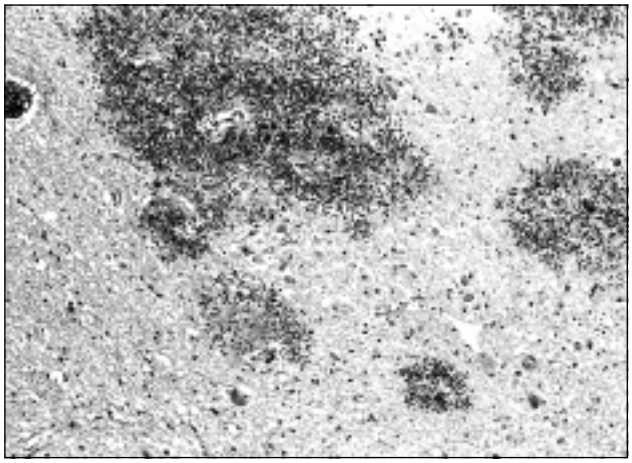

Fig 2. Photomicrograph of the medulla oblongata beneath the floor of the fourth ventricle showing prominent vessels with perivascular haemorrhage (H&E, x100)
Note the presence of well-preserved neurons

that cleave carbon-carbon bonds and is synthesised by a variety of plants and micro-organisms but not by animals. The capacity for human intestinal absorption of thiamine is about 5 mg/d.[1] Approximately 25 to 30 mg of thiamine are stored in the body and the recommended daily allowance is 1.0 to 1.5 mg. Thiamine requirement is increased by a raised carbohydrate intake and by pregnancy, lactation, thyrotoxicosis, and fever.

From experimental studies, biochemical evidence of thiamine deficiency and neuromuscular symptoms start to appear about 1 week after instituting a thiamine-deficient diet.[1] In developing countries, thiamine deficiency may occur following the consumption of milled rice, or food containing thiaminase or other antithiamine factors. In developed countries, thiamine deficiency occurs mainly in chronic alcoholism but also in a wide variety of conditions that are associated with sustained poor feeding or malabsorption. These conditions include food faddism, uraemia, chronic dialysis, neoplasms of the gastrointestinal tract,[2] prolonged intravenous therapy,[3] gastric plication as treatment for obesity,[4] malabsorption, hyperemesis gravidarum, and chemotherapy for malignancy. The two major clinical manifestations of thiamine deficiency involve the cardiovascular system (wet beriberi) or the nervous system (beriberi neuropathy and Wernicke-Korsakoff syndrome). Usually, both systems are involved. In some patients, purely cardiovascular, neuropathic, or cerebral diseases occur; the disease type may be related to the duration and severity of the deficiency, the degree of physical exertion, and the caloric intake.[1]

The neuropathological findings of WE are characteristic and allow autopsy diagnosis even in the absence of a clinical diagnosis. Autopsy diagnosis is based on a combination of the topographical distribution and histology of the brain lesions.[5] The mammillary bodies are invariably affected. Other affected areas are more variable and may include the hypothalamus, periventricular region of the thalamus and third ventricle, grey matter of the upper brain stem, and the floor of the fourth ventricle. In the acute phase, there is a marked prominence of capillaries that contain swollen endothelial cells, perivascular haemorrhage, necrosis, spongiosis, and relative sparing of neurons. In the chronic phase, there is a loss of brain tissue, spongiosis, astrocytosis, and minor neuronal loss. Ng[6] reported a characteristic pattern of hypotensive symmetrical haemorrhagic necrosis of the basal ganglia and brain stem in patients with intractable hypotension. In the present case, there was sustained hypotension before death. The distribution of haemorrhage in the floor of the fourth ventricle overlapped with the pattern described by Ng. Two distinctive pathological features, however, differentiate the present case of acute WE from Ng's series. The first is the characteristic involvement of mammillary bodies in acute WE which is absent in Ng's series. The second is the histopathological change of vascular prominence and preservation of neurons in acute WE (Fig 2) which contrasts with the ischaemic necrosis affecting the brain substance and neurons in Ng's series.

In a series of autopsies, neuropathological evidence of WE was encountered in 0.8% to 2.8%.[5] Harper[7] reported a large autopsy series from Australia; 131 cases of WE were diagnosed from 4677 adult brains, giving an overall frequency of 2.8%. Seventy-five percent of the subjects were male and the peak age of incidence was in the fifth decade. Ninety percent of the cases were associated with alcoholism. The most common findings (66%) were shrinkage and brown discoloration of the mammillary bodies which are indicative of chronic WE. The acute lesion, as characterised by mammillary body and periventricular haemorrhage (as in the present case), was present in 17% of cases. The remaining 17% were classified as a combination of both acute and chronic lesions. On review, a clinical diagnosis of Korsakoff's psychosis or WE was noted in only 20%. This discrepancy may be due to a subclinical encephalopathy in the chronic cases. Of the 97 cases with detailed clinical information, only 16.5% showed the classical triad (eye signs, ataxia, and mental signs) whereas 27.8% and 37.1% showed two signs and one sign, respectively.[8] The remaining 18.6% showed no signs. The authors suggested that the classical triad for diagnosis should be relaxed. In the present case, mental and eye

signs were probably present, whereas ataxia was not documented.

The present case illustrates the need for a high clinical awareness of WE as a complication of malnutrition due to any cause. In this patient, a detailed history on alcohol intake was not documented. His admission following a slip and fall, and the detection of alcohol in his breath indicated that he probably had significant alcoholism. This might have been an underlying predisposing factor, because his bodily reserve of thiamine may have been subnormal. There is no doubt, however, that the persistent and complete small bowel obstruction was the cause of acute thiamine deficiency.

Clinicians should be aware that the clinical triad of eye signs, ataxia, and mental signs occur in only a minority of patients. Various biochemical tests to detect thiamine deficiency have been used.[1] These include detecting the thiamine level in the blood or red blood cells, testing urinary thiamine excretion, and assaying for red blood cell transketolase activity. These tests are unavailable in most hospitals in Hong Kong, however. In suspected acute cases, computed tomography or magnetic resonance imaging of the brain may provide diagnostic clues because the pattern of involvement is characteristic. Brain stem auditory-evoked potentials have also been reported as a sensitive indicator for the early diagnosis of WE, and can differentiate it from uncomplicated delirium tremens.[9]

The relatively small bodily reserve of thiamine indicates that WE could affect patients in a relatively short time. In the present report, the patient had acute WE approximately 6 weeks after unrelieved small intestinal obstruction. This is in keeping with the reported time lag of 4 to 8 weeks from the onset of a thiamine-deficient diet to symptomatic presentation of WE.[10-12] Prophylactic parenteral thiamine is therefore suggested for the high-risk patient group. Fortification of alcoholic beverages with thiamine has even been proposed as a method to decrease the cost of medical care for chronic alcoholics with Wernicke-Korsakoff syndrome.[13]

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