Wernicke's encephalopathy in a patient with hyperemesis gravidarum and thyrotoxicosis

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Wernicke's encephalopathy is known to be associated with chronic alcoholism. However, it may not be easily recognised in other conditions such as starvation, anorexia nervosa, malabsorption or hyperemesis gravidarum. Although Europeans have been reported to be more prone to Wernicke's encephalopathy, Asians can develop similar problems especially when they have multiple risk factors. We report a young Indo-Asian woman with Wernicke's encephalopathy complicating hyperemesis gravidarum and thyrotoxicosis, and the possible mechanism by which both conditions led to encephalopathy is discussed.

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Key words: Wernicke's encephalopathy; Hyperemesis gravidarum; Thyrotoxicosis; Thiamine deficiency

Introduction

In 1881, Carl Wernicke described an acute-onset illness characterised by paralysis of eye movements, ataxia of gait, and mental confusion. Swelling of the optic discs and retinal haemorrhages were also said to be present. His observations were made on three patients, of whom two were alcoholics and one was a young woman with persistent vomiting following the ingestion of sulphuric acid.[1]

Wernicke's encephalopathy has been well described in the literature in patients with chronic alcoholism and malnutrition. Its association with hyperemesis gravidarum has been reported since 1939.[2,3] A few cases have been recorded with co-existing central pontine myelinolysis.[4,5] We describe here what we believe to be the first known case associated with probable thyrotoxicosis in Hong Kong.

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Case report

A 23-year-old primigravida Indo-Asian woman with a 12-week pregnancy presented to us with sudden onset of diplopia of 1 day's duration. She was admitted to hospital in the 8th week of her gestation because of excessive vomiting associated with the pregnancy. Over the next 4 weeks she could not tolerate any oral intake, lost 6 kg in body weight, and was given intravenous dextrose solution solely for fluid replacement.

Her diplopia was mainly horizontal and more obvious when looking sideways. She had no other complaint except for some bouts of palpitation and a family history of thyrotoxicosis. She had a normal diet and was a non-drinker. On physical examination, she was observed to be thin, with moist and sweaty palms. There was no obvious goitre. She had impaired abduction of both eyes with a horizontal nystagmus, especially when looking to the left. Fundoscopy revealed two small patches of haemorrhage over her right fundus. She had no pyramidal or cerebellar signs; reflexes were normal. Initial differential diagnoses included multiple sclerosis, cerebral lupus, and brainstem encephalitis.

Investigations that included blood tests for complete blood profile, renal and liver function tests, antinuclear factor and anti-DNA antibodies, glucose, mag-

nesium, calcium, and phosphate levels were all normal. Thyroid function tests confirmed that she has thyrotoxicosis (free thyroxine, 38.9 pmol/L [normal range, 10.0 - 36.0 pmol/L], thyroid stimulating hormone, 0.08 mU/L ([normal range, 2.0 - 11.0 mU/L]). Results of other investigations including a magnetic resonance image of the brain, electroencephalogram, and nerve conduction tests were all normal. Lumbar puncture was performed and the cerebrospinal fluid was normal.

She was diagnosed as having hyperemesis gravidarum with thyrotoxicosis and was given propylthiouracil 100 mg, three times daily. Two days after the onset of diplopia, it was observed that she had truncal ataxia when walking. A clinical diagnosis of Wernicke's encephalopathy was made. She was given thiamine 100 mg, intramuscularly, daily. Her condition then improved dramatically; within 1 day the sixth nerve palsies disappeared, and within 3 days the nystagmus subsided. Finally, her vomiting stopped, and the ataxia resolved after approximately 2 weeks.

A subsequent red blood cell transketolase result using a Beckmann DU. 7500 spectrophotometer (Fullerton, Ca, US) was 4.6 (normal range, 4.5 - 9.0 mmol/L) and the thiamine pyrophosphate (TPP) effect was 32% (normal range, 4 - 40%). She was discharged 2 weeks later on oral thiamine, 10 mg daily. At follow up, 4 weeks later, she had completely recovered from her neurological disability and was gaining weight. Results of her thyroid function tests also returned to normal.

Discussion

A diagnosis of Wernicke's encephalopathy can be readily made on ocular abnormalities which are present in nearly all cases. These abnormalities are (in decreasing order of frequency): nystagmus, lateral rectus palsy, and paralysis of conjugate gaze. Horizontal nystagmus is more common, although 50% of cases also show some vertical nystagmus. Lateral rectus palsy is always bilateral but may not be symmetrical. Ptosis and small retinal haemorrhage may occur but other features of the third and fourth nerve palsies are absent. Papilloedema was not seen in the 232 cases Victor reports.[1] Ataxia of gait affects the vast majority of patients and may be sufficiently severe to prevent normal walking. Ten per cent of patients with Wernicke's encephalopathy have no disturbance of mental state but memory and cognitive deficits would no doubt be detected in a large proportion, if formal neuropsychological evaluations were undertaken. Approximately one-third have symptoms of polyneuropathy at presentation but signs may be detected in more than 80%.

Our patient showed all the clinical features of bilateral lateral rectus palsies, horizontal nystagmus, ataxia of gait, and small retinal haemorrhages which are typical of Wernicke's encephalopathy. Although memory loss and symptoms and signs of polyneuropathy were absent, the laboratory findings supported the diagnosis. The setting of hyperemesis gravidarum complicated by prolonged intravenous dextrose infusion without multivitamin supplementation should hint at such a diagnosis. Our case responded well to thiamine injections, and her ophthalmoplegia disappeared within 1 day. The retinal haemorrhages resolved, and her ataxia was markedly improved a few days later.

Wernicke's encephalopathy is due to a deficiency of thiamine which acts as a coenzyme in various stages of carbohydrate metabolism. Transketolase, one of the enzymes of the hexose monophosphate shunt, requires TPP as a coenzyme. A fall in the activity of transketolase is one of the earliest changes in thiamine deficiency. On the other hand, transketolase activity can be enhanced by the addition of exogenous thiamine pyrophosphate (TPP effect). If the activity of the enzyme is increased more than 15% by the added thiamine diphosphate, a deficiency state is probably present.

The propensity of Europeans for developing Wernicke's encephalopathy compared with non-Europeans consuming a similar thiamine-deficient diet may be explained by the difference in binding affinity between transketolase and TPP found in different racial groups.[6] Apart from genetic predisposition, an environmental challenge (i.e. thiamine deficiency) is necessary for development of the disease. As thiamine is not stored in the body to any degree, the deficiency in this patient could have been due to increased thiamine depletion because of the pregnancy and dextrose infusion as well as inadequate replacement because of the excessive vomiting.[7]

A transient hyperthyroid status occurs occasionally in normal early pregnancy. Human chorionic gonadotropin (hCG), which increases to a maximum level in early pregnancy, has been suggested to be the thyrotrophic factor during early pregnancy, although discrepant results have been obtained.[8] Interestingly, a high hCG concentration has also been suggested to have a causal relationship with hyperemesis gravidarum.[9]

Whether thyrotoxicosis contributes to the development of thiamine deficiency is as yet undefined. The accelerated metabolic rate in thyrotoxicosis was previously thought to be the possible mechanism. However, a study that compared the erythrocyte transketolase activities of thyrotoxic patients with those of normal subjects showed that decreased transketolase activity was not accompanied by an elevated TPP effect in the former group.[10] Therefore, further studies are required to clarify the relationship of hyperthyroidism to thiamine metabolism in humans.

In conclusion, any pregnant woman who develops severe and prolonged hyperemesis gravidarum with a concomitant calorie loss should receive thiamine supplements. If ophthalmoplegia, ataxia, or confusion develops, parenteral thiamine (at least 50 mg daily) should be given. Blood should be taken for biochemical evaluations but the administration of thiamine must not be delayed.

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