WERNICKE’S ENCEPHALOPHY ASSOCIATED WITH HYPEREMESIS GRAVIDARUM – A CASE REPORT

Wahinuddin Sulaiman, Azerin Othman, Monniaty Mohamad, Hj. Rosemi Salleh, Lily Mushahar

Department of Medicine, Hospital Kota Bharu, 15586 Kota Bharu, Kelantan, Malaysia.

Two cases of Wernicke’s encephalopathy due to hyperemesis gravidarum are described. The first patient presented with bilateral papilloedema, altered sensorium and the second with bilateral retinal haemorrhages, ophthalmoplegia and nystagmus. Both patients were diagnosed with Wernicke’s encephalopathy on clinical ground since there were no laboratory facilities to measure red cell transketolase and thiamine pyrophosphate levels. This is a rare but treatable complication of hyperemesis gravidarum (HG) and due to lack of diagnostic tools, there is often diagnostic uncertainty, delay in commencing appropriate treatment, as well as irreversible damage to the upper brain stem and death.

Key words: Wernicke’s encephalopathy, hyperemesis gravidarum

Introduction

Wernicke’s encephalopathy is usually associated with chronic alcoholism(1). Hyperemesis gravidarum is one of many other causes of Wernicke’s encephalopathy in clinical practice (2,3). Other causes include undernutrition, starvation, anorexia, intravenous feeding (2,3), and chemotherapy. It may be precipitated by glucose administration to patients especially those with thiamine deficiency.

We report 2 cases of severe Wernicke’s encephalopathy where the presence of papilloedema resulted in the delay in diagnosis and unfortunately death in the first case, and severe coagulopathy with respiratory failure requiring ventilatory support in the second.

Case report

Case 1

A 42-year old housewife presented in the 16th week of her fifth pregnancy. Her previous pregnancies were uneventful. She denied history of alcohol consumption. She was treated as hyperemesis gravidarum because she had been vomiting for 8 weeks continuously despite various antiemetics. At 16 weeks of gestation she became drowsy and unresponsive to call with impaired hearing and vision. Further history obtained revealed that she also had unsteadiness of gait few days prior to admission.

On admission, she was drowsy and unable to obey simple commands. There was intermittent right facial muscle twitching. However, she moved all four limbs on pain stimuli. She had a diffuse goitre but was clinically euthyroid. There was neither meningism nor cerebellar signs. The reflexes were normal with negative Babinski response. Fundoscopy showed bilateral papilloedema with multiple haemorrhagic spots. Her blood pressure was 170/100 mmHg.

Based on the clinical findings, she was diagnosed as having encephalitis with a differential diagnosis of cerebral sagittal sinus thrombosis. Computer tomographic (CCT) scan of the brain was normal. Magnetic Resonance Imaging (MRI) was deferred in view of patient’s clinical instability.
Echocardiography showed no clot in the cardiac chambers, and no structural or functional abnormality. She had a deranged coagulation profile suggestive of early disseminated intravascular coagulopathy. Other laboratory investigations (collagen screening, blood counts, septic screening, viral serology) were unremarkable. Lumbar puncture was suggested but refused by the patient's family.

She was ventilated and a diagnosis of Wernicke’s encephalopathy was made by clinical and laboratory exclusion of other possible differential diagnoses and was given intravenous thiamine. Unfortunately, she could not be weaned off ventilatory support and despite high dose thiamine and other supportive measures, she succumbed to the illness and died 4 days after admission.

Case 2.

A 25-year old gravida two Malay lady, who was twelve weeks pregnant was admitted to Hospital Kota Bharu following a week’s history of giddiness and unsteady gait with blurring of vision. She was hospitalised earlier at a district hospital for hyperemesis gravidarum at eight weeks of gestation for a month. She was given antiemetics but no vitamins. She was otherwise premorbidly well and healthy.

Throughout her hospitalisation at the district hospital, she was given intravenous dextrose and saline. On admission she was noted to have slow mentation, but able to follow commands, afebrile, with stable vital signs. Nystagmus was present in both vertical and horizontal direction but the range of eye movement were full. The pupils were reactive. There was flame shape haemorrhages in both fundi but no papilloedema. She moved all limbs spontaneously but was unable to cooperate to test the gait. Sensation was intact and cerebellar signs absent. Clinically she had no goitre.

A clinical diagnosis of Wernicke’s encephalopathy was made after excluding other possibilities such as systemic lupus erythematosus, by laboratory investigations (serum C₁ and C₄, and antinuclear antibody). However, she had a prolonged International Normalised Ratio (INR) and raised free T4 (59.16 nmol/L), free T3 (6.98 nmol/L) with a low serum TSH levels (< 0.03 mU/L), which suggested thyrotoxicosis. CT scan of the brain was normal. She was treated with high dose intravenous thiamine 300 mg daily, propylthiouracil and methylprednisolone. She had a spontaneous abortion a week after admission. Following the administration of thiamine, she made a great improvement in her neurological function within a month in the ward. Her mentation and memory gradually improved. She was allowed to go home with close supervision by her family members. She was advised to continue the oral thiamine until she regained her normal function. During her assessment in the outpatient clinic at 8 weeks after discharge, she managed to resume her daily activities although still not ambulating well due to residual weakness of both lower limbs and she was clinically and biochemically euthyroid.

**Discussion**

Wernicke’s encephalopathy (WE) was first described by Carl Wernicke in 1881 as a classical triad of acute mental confusion, ataxia and ophthalmoplegia and was first reported in 1914 as a complication of hyperemesis gravidarum and subsequently increasing number of cases have been reported (4 - 12). Wernicke’s encephalopathy is a consequence of thiamine (vitamin B1) deficiency which is essential for carbohydrate metabolism and can be fatal if not treated. It was previously believed that WE is commonly associated with alcoholism (1). Nevertheless, it also should be considered in patients with anorexia nervosa (13), prolonged vomiting associated with chemotherapy, elderly patients living alone, gastrointestinal disease, peritoneal dialysis and haemodialysis (14) and human immunodeficiency virus infection. It can be precipitated in the hospital by glucose administration to patients with thiamine deficiency.

Due to its rarity, especially among the Malay race of Muslim religion in this part of the country where alcohol is forbidden, Wernicke’s encephalopathy may not carry a high index of suspicion. Wernicke’s encephalopathy is still an uncommon complication of hyperemesis gravidarum, which is fairly common.

We believe that both our patients with a background history of severe and prolonged hyperemesis gravidarum eventually developed Wernicke’s encephalopathy.

Diagnostic uncertainty led to the delay in appropriate treatment to our first patient who eventually succumbed and died. Although the presentation may not be so obvious and the classical triad of Wernicke’s encephalopathy was not present, the combination of hyperemesis gravidarum and
neurological manifestations i.e. visual blurring and unsteadiness of gait, papilloedema with retinal haemorrhages prompted us to make the diagnosis of Wernicke’s encephalopathy, albeit too late.

However, Wernicke’s encephalopathy was well illustrated in the second patient. The immediate replacement with high dose parenteral thiamine and other supportive measures, including ventilatory support, gradually improved her symptoms.

Papilloedema has not been described as an associated physical sign in a large retrospective study (15) and it is a rare finding as reported in previous analyses (4). Retinal haemorrhages, however, has been found to be a more frequent manifestation (16) of Wernicke’s encephalopathy. The pathophysiology of papilloedema in Wernicke’s encephalopathy is still unclear. As in our cases, both had retinal haemorrhages and the first patient had papilloedema, for which there was no evidence to suggest increased intracranial pressure as showed by normal brain CT.

There have been case reports of gestational thyrotoxicosis associated with hyperemesis gravidarum manifesting as Wernicke’s encephalopathy (17,18). As shown in the second patient, thyrotoxicosis was diagnosed based on the biochemical result. The cause of the thyrotoxicosis has previously been identified to be closely associated with human chorionic gonadotropin (hCG). Both the thyrotoxicosis and a catabolic state due to the hyperemesis were thought to induce B1 deficiency, causing Wernicke’s encephalopathy.

Although, in our second case, thyroid storm may not be disputed, the clinical finding was much less milder than those expected for hyperthyroid Graves’ disease. Corticosteroid have shown to have beneficial effect on Wernicke’s encephalopathy (19).

The red cell transketolase and thiamine pyrophosphate activities will help to support the clinical diagnosis of Wernicke’s encephalopathy. However, one should not await the result of this assay if Wernicke’s encephalopathy is highly suspected and thus administration of thiamine should not be delayed. These supportive investigations however, are not available in our laboratory. MRI of the brain should be done when investigating for Wernicke’s encephalopathy as reported in previous analyses (20,21,22). The MRI of the brain will show increased T2 weighted signal intensity in various areas such as the mamillary bodies, paraventricular regions of the thalamus and in periaqueductal regions of the midbrain. However, the MRI findings in our second patient was unremarkable.

Our present cases illustrate the importance of knowing that Wernicke’s encephalopathy may complicate clinical conditions that deplete thiamine and that all patients with prolonged vomiting of any cause including hyperemesis gravidarum with poor nutritional status and impaired conscious level should be treated with high dose parenteral thiamine, whether the classical features of Wernicke’s encephalopathy are present or not. In both cases, the diagnosis can not be 100 % verified as MRI was not available in the first case and other differential diagnosis need to be considered. One should also consider other intracranial pathologies which may cause papilloedema, which is infrequently associated with Wernicke’s encephalopathy, and the administration of thiamine should not be delayed just because of the presence of papilloedema. These two cases illustrates that the diagnosis of Wernicke’s encephalopathy should be high in the list of differential diagnoses in patient with hyperemesis gravidarum presenting with clinical features of upper brainstem signs.

Acknowledgement

I would like convey many thanks to Professor Dr. Eddy Nyunt Win, Consultant Neurologist/Head of Department of Medicine, International Medical University for his tremendous encouragement, advise and editing this report.

Correspondence:

Dr. Wahinuddin Sulaiman
Department of Medicine,
Hospital Taiping,
34000, Taiping,
Perak.

Reference


Myiasis occurs when living tissues of mammals are invaded by eggs or larvae of flies, mainly from the order of Diptera. Most of the previously reported cases are in the tropics and they were usually associated with inadequate personal hygiene, sometimes with poor manual dexterity. This report describes two cases of oral myiasis in cerebral palsy patients in Seremban General Hospital, Malaysia. This article also discusses the therapeutic property of maggots and highlights the importance of oral health care in the special needs patients.

Key words: Oral myiasis, cerebral palsy, case report

CASE REPORTS

Case No.1

A 15 year old Chinese boy with cerebral palsy was seen at the Casualty Department, Seremban General Hospital. He presented with persistent mouth opening and poor oral hygiene. Intraoral examination revealed a 2 cm by 2 cm perforation of the anterior palate, about 2 mm from the gingival margin of the upper right central incisor. The cavity was filled with hundreds of maggots. The first attempt was to flush the cavity with normal saline which proved ineffective. A cotton bud impregnated with turpentine was then placed at the opening of the cavity for 10 to 15 minutes. Dozens of maggots ‘rushed’ out from the cavity. This procedure was performed out twice daily.

By the third day, the oral cavity was free from maggots. However, it was then noted that the maggots started to appear from the patient’s right ear. He was then referred to the Ear, Nose and Throat Department for further management. However, he failed to attend the review clinic.

Case No.2

A 19 year old Indian boy with cerebral palsy was referred to the Specialist Dental Clinic, Seremban General Hospital by a medical officer. This boy presented with a 1 cm x 1 cm perforation of the anterior palate, about 2 mm from the gingival margin of the upper right central incisor. The cavity was filled with hundreds of maggots. The first attempt was to flush the cavity with normal saline which proved ineffective. A cotton bud impregnated with turpentine was then placed at the opening of the cavity for 10 to 15 minutes. Dozens of maggots ‘rushed’ out from the cavity. This procedure was performed out twice daily.

By the third day, the oral cavity was free from maggots. However, it was then noted that the maggots started to appear from the patient’s right ear. He was then referred to the Ear, Nose and Throat Department for further management. However, he failed to attend the review clinic.
of the palate adjacent to the upper left lateral incisor. He too had persistent mouth opening and poor oral hygiene with unpleasant odour. He lives with his elderly grandmother who neglected his oral hygiene. As in the first case, the cavity was filled with maggots. The same method of cleansing was performed. It took two days to get the cavity cleaned and free from the maggots. He was then discharged. He too failed to attend the review appointment.

For both cases, broad spectrum amoxycillin 250 mg three times daily was prescribed as there were signs of infection. Oral hygiene instructions and reinforcement (to the parents and guardians) was carried out extensively. The parents and guardians were given extensive hygiene instruction and reinforcements.

### Discussion

Oral myiasis can either be primary or occasionally, secondary to nasal involvement, especially when the maggots penetrate to the paranasal sinuses or palate (4). Primary oral myiasis commonly affects the anterior part of the mouth particularly the palate (4).

The classification of myiasis is as follows (8):

1) Those in which the larvae live outside the body
2) Those in which the larvae burrow into unbroken skin and develop under it.
3) Those which live in the intestinal or urinary passages.
4) Those in which eggs or young larvae are deposited in the wounds or natural cavities in the body.

These two case reports correlates with the fourth group in the above classification.

It was predicted that the flies were attracted to the bad mouth odour due to neglected oral hygiene or fermenting food debris. Persistent mouth opening facilitates the deposition of the eggs by the adult fly. Conditions which are likely to cause prolonged mouth opening include mouth breathing during sleep, senility, alcoholism, mental retardation and hemiplegia and cerebral palsy (1).

### Entomology

The genera commonly reported are Sarcophagidae and Muscidae from the Diptera order (9). The life cycle of a fly begins with the egg stage followed by the larva, the pupa and finally the adult fly.

Sood et al described that the larva can be divided into three stages depending upon the size and life span (9). During the first and second stage, the larva has segmental hooks which are directed backward. This hooks helps the larva to anchor itself to the surrounding tissue. The presence of these hooks made removal of the larva from its host difficult.
The larval stage lasts from six to eight days in which period they are parasitic to human beings. They are photophobic and therefore tend to hide themselves deep into the tissues and also to secure a suitable niche to develop into pupa.

Sood et al, further mentioned that the larvae release toxins to destroy the host tissue (9). Proteolytic enzymes released by the surrounding bacteria decompose the tissue and the larvae feed on this rotten tissue (8). The infected tissue frequently releases foul smelling discharge. As described in case 1 the interaction of toxin or enzyme released by the larvae-bacteria can also cause bony erosion (8).

**Treatment**

Treatment comprises systemic and local measures. Systemic treatment includes broad-spectrum antibiotics such as ampicillin and amoxycillin especially when the wound is secondarily infected (10).

Topical treatment consists of application of turpentine larvicidal drug like Negasunt (by Bayer) (3), mineral oil, ether, chloroform, ethyl chloride, mercuric chloride, creosote, saline, systemic butazolidine or thiobendazole and removal of the larvae (4,5).

Turpentine is a toxic chemical as it can induce tissue necrosis. When applied topically, it can produce epithelial hyperplasia, hyperkeratosis and ulceration (11,12,13). However, the damage is reversible, the hyperplasia will only persist when the stimulus is continuously applied and regresses once it is withdrawn (11).

**Maggot Debridement Therapy**

Despite frequently being associated with dirty environment, the maggots can be used therapeutically to debride and enhance healing in chronic wounds such as the pressure ulcers and venous stasis ulcers. The maggots clear away the dead and necrotic tissue and at the same time secrete substance such as allantoin, which promotes wound healing (3).

The practice of using maggots to treat bone and soft tissue infections was established especially in North America since the 1930s. The maggots are grown and kept in special, sterile containers prior to being used.

**Oral health care in special needs patients**

Special needs patients include patients with mental and/or physical disability. Most of these patients have difficulties in maintaining good oral hygiene due to poor manual dexterity, parents/guardians are too busy concentrating on the patients’ social or other health aspects, parents or guardians are not aware of the importance of oral hygiene or have difficulty in gaining access to a dental clinic.

A special needs patient should be exposed to the dental intervention as early as possible to promote co-operation and confidence and to prevent disease.

**Acknowledgement:**

The authors would like to thank Professor Malcolm Harris, Head and Consultant, Department of Oral and Maxillofacial Surgery, Eastman Dental Institute, London, for his support and advice.

**Correspondence:**

Miss Roszalina Ramli
Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Universiti Kebangsaan Malaysia, 50300 Jalan Raja Muda Abdul Aziz, Kuala Lumpur, Malaysia.

**Reference**


