THE NORTHERN HOSPITAL

WERNICKE'S ENCEPHALOPATHY

"Harlequin's Carnival" oil on canvas, Joan Miro, 1924-25, Albright-Knox Art Gallery, Buffalo NY, USA.

"I was living on a few dried figs a day. I was too proud to ask my colleagues for help. Hunger was a great source of hallucinations. I would sit for long periods looking at the bare walls of my studio trying to capture these shapes on paper or burlap…Harlequin's Carnival was the product of hallucinations brought on by hunger!"

Joan Miro

The Catalan artist Joan Miro, (1893-1983) was famed for his so-called "automatic surrealist" works. He agonized over his inner subconscious mind, and tried to depict its images in his paintings.

In his own words…

"How did I think up my drawings and my ideas for painting? Well I'd come home to my Paris studio in Rue Blomet at night, I'd go to bed, and sometimes I hadn't any supper. I saw things, and I jotted them down in a notebook. I saw shapes on the ceiling..."

In the 1920s he was living in a bleak Paris apartment, so poor he was often unable even to afford to eat. His hunger on one occasion became so bad, he began to suffer from hallucinations. During this bleak period he produced his greatest and most recognized work, the "Harlequin's Carnival".

"I was living on a few dried figs a day. I was too proud to ask my colleagues for help. Hunger was a great source of hallucinations. I would sit for long periods looking at the bare walls of my studio trying to capture these shapes on paper or burlap…Harlequin's Carnival was the product of hallucinations brought on by hunger!"

In this work he imagined a host of imaginary beings, or "harlequins" partying within his apartment, but really within his own mind, the images seemingly projected onto the bare walls of his stark apartment. In the left of the picture a forlorn, even melancholy moustached figure stares back at him. Perhaps this figure represented himself, a lonely figure among the fantastic surrealist revellers that filled his room. On the right a window opens out to the "real" world, but even this seems to be distorted.

He died bedridden at his home in Palma, Mallorca on Christmas day December 25, 1983. Today his works sell in the world of "high art" for hundreds of thousands of dollars, some for millions of dollars.

Starvation leads to a myriad of nutritional disorders, not now commonly seen in modern Western society. Among these is acute thiamine deficiency that may lead to confusion, even hallucinations. Perhaps it was this condition which led to the creation Miro's masterpiece the "Harlequin's Carnival" in 1924. Uncommon as starvation is, in modern day Australia, some nutritional deficiencies may still nonetheless manifest in the form of medical conditions which are associated with a significant impairment of eating. In modern Western society, this is most commonly seen in the form of chronic alcoholism.

WERNICKE'S ENCEPHALOPATHY

Introduction

Wernicke's encephalopathy is a neurological disorder of acute onset caused by **thiamine (ie vitamin B1)** deficiency.

The condition is characterised by **ocular abnormalities, ataxia** and **confusion or altered conscious state.**

It is most commonly seen in chronic alcoholics.

It represents a **medical emergency**, as the condition is progressive if left untreated and may result in Korsakoff's psychosis. About 25 % of patients with Korsakoff's psychosis do not recover.

Pathophysiology

- The condition results from a deficiency of thiamine, an essential coenzyme in intermediate carbohydrate metabolism, the pentose-phosphate pathway and the Krebs cycle.
- Alcohol interferes with the active GIT transport of thiamine.
- Further, in chronic liver disease, activation of thiamine pyrophosphate from thiamine is decreased, and capacity of the liver to store thiamine is decreased.
- Left untreated Wernicke's encephalopathy progresses to a subacute and then chronic encephalopathy, known as **Korsakoff's psychosis.** This manifests as retrograde amnesia (inability to recall information), anterograde amnesia (inability to assimilate new information) and confabulation.

Causes:

1. Starvation.

   Starvation is rare in Australia.

   Thiamine deficiency may occur in settings of medical conditions leading to poor nutrition with protracted vomiting, including:

   - **Chronic alcohol abuse (by far the commonest cause) in modern Western society.**
   - Hyperemesis gravidarum.
   - Eating disorders (anorexia nervosa, severe fasting).
   - Chronic gastrointestinal disorders.

2. It has been associated with patients on hyperalimentation.

3. Rare genetic transketolase abnormalities.

Clinical Features

Patients present with the "classic triad" of:

1. Confusion/altered conscious state
2. Ataxia
3. Ophthalmoplegia

It is important to note however that only about a third of patients will have the full classic triad.

Ophthalmoplegia

The ocular abnormalities are the hallmarks of Wernicke's encephalopathy.

This may present in a number of ways including most commonly:

- Horizontal nystagmus.
- Paralysis of the lateral rectus muscles (usually bilateral)
- Conjugate (internuclear) gaze palsies.

Altered conscious state

This may manifest in a variety of ways:

- Confusion
- Drowsiness
- Coma may rarely be the sole manifestation of Wernicke's encephalopathy.

Ataxia

The acute ataxia in the early stage of the disease, is a result of vestibular dysfunction.

- The wide based ataxic gait seen in the subacute and chronic phases of the illness results from cerebellar dysfunction, either alone or in combination with vestibular dysfunction.
- In addition to the classic triad of features, hypothermia and hypotension may also occur.

When assessing these patients it is important to look for other manifestations of thiamine deficiency, such as "wet beri-beri" (congestive cardiac failure) and nutritional polyneuropathy.

Investigations

Wernicke's encephalopathy is largely a clinical diagnosis, but MRI findings can also be very suggestive.

Investigations will also be aimed at *excluding other/associated pathology.*

Blood tests

- FBE
- U&Es/glucose
- Magnesium
- LFTs
- Blood alcohol
- Clotting profile.
- Others as clinically indicated.

CXR

- For evidence of infection in particular.

ECG

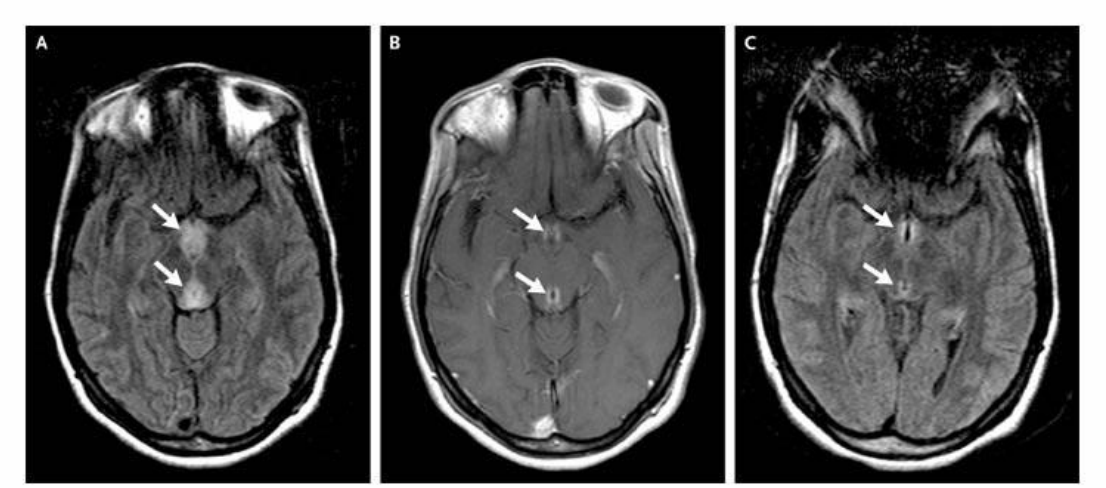
- As for any unwell patient.

CT scan brain

- CT brain as for any patient with confusion or altered conscious state.
- This will not make the diagnosis of Wernicke's, but will be needed as an initial screen to rule out other pathology, such as extra-axial hematomas

MRI

- This is the best investigation for suspected Wernicke's encephalopathy.
- **Lesions of the mamillary bodies on T1 weighted gadolinium enhanced images are very characteristic and considered "pathognomonic" by some authors.**
- Peri-aqueductal and peri-ventricular gray matter lesions may also be seen. These lesions are bilateral and symmetrical.
- Acute lesions seen on MRI are reversible with early treatment.



MRI showing the typical features of Wernicke's encephalopathy with panels A and B showing hyperintensity of the mamillary bodies and peri-aqueductal gray matter. Panel C, one week after treatment, shows almost complete resolution of the MRI changes [2]

Management

1. IV fluids:

    - Correct any dehydration.

2. Sedation:

    - May need sedation with diazepam and/or haloperidol if significantly confused or agitated or for impending delirium tremens.

3. Thiamine:

    Treatment with thiamine is urgent to prevent possible progression to an irreversible Korsakoff's syndrome.

    - **Thiamine 500 mg IV infusion over 30 minutes, 3 times daily for 2 to 3 days** [1]

      Then thiamine 250 mg IV or IM, daily for 3 to 5 days or until clinical improvement ceases. [1]

    - The ocular symptoms may be reversed relatively quickly (within 1-6 hours). Ataxia and confusion may take longer to resolve, days or even months.

    - **Thiamine must be given *prior* to any IV glucose solutions, as carbohydrate loading in the presence of marginal or depleted thiamine stores may worsen or precipitate a Wernicke's encephalopathy. The CHO "drives" the Krebs cycle, thus depleting the last stores of thiamine, which is used in the cycle. *Because of this give thiamine should be given prior to any glucose*** [1]

4. Correct any associated electrolyte disturbances:

   - Hypomagnesaemia (magnesium is a necessary cofactor in thiamine dependant metabolism and should be corrected if the patient is hypomagnesaemic)
   - Hypokalaemia
   - Hypoglycaemia (after thiamine)

Disposition:

- All patients with suspected Wernicke's encephalopathy must be admitted, as it is associated with 10% mortality rate without adequate treatment.

References:

1. Gastrointestinal Therapeutic Guidelines 5th ed 2011.
2. Images in Clinical Medicine, Wernicke's Encephalopathy, NEJM, May 12, 2005
3. Spampinato V, Magnetic Resonance Imaging Findings in Substance Abuse, Top Magn Reson Imaging, vol 16, no (3), June 2005
4. Reuler J B et al Wernicke's Encephalopathy: NEJM vol 312 no 16 April 18 1985

Dr J Hayes

Reviewed March 2013