Wernicke's encephalopathy and central pontine myelinolysis associated with hyperemesis gravidarum

P S Bergin, P Harvey

Thiamine supplementation is urgently required in anybody suffering prolonged vomiting; otherwise carbohydrates—particularly dextrose—may precipitate Wernicke's encephalopathy

When a known alcoholic develops abnormal ocular movements, ataxia, and confusion Wernicke's encephalopathy is usually considered. However, when these signs develop in other circumstances the diagnosis may not be suspected. Wernicke's encephalopathy was recognised as a complication of hyperemesis of pregnancy in 1914.[1] Unfortunately, cases continue to occur.[2-5] We report a case in which the patient was in hospital for six weeks before developing combined Wernicke's encephalopathy and central pontine myelinolysis.

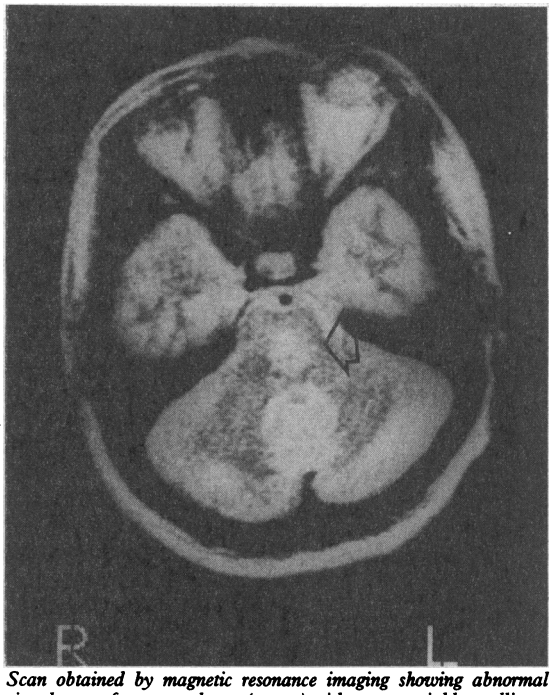
Case report

A 25 year old West Indian woman who was nine weeks pregnant was admitted to her local hospital for hyperemesis gravidarum. She had previously been well and had had a normal diet before becoming pregnant. She did not drink alcohol. This was her first pregnancy, and she had been vomiting for four weeks. Despite metoclopramide, prochlorperazine, cyclizine, and transdermal hyoscine the vomiting continued, though she was apparently able to keep down some food. Throughout her hospital stay she was treated with intravenous dextrose and saline but received no vitamin supplements. At 15 weeks' gestation she became confused and mildly ataxic. Family members reported that she no longer recognised them. She was noted to have tachycardia. Two days later she developed pronounced dysphagia and dysarthria, and she was transferred to the regional neurology unit.

On admission she was drowsy and unable to follow commands. She was dysarthric and unable to swallow water or saliva but had normal palatal and tongue movements and normal gag reflex. Coarse nystagmus was present in all directions of gaze She moved all limbs spontantously but was unable to cooperate sufficiently to test power, sensation, or gait. The reflexes were symmetrically exaggerated, and the right plantar was extensor.

A clinical diagnosis of combined Wernicke's encephalopathy and central pontine myelinolysis was made. Concentrated intravenous injections of the vitamin B complex and ascorbic acid (Parentrovite) and parenteral feeding were started. Two days after transfer she had a spontaneous abortion, and her subsequent course was complicated by intermittent upper airway obstruction. Her level of consciousness gradually improved but she was left with major impairment of short term memory. She experienced ongoing vertigo, and her gait remained ataxic. She was discharged home after nine weeks, still requiring constant supervision.

The diagnosis of Wernicke's encephalopathy was confirmed by low red cell transketolase activity (16 U/l, normal 34-90) and a raised thiamine pyrophosphate effect (224%, normal 4-40%). Magnetic resonance imaging was performed three weeks after onset of the neurological symptoms. The images obtained were degraded by movement artefact but showed a definite abnormality of signal return from the central pons that was not associated with any appreciable swelling. This appearance is typical of central pontine myelinolysis.[6,7]



Scan obtained by magnetic resonance imaging showing abnormal signal return from central pons (arrow) without appreciable swelling

Discussion

Wernicke's encephalopathy is due to a deficiency of thiamine (vitamin B-1), an essential cofactor in various stages of carhohydrate metabolism.[8] Transketolase is a thiamine dependent enzyme in the pentose phosphate pathway, and in Wernicke's encephalopathy activity is usually low.[8] The thiamine pyrophosphate effect is the increase in activity of transketolase when thiamine pyrophosphate is added to a preparation of the patient's red cells. A pronounced increase in thiamine pyrophosphate effect is probably the most reliable test of thiamine deficiency.[9]

Hyperemesis gravidarum is fairly common, but Wernicke's encephalopathy is an uncommon complication. This may reflect differences in genetic susceptibility as there is evidence that people who develop Wernicke's encephalopathy have a form of transketolase that binds thiamine less avidly than that of controls.[10] Requirements for thiamine vary with age and sex and increase during pregnancy to 1·5 mg daily.[11] Once body stores of thiamine become critically depleted, then Wernicke's encephalopathy can be hastened by ingestion of carbohydrate rich food. Intravenous dextrose will aggravate matters further. (It is sometimes incorrectly assumed that eating any food will protect someone from Wernicke's encephalopathy.)

Any pregnant women who develops hyperemesis

Royal Free Hospital, London NW3 2QG
P S Bergin, *neurology registrar*
P Harvey, *consultant neurologist*

Correspondence and requests for reprints to: Dr P S Bergin, Department of Clinical Neurophysiology, National Hospital for Neurology and Neurosurgery, Queen Square, London WC1N 2AN.

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should receive thiamine supplements as, indeed, should any patient with prolonged vomiting from any cause. If confusion, ataxia, or ocular signs (usually a sixth nerve palsy, gaze palsy, or nystagmus) develop parenteral thiamine (at least 50 mg daily) should be given until a normal diet is reinstituted. Blood should be taken to measure red cell transketolase activity or the thiamine pyrophosphate effect, but administration of thiamine must not await the result of this assay.

Not all this patient's problems could be explained on the basis of Wernicke's encephalopathy. Bulbar dysfunction and pyramidal signs are not features of Wernicke's encephalopathy. Reflexes are usually absent rather than exaggerated. The clinical consequences of central pontine myelinolysis vary considerably but pseudobulbar palsy and pyramidal tract signs along with depressed levels of consciousness are common manifestations.[12] Wernicke's encephalopathy and central pontine myelinolysis occur together more often than can be explained by chance.[12 13] There are two other reports of the conditions coexisting during pregnancy.[2 14]

There is still controversy over the pathogenesis of central pontine myelinolysis, but it is widely regarded as being the result of rapid correction of hyponatraemia.[15 16] Our patient's serum sodium concentration never fell below 126 mmol/l, though electrolyte values were measured only weekly. No attempt was made to correct the hyponatraemia, and hypertonic saline was never given. In the two other cases of combined Wernicke's encephalopathy and central pontine myelinolysis in pregnancy the lowest serum sodium concentration recorded was also 126 mmol/l.[2 14] Possibly, therefore, thiamine deficiency somehow makes the myelin sheaths of the central pons more sensitive to changes in serum sodium value. Certainly we agree with the advice of other authors that chronic hyponatraemia should be corrected slowly, but we also emphasise the need for thiamine supplementation if there is any possibility of deficiency of this vitamin.

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Correction

Any Questions

Owing to an editorial error the name of one of the experts who answered the question on the "golden hour" in major trauma (22 August, p 459) was omitted. The expert is Dr Fiona Gibson, registrar in accident and emergency medicine, Peterborough.

ANY QUESTIONS

One of my patients has been supplied with "Electron-Plus" tablets by an osteopath, which, as well as containing the usual panoply of vitamins and minerals, include "extract of raw bovine tissue" (comprising brain, spleen, pituitary, and parotid tissue). In view of the persistence of bovine spongiform encephalopathy in cattle should this preparation be regarded as potentially infected and is it therefore contraindicated?

There are two considerations—the legal issue and the scientific argument. The sale of bovine offal for human consumption (including brain and spleen, spinal cord, thymus, intestines, and tonsils from animals older than 6 months) was prohibited in England and Wales from November 1989 and in Scotland and Northern Ireland from February 1990. The banned tissues are thought to be likely replication sites for the agent causing bovine spongiform encephalopathy.[1] The questioner does not indicate the amount of material derived from cattle in the prescribed tablets, but the sale of a preparation containing raw extracts of bovine brain or spleen in the United Kingdom seems to contravene present legislation, unless the material is from calves younger than 6 months or from herds which are free of bovine spongiform encephalopathy in other countries.

Would the ingestion of such tablets be hazardous? The amount of material derived from cattle is presumably small. The oral route of challenge is inefficient for the experimental transmission of bovine spongiform encephalopathy to other species. A course of tablets would, at worst, represent possible sequential doses by an inefficient route if, in the first instance, potentially infected raw brain or spleen was involved in the preparation. While normal cooking temperatures do not definitely inactivate the agent causing bovine spongiform encephalopathy, they can reduce the infectivity. The agent does not occur at high concentration in muscle (meat). Eating properly cooked beef (or lamb for that matter) is safe for humans, but I would advise against eating bovine (or ovine) brain or spleen because these tissues are recognised as likely replication sites.[2] It seems rational to extend this exclusion to untreated extracts of bovine brain or spleen, even if the possible hazard cannot be quantified. It would be fair, of course, to determine exactly the details of the source of the material concerned.—J G COLLEE, *retired professor of medical microbiology, Edinburgh*

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