Lesson of the Week

Neurological complications associated with parenteral treatment: central pontine myelinolysis and Wernicke's encephalopathy

P D THOMPSON, R F GLEDHILL, N P QUINN, M N ROSSOR, P STANLEY, E N COOMES

Infusion of intravenous fluids is part of the routine management of patients presenting with severe metabolic and electrolyte derangements. Usually such treatment is free of neurological complications, but under certain circumstances these patients may develop two potentially serious disorders—namely, central pontine myelinolysis and Wernicke's encephalopathy.[1] Our recent experience of three such patients, two of whom had both central pontine myelinolysis and Wernicke's encephalopathy while the third had central pontine myelinolysis alone, suggests that these conditions may be more common than is generally thought. We report on these patients to highlight the circumstances in which these two complications arose as both may be prevented by timely intervention.

The correction of chronic hyponatraemia with intravenous fluids should be undertaken with caution; any accompanying malnutrition warrants the administration of thiamine, particularly if glucose is prescribed

Case Reports

CASE 1

An 18 year old woman presented with lethargy in the 20th week of her second pregnancy. She had vomited at least 10 times daily throughout gestation and had lost 1·3 kg in weight. She was able to walk into the emergency room, and on examination had no abnormal neurological signs but was pale and dehydrated. The plasma sodium concentration was 126 mmol(mEq)/l, plasma potassium 2·3 mmol(mEq)/l, and blood urea 86·5 mmol/l (519 mg/100 ml). During the first two hospital days she received 16 litres of intravenous fluid, comprising 10 litres of physiological saline (154 mmol sodium/l) and 6 litres of 5% dextrose. She was also given transfusions of four units of packed red blood cells. After these measures the plasma sodium concentration was 145 mmol/l, potassium 4 mmol/l, and blood urea 14·7 mmol/l (88 mg/100 ml).

On the fourth hospital day she did not speak or respond to verbal commands, and the next day she was irritable and confused. Bilateral abducens palsies, horizontal nystagmus, and bilateral weakness of the lower face were present. The corneal reflexes were normal. She moved all limbs spontaneously, but the left plantar response was extensor. Parenteral thiamine (250 mg) was administered, and the next day the abnormal ocular movements were less pronounced. Over the next two weeks her mental state improved but neurological examinations showed the evolution of a spastic quadriparesis. By the 17th hospital day she was alert and it became apparent that she had severe spastic dysarthria and intact sensation. Thereafter her neurological deficits rapidly improved, and eight weeks after admission she was independent for daily activities. At 37 weeks' gestation she was delivered of a normal male infant.

CASE 2

An 82 year old woman presented with a one week history of vomiting due to a strangulated femoral hernia with intestinal obstruction. Her only known medication was bendrofluazide. On admission the plasma sodium concentration was 124 mmol/l, potassium 4·1 mmol/l, blood urea 60·9 mmol/l (365 mg/100 ml), and blood glucose 3·6 mmol/l (65 mg/100 ml). Resection of the small bowel and saline peritoneal lavage were performed under regional anaesthesia. During the first hospital day she received roughly 10 litres of intravenous fluid, comprising 6·5 litres of physiological saline, 2 litres of Hartmann's solution (131 mmol sodium/l), 1 litre of plasma protein fraction (130-160 mmol sodium/l), 500 ml of 5% dextrose, and 50 ml of 50% dextrose. Postoperatively, the plasma sodium concentration was 136 mmol/l and blood urea 53·9 mmol/l (324 mg/100 ml). Over the next two days she received 1 litre of 5% dextrose water, 250 ml of 50% dextrose, 800 ml of plasma protein fraction, and 400 ml of 8·4% sodium bicarbonate (1000 mmol sodium/l). Two days later parenteral nutrition was begun, including 1·24 mg thiamine.

On examination on the ninth hospital day she was awake and responded to her name, with almost complete external ophthalmoplegia and brisk facial reflexes. Corneal reflexes and the remainder of the cranial nerves were normal. She was unable to move any limb to command but withdrew all limbs to pain. Tone in the legs was increased, and the plantar responses were extensor. She could appreciate painful stimuli throughout. She developed septicaemia and died later that day. The brain was not included in the postmortem examination.

CASE 3

A 52 year woman presented with drowsiness and a one week history of vomiting and diarrhoea. She was taking one tablet of atenolol 100 mg and chlorthalidone 25 mg (Tenoretic) daily, spironolactone 50 mg daily, and one tablet of cyclopenthiazide 0·25 mg and potassium chloride 600 mg (Navidrex K) daily for hypertension. She adhered strictly to a salt free diet. On admission she was confused but without other abnormal neurological signs. Shortly after admission she suffered a generalised seizure. The plasma sodium concentration was 99 mmol/l, potassium 1·7 mmol/l, and blood urea 3 mmol/l (18 mg/100 ml). Over the next three days she received 2 litres of 2% saline (308 mmol sodium/l), 2·5 litres of physiological saline, parenteral frusemide, and oral sodium chloride and dextrose powder. The plasma sodium concentration rose to 123 mmol/l. During the next two weeks she found it increasingly difficult to speak and move her limbs. Two weeks later she was observed to be alert but anarthric. Ocular movements and corneal reflexes were normal and she had a pseudobulbar palsy and spastic quadriparesis with extensor plantar responses. Limb sensation was normal. She was fully mobile and independent when discharged two months later.

University Department of Neurology, King's College Hospital, and Institute of Psychiatry, London SE5 8AF

P D THOMPSON, MB, FRACP, honorary senior registrar in neurology
R F GLEDHILL, MD, MRCP, senior lecturer in neurology
N P QUINN, MA, MRCP, lecturer in neurology
M N ROSSOR, MA, MRCP, senior neurology registrar

St Stephen's Hospital, Chelsea SW10 9TH

P STANLEY, MRCP, medical registrar
E N COOMES, MD, FRCP, consultant physician

Correspondence to: Dr Thompson.

Discussion

After the rapid correction of chronic hyponatraemia with intravenous fluids these three patients developed progressive spastic quadriparesis and pseudobulbar palsy with preservation of consciousness and sensation. Such neurological findings are compatible with a lesion affecting the basis pontis, the sparing of the tegmental structures accounting for the preservation of consciousness and sensation. In severe illnesses in which electrolyte disturbances, particularly hyponatraemia, were prominent these signs suggested a clinical diagnosis of central pontine myelinolysis.[2 3] To our knowledge there has been only one previous report of central pontine myelinolysis occurring during pregnancy.[4] The remarkable degree of recovery that can occur after central pontine myelinolysis is well illustrated by two of our patients (cases 1 and 3). In most of the reported cases the diagnosis of central pontine myelinolysis has been made post mortem. Consequently the incidence of non-fatal cases is unknown as the early clinical features may escape notice in critically ill patients. The recovery observed in the present cases serves to emphasise the need to consider the diagnosis and to continue active care in those patients whose underlying medical condition is potentially reversible.

Though the pathogenesis of central pontine myelinolysis remains unclear, a rapid or excessive rise in plasma sodium concentration during the treatment of chronic hyponatraemia may be a crucial factor.[5-7] Those patients in whom hyponatraemia has developed gradually may be especially at risk.[5]

Though the appropriate management of hyponatraemia depends on the underlying cause, the role of parenteral sodium in its correction is controversial.[8-10] In cases in which hyponatraemia is complicated by seizures or encephalopathy the use of hypertonic saline has been advocated, but only in quantities sufficient to control these features.[6 11] A consensus is emerging that parenteral sodium should be administered with caution, so as to avoid unduly rapid or excessive correction and hence minimise the risk of central pontine myelinolysis.[5-7 11] Based on the clinical study of Norenberg *et al*, it would seem advisable to restrict the increase in plasma sodium concentration to about 10 mmol/l above the lowest recorded value during the first week of treatment and to avoid hypernatraemia.[6] In addition, even when parenteral sodium is thought to be indicated it may not be necessary to replace the calculated sodium deficit.[10] Finally, the oral route may be the more satisfactory method for correcting hyponatraemia.[8]

Two of our patients had the ocular signs of Wernicke's encephalopathy, which is known to coexist in patients with central pontine myelinolysis.[1] In case 1 this may be explained by thiamine deficiency resulting from persistent vomiting in pregnancy,[12] and in case 2 thiamine deficiency was probably precipitated by the administration of a large quantity of dextrose without vitamin supplements. The risks of precipitating Wernicke's encephalopathy by administering glucose to patients predisposed to thiamine depletion have been emphasised,[13] and it would seem appropriate to prescribe thiamine supplements in all malnourished patients requiring parenteral treatment.

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An 89 year old patient suffers from repeated extravasation of blood into the skin of her hands and legs, presumably due to capillary fragility? All blood tests and other investigations have given normal results. Is there any way in which this type of senile purpura can be diminished as the cosmetic appearance is somewhat embarrassing?

Senile purpura is extremely common in the elderly, as it is in patients using excessive quantities of topical steroids and who have taken oral corticosteroids for some time. The mechanism of action in these conditions is similar. The quantity and quality of dermal collagen are reduced, producing inadequate support for the dermal blood vessels.[1 2] As a result of minor trauma the blood vessels rupture, producing purpura; in a healthy, active, normal individual the presence of red cells in the dermis stimulates phagocytosis of the red cells.[2] In the elderly, however, this phagocytic function is appreciably impaired and therefore the purpura lasts for many weeks or months. Characteristically, investigations, in particular investigations of clotting factors, are normal. Senile purpura may be disguised by cosmetics and make up is available in the form of Covermark, Dermacolor, Keromask, and Veil Cover Cream. The general practitioner may refer the patient to the local Red Cross Association (details obtainable from the British Red Cross Society, 9 Grosvenor Crescent, London SW1X 7EJ. Tel 01-235-5454), which gives free advice on the use of cosmetics for covering up skin blemishes. The association will recommend to the general practitioner which cosmetic camouflage material is best for that patient, and these preparations, although classified as borderline substances, may be prescribed in the NHS.—W J CUNLIFFE, consultant dermatologist, Leeds.

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What is the value of beta-sympathomimetic agents in suppressing preterm labour and are there any special indications for their use in obstetrics?

Beta-sympathomimetic agents are the drugs of choice for treating preterm labour, and several controlled trials have shown that they can significantly prolong pregnancy.[1 2] Nevertheless, treatment is appropriate for only a few patients, the most suitable candidates being women in labour early in the third trimester, when even a short delay in delivery may benefit the fetus.[1] Obstetric complications such as antepartum haemorrhage may contraindicate tocolytic treatment, and the most appropriate patients for this treatment are those who present before 33 weeks with intact membranes at less than 4 cm dilatation and who have no associated obstetric pathology.[3] Side effects include alterations in carbohydrate metabolism, tachycardia, and other cardiovascular effects (which may, however, be mitigated by tachyphylaxis), and the rare but serious side effect of pulmonary oedema.[1 4] Relative contraindications therefore include heart disease and diabetes,[4] though diabetics may be treated under strictly controlled conditions.[5] Another possible indication for short term treatment is uterine hyperactivity that is causing fetal hypoxia.[4] In all cases careful monitoring of mother and baby is essential.[1]—JAMES OWEN DRIFE, senior lecturer in obstetrics and gynaecology, Leicester.

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