ml). Her condition improved slowly, and she was discharged after three weeks. Four months after the initial episode, taking no medication, she was considered to be cured; laboratory results are shown in the table.

Main laboratory data on admission and after full recovery

	On admission	Four months later
Serum		
Glucose (mmol/l)	4·6	5·0
Blood urea nitrogen (mmol/l)	5·0	5·7
Creatinine (μmol/l)	88	71
Uric acid (μmol/l)	125	262
Sodium (mmol(mEq)/l)	141	143
Potassium (mmol(mEq)/l)	2·9	4
Chloride (mmol(mEq)/l)	112	101
Bicarbonate (mmol(mEq)/l)	3·7	21·2
Arterial pH	7·12	7·38
Oxygen pressure (mm Hg)	111	88
Carbon dioxide pressure (mm Hg)	12·4	34·4
Calcium (mmol/l)	2·5	2·4
Phosphorus (mmol/l)	0·39	1·2
Magnesium (μmol/l)	782	ND
Ketones	Negative	ND
Lactate (μmol/l)*	921	ND
Amylase (Somogyi units/l)	900	ND
Anion gap (calculated mmol/l)	25·3	10·8
Urine		
pH	6	6·8
Proteinuria	+ + +	Negative
Glucosuria	+ + +	Negative
Sodium (mmol(mEq)/l)	113	ND
Potassium (mmol(mEq)/l)	43	ND
Uric acid (mmol/24 h)	200	132
Sediment	10 white cells/ high-power field	Normal
Phosphate clearance (ml/min)	94	15

*Normal range 0·5–2 mmol/l.
ND = Not done.
Conversion: SI to traditional units—Blood glucose: 1 mmol/l ≈ 18 mg/100 ml. Blood urea nitrogen: 1 mmol/l ≈ 2·8 mg/100 ml. Creatinine: 1 μmol/l ≈ 11·3 μg/100 ml. Uric acid: 1 μmol/l ≈ 16·8 μg/100 ml. Calcium: 1 mmol/l ≈ 4 mg/100 ml. Phosphorus: 1 mmol/l ≈ 3·1 mg/100 ml. Magnesium: 1 μmol/l ≈ 2·4 μg/100 ml. Lactate: 1 μmol/l ≈ 9 μg/100 ml. Anion gap: 1 mmol/l ≈ 00 mg/100 ml. Urinary uric acid: 1 mmol/24 h ≈ 6 mg/24 h.

Biochemical analysis of the remaining tablets kept in the original cardboard box detected the presence of 4-epianhydrotetracycline and anhydrotetracycline in a proportion of 60%; the maximum tolerated content of these compounds is less than 3%.

Comment

This patient showed all the main features of the Fanconi syndrome. The finding of degradation products in the tetracycline tablets provides strong evidence for their being the cause of this renal tubular dysfunction.

Severe metabolic acidosis was prominent. Renal tubular acidosis due to the Fanconi syndrome was undoubtedly partly responsible for this. The existence of hyperchloraemia and an inappropriately high urinary pH endorse this interpretation. An inappropriately high urinary pH implies a distal acidification defect, which is sometimes present in the Fanconi syndrome[2] and adds to the generalised proximal tubular dysfunction. The increased anion gap, however, cannot be accounted for by renal tubular acidosis and was caused by the lactic acidosis, as shown by the raised serum lactate concentrations and the absence of other causes of high anion gap metabolic acidosis.[3] Since lactic acidosis appeared simultaneously with the Fanconi syndrome and no other reason for it could be found[4] it seems logical to assume that the degraded tetracycline tablets were also responsible for its development. The possibility of a coincidental spontaneous lactic acidosis is unlikely in this case.

We can find no report of an association between lactic acidosis and tetracycline intake in the absence of other drugs or diseases capable of inducing lactic acidosis by themselves. The mechanism by which degraded tetracycline may produce lactic acidosis remains unknown. The condition might result from a toxic effect of the drug at the cellular level, but direct evidence is lacking. Nevertheless, we believe that this observation should alert doctors to the possibility of intake of altered tetracycline in cases of lactic acidosis of obscure origin.

We thank Dr M Rodés, from the department of metabolopaties, Institut de Bioquimica Clinica "Flor de Maig," Fundació "Juan March" Cerdanyola (Barcelona), for measuring the urine amino-acids; Dr A Moreno and other staff from the medical department of the Compañía Española de Penicilina y Antibióticos SA (Madrid) for performing the biochemical analysis of the altered tablets; and Ms Isabel Roselló for secretarial help.

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Severe peripheral neuropathy complicating legionnaires' disease

Neurological disturbance, particularly mental confusion, is a common complication of legionnaires' disease. Case reports draw attention to evidence of central nervous system dysfunction,[1 2] but we have found only a single example of clinically severe peripheral nerve disease.[3] We report a case of legionnaires' disease complicated by a profound but reversible neuropathy.

Case report

A 43-year-old porter was found in a confused state at home after a week of flu-like symptoms. On admission to hospital he was feverish (38·8°C) and dehydrated with clinical evidence of left lower-lobe pneumonia. He was disorientated but there were no focal neurological deficits. All the deep reflexes were difficult to obtain, and the plantar responses were extensor. The white cell count was normal ($8·2 \times 10^9$/l (8200/mm^3); 86% neutrophils, 8% lymphocytes) but the plasma urea concentration was 11·7 mmol/l (70·5 mg/100 ml) and the serum aspartate aminotransferase activity 260 IU/l. Chest radiography confirmed extensive consolidation in the left lung. Cerebrospinal fluid was normal (white cell count $2·0 \times 10^6$/l, protein concentration 0·4 g/l, glucose concentration 4·0 mmol/l (72·1 mg/100 ml)). Subsequently *Legionella pneumophila* infection was diagnosed on the basis of a fourfold rise in fluorescent antibody titre.

Bulbar weakness with dysarthria, dysphagia, and nasal regurgitation of fluid became apparent on the fifth hospital day. Thereafter, as the confusion lessened increasingly severe limb weakness became apparent. The patient complained of distal numbness in arms and legs together with tingling and pronounced unsteadiness on attempting to walk. By his third week in hospital the bulbar palsy had disappeared. Examination then showed bilateral facial weakness but otherwise normal cranial nerves. Symmetrical wasting of the small hand muscles was evident together with noticeable distal weakness in arms and legs. The arms showed tremor on posturing and mild ataxia with use. There was moderate ataxia of the legs tested in the lying position and a more pronounced disturbance of gait and stance. The deep reflexes had disappeared but the plantar responses remained extensor. Subjective perversion of sensation to touch was present below the mid-calf on each side, and position sense was impaired at the fingers and toes. Vibration sense was lost below the iliac crests.

Nerve-conduction studies showed absent sensory action potentials in the arms and moderate slowing of motor conduction (25 m/s in the median nerve). A further specimen of cerebrospinal fluid four weeks after admission showed a protein concentration of 0·6 g/l.

During the next two months the patient's weakness and sensory signs gradually resolved, though the tendon reflexes remained absent and the plantar responses extensor.

Comment

Though there was evidence of disturbance of the central nervous system (mental disorientation and extensor plantar responses), the neurological signs that developed in this patient with legionnaires' disease indicated predominant peripheral nerve dysfunction. Cerebellar ataxia has been noted as a complication of legionnaires' disease,[4] but our patient's weakness and sensory loss were the likely cause of his ataxia.

Acute polyneuropathy, commonly designated Guillain-Barré syndrome, is a well-recognised complication of many specific infective processes. A rising cerebrospinal fluid protein concentration reaching high values in four to six weeks is characteristic. Whether the

inflammatory damage to peripheral nerves is caused by the infective agent and its toxins or by an immunological response triggered by them has long been debated. Much evidence supports an immunological cause for this condition, but it is not clear whether our patient's neuropathy was of this type or a specific feature of legionnaires' disease. Kennedy *et al*[3] found neurophysiological evidence for an acute axonal neuropathy in five patients with legionnaires' disease, though clinical manifestations were evident in only a single case. Their findings and the small rise in cerebrospinal fluid protein concentration in our patient offer some support for a specific neuropathy accompanying legionnaires' disease.

We thank Dr A Pringle for permission to report this case.

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Acute polymyopathy during total parenteral nutrition

Total parenteral nutrition is often used as nutritional support[1]; deficiency states of various nutrients have been recognised in association with it. We report four cases of an acute myopathy associated with total parenteral nutrition that improved dramatically either when the nutrition was stopped or with intravenous lipid supplementation.

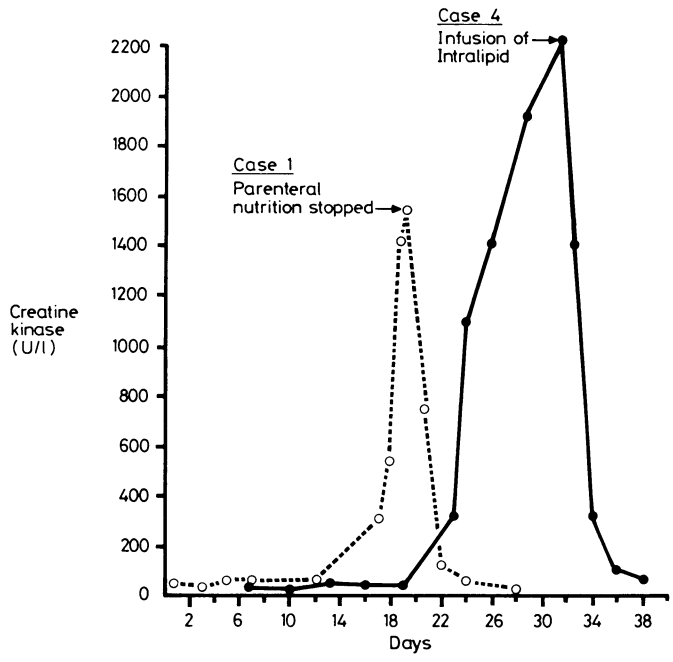
Case reports

Case 1—A 59-year-old woman with coeliac disease and previously treated oesophageal carcinoma was started on total parenteral nutrition. Weight gain was 6 kg in 34 days. A lipid supplement (Intralipid 10%, Vitrium) was initially part of the regimen but was stopped because of thrombophlebitis at infusion sites. The figure shows plasma creatine kinase activities (normal <140 U/l) from the day after the last infusion. Aspartate aminotransferase activity rose transiently on day seven, but no associated increase in bilirubin concentration or alkaline phosphatase activity occurred. Parenteral nutrition was stopped on day 20 because of muscle pain, tenderness, swelling, and tachycardia. By day 21 muscle symptoms had abated and by day 22 creatine kinase activity was normal. The ratio of 5,8,11-eicosatrienoic acid to arachadonic acid in plasma lipids was 1·4 on day 20 (normal <0·4). Seven days after parenteral nutrition was stopped the ratio was 0·3, and after 14 days no 5,8,11-eicosatrienoic acid was detected.

Cases 2 and 3—Two further patients with similar symptoms and responses to total parenteral nutrition were seen; they did not receive lipid supplementation.

Case 4—A 54-year-old woman was started on total parenteral nutrition for small-bowel fistula after gastrectomy for carcinoma of the stomach and gained 7 kg in weight. On day 23 she complained of muscle weakness and plasma creatine kinase activity was raised (figure). By day 29 she had developed muscle pain and tenderness. On day 32 a lipid infusion (Intralipid 10%, 500 ml) was started and total parenteral nutrition continued. Muscle pain immediately lessened and then disappeared. Creatine kinase activity reached normal values by day 36. The ratio of plasma 5,8,11-eicosatrienoic acid to arachadonic acid on day 32 was 1·9. No eicosatrienoic acid was detected seven days after the start of lipid treatment. Parenteral nutrition was continued until day 40 without further complications.

Methods—Total parenteral nutrition was performed by standard techniques and provided up to 16·7 MJ(4000 kcal)/day. Recommended allowances of vitamins and trace elements were administered. Biochemical and haematological tests were performed thrice weekly and concentrations of vitamins A, C, and E, β-carotene, thiamine, and pyridoxine measured weekly. Electromyography confirmed an acute myopathy. Muscle biopsy specimens could not be obtained. The constituent fatty acids in plasma were analysed by gas-liquid chromatography after extraction and hydrolysis. Deficiency of essential fatty acids was diagnosed when the ratio of 5,8,11-eicosatrienoic acid to arachadonic acid was greater than 0·4.[2]



Creatine kinase activity during total parenteral nutrition in cases 1 and 4.

Comment

The acute myopathy in these patients was clearly related to parenteral nutrition. Stopping the regimen resulted in clinical and biochemical improvement within hours and complete resolution of the myopathy within days. Hepatomegaly was not detected clinically, and there was no biochemical evidence of hepatic dysfunction.

The cause of the myopathy was not established, though deficiency of essential fatty acids probably played a part. Characteristic chemical evidence for such a deficiency was detected. Though measurable amounts of 5,8,11-eicosatrienoic acid are expected after parenteral nutrition without lipid supplementation, a ratio of eicosatrienoic to arachadonic acid of the magnitude seen here indicates severe deficiency.[3] Parenteral nutrition causes high circulating insulin concentrations, which suppress release of endogenous essential fatty acids from adipose tissue stores, resulting in a relative deficiency. Stopping parenteral nutrition thus allows release of these acids. The rapid clinical and biochemical response brought about by adding a lipid supplement to the regimen (case 4) is consistent with this hypothesis. Deficiencies of phosphate, vitamin E, and selenium have been associated with myopathies and muscle damage but were excluded in these cases.

No further cases of acute myopathy occurred after intravenous lipid supplementation was added on a regular basis to the nutritional support protocol. Whether a pure deficiency of essential fatty acids was the direct cause of this syndrome was not established. The lipid supplement may provide another as yet unidentified nutrient or, alternatively, essential fatty acids may reverse the abnormality without correcting the basic defect. Whatever the mechanism, lipid supplementation seems to prevent and reverse the muscular syndrome without the need to stop the nutritional support.

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