SHORT REPORTS

Acute interstitial nephritis in a patient taking tienilic acid

A patient taking the uricosuric diuretic tienilic acid or ticrynafen (2,3-dichloro-4-(2-thienyl-carbonyl) phenoxyacetic acid)—marketed as Selacryn, (Smith, Kline and French Laboratories 62698) developed acute renal failure due to acute allergic interstitial nephritis.

Case report

A 61-year-old housewife of Lithuanian extraction had been attending the nephrology hypertension clinic at the Royal Melbourne Hospital for 16 years. She had mild essential hypertension controlled by chlorothiazide 0·5 g twice daily and was also receiving thioridazine 50 mg daily. She entered a double-blind cross-over trial comparing tienilic acid (250 mg daily) with hydrochlorothiazide (50 mg daily). After a four-week placebo phase she started on active treatment (retrospectively noted to have been with hydrochlorothiazide) for 12 weeks. During this phase her renal function was normal (serum creatinine concentration 0·08 mmol/l (0·9 mg/100 ml)) but she had mild hyperuricaemia (serum uric acid concentration 0·53 mmol/l (9 mg/100 ml)). After 16 weeks treatment was crossed over to tienilic acid. Nine days later her renal function was much impaired. Her serum creatinine concentration was 0·70 mmol/l (7·9 mg/100 ml) and her serum uric acid concentration >0·70 mmol/l (13·9 mg/100 ml). At this time she was mildly hypertensive (blood pressure 162/92 mm Hg) and complained of nausea, vomiting, and anorexia. Percutaneous renal biopsy showed acute tubular necrosis, interstitial oedema, and a heavy interstitial cellular infiltrate in which eosinophils were predominant. Although the infiltration was patchy the changes were interpreted as those of an acute hypersensitivity interstitial nephritis. Tienilic acid was stopped. Renal function improved spontaneously, returning to normal six weeks later (serum creatinine 0·08 mmol/l (0·9 mg/100 ml).

Comment

Tienilic acid, an orally active diuretic with uricosuric properties, is an effective antihypertensive in cases of mild-to-moderate hypertension.[1] Acute renal failure within hours of giving the drug has been reported and has usually been attributed to acute urate nephropathy.[2] Some cases of acute renal failure may be precipitated during dehydration, particularly at cross-over periods from thiazide diuretics to tienilic acid and in the presence of hyperuricaemia. A reaction is described characterised by loin pain, abdominal pain, nausea, vomiting, and mild fever. Oliguria and acute renal failure may intervene, but is usually reversible.[3] Renal biopsy in some cases has shown an unusual accumulation of vacuoles of a lysosomal type in the proximal tubules.[4] No uric acid crystals are seen in the urinary sediment of such patients, although the reaction is thought to be due to the presence of urate in the collecting ducts or the deep loops of Henle. The incidence of this nephrotoxic reaction is estimated at 0·05%.[3]

Acute allergic interstitial nephritis, a condition distinct from urate nephropathy, has been reported 10 weeks after starting treatment with tienilic acid.[5] In our case it occurred nine days after starting the drug. The patient did not have pain but complained of nausea and vomiting. She had recently changed medication from hydrochlorothiazide to tienilic acid. She was also hyperuricaemic when she began taking tienilic acid. Uric acid crystals were not seen in either the renal biopsy or the urinary sediment and the histological features were similar to those described by Huang and his colleagues.[5] There was no vacuolisation of the proximal tubular cells. Although acute renal failure may be caused by acute urate nephropathy or an unusual tubular vacuolisation of the lysosomal type, we conclude that acute allergic interstitial nephritis may also be responsible for acute renal failure in patients receiving tienilic acid.

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Proximal myopathy after prolonged total therapeutic starvation

Myopathy of the proximal limb muscles developed in a patient after prolonged total therapeutic starvation for refractory obesity. Recovery was spontaneous. We know of no report of a similar case.

Case report

A 19-year-old man was admitted to hospital for total therapeutic starvation for refractory obesity. The fast lasted about 17 weeks, during which time his weight fell from 130 kg to 82 kg. During the fast he received supplements of potassium (as Slow K), allopurinol (300 mg/day), folic acid, and vitamins A, B, C, and D (as Multivite). Detailed haematological and biochemical monitoring was undertaken and twice weekly electrocardiographs (ECG) performed. As often occurs in such patients he developed a normochromic anaemia (haemoglobin 10·4 g/dl) and neutropenia (lowest neutrophil count $1{\cdot}426 \times 10^9$/l). Serum electrolyte concentrations remained normal throughout the fast except for serum bicarbonate which indicated consistent but mild metabolic acidosis (HCO_3^- 14-17 mmol(mEq)/l). Urate concentrations were well controlled at all times (<430 μmol/l; < 7·22 mg/100 ml). Serum magnesium concentrations fell just below normal (0·67 mmol/l (1·63 mg/100 ml); normal range 0·7-1·0 mmol/l (1·7-2·43 mg/100 ml)) towards the latter part of the fast, and serum calcium concentrations remained normal. The mean phosphate concentration was 1·40 mmol/l (4·34 mg/100 ml) with a range of 0·95-1·70 mmol/l (2·94-5·27 mg/100 ml). Towards the end of the period of starvation the ECG showed prolongation of the Q-T interval (maximum 0·6 seconds) but was otherwise normal.

Nine days after refeeding started he developed recurrent ventricular fibrillation and ventricular tachycardia but was successfully resuscitated using repeated DC counter shock, lignocaine, and phenytoin; phenytoin proved a successful prophylactic and was continued for six weeks. Subsequent recovery was uncomplicated until seven weeks after refeeding, when he developed considerable weakness of his proximal limb muscles, particularly in his legs. On examination no muscle wasting was evident and no fasciculation was observed. The deep tendon reflexes and plantar responses were normal, and there were no sensory abnormalities. Nerve conduction studies showed normal nerve conduction velocities. Electromyography revealed no spontaneous activity, and on voluntary activity the interference pattern was slightly reduced. There was a mild excess of polyphasic units. The creatinine phosphokinase level was 142 units/l with no significant amount of cardiac isoenzyme present. After about four weeks muscle power began to improve progressively and had recovered completely by 14 weeks—that is, five months after the end of the fast.

Comment

Accounts of muscle disorder as the sequel to prolonged fasting are comparatively rare. The most dramatic report was that of Garnett *et al*,[1] who described fragmentation of the cardiac myofibrils in a young woman after therapeutic starvation. Their patient presented with sudden ventricular fibrillation, which proved fatal, and the appearances of the cardiac muscle were subsequently studied by electron microscopy. Our own patient presented with a similar serious disorder of cardiac function before the development of the voluntary muscle disorder. By analogy with the earlier case, the two phenomena may have been symptoms of a generalised muscle condition.

The cause of the myopathy remains obscure. Allopurinol and phenytoin have both been implicated, rarely, as causes of peripheral neuropathy, but there are no reports of these drugs causing myopathy. Loss of normal body potassium and magnesium stores has been

reported to cause muscle fibre necrosis,[2] and magnesium was not given to our patient during his fast. Likewise vitamin E deficiency is described as a cause of obscure proximal myopathy[3] and the serum concentration of this vitamin fell just below normal (14 μmol/l; normal range 16·3-30·7 μmol/l) by the end of the fast. The fact that a clinically evident myopathy did not appear until seven weeks after the fast was broken might suggest that its appearance was facilitated by the fluid retention which occurs in the early weeks of refeeding and might point to electrolyte shifts in the production of the syndrome.

Whatever its cause, clinical myopathy as the sequel to prolonged fasting appears to be a rare and self-limiting condition. Nevertheless, in view of its association with near-fatal cardiac arrhythmias in our patient it seems worth while to make regular measurements of voluntary muscle function during therapeutic starvation, to use evidence of muscle dysfunction as an indication to terminate the fast, and to monitor cardiac function in these patients with great care during the early weeks of refeeding.

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Hydatidiform mole with coexistent viable fetus detected by routine AFP screening

Measurement of maternal serum α-fetoprotein (AFP) concentrations may soon become routine between 16 and 20 weeks of pregnancy as a screening test for fetal neural tube defects.[1] Concentrations may also be raised in several other conditions, including threatened, inevitable, and missed abortion[2] and various congenital abnormalities of the fetal gastrointestinal tract and other sites.[3] We report a case in which a hydatidiform mole coexistent with a viable fetus was detected by routine maternal AFP screening.

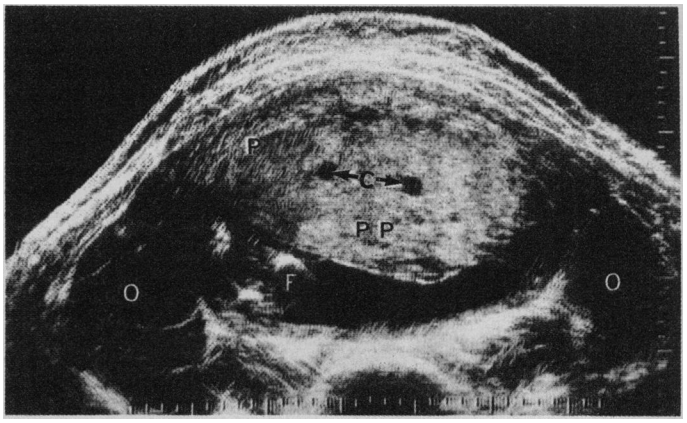
Case report

A 29-year-old primigravid Caucasian patient was found at 16 weeks' gestation to have a grossly raised maternal serum AFP concentration of 2800 μg/l (90% confidence limits at 16 weeks 20-130 μg/l). The antenatal course had been unremarkable but the uterine size was consistent with 18-20 weeks' gestation. Fetal movements were felt and there was no vaginal bleeding. Ultrasound examination two weeks later showed a single live fetus (estimated gestation 18-19 weeks) compressed by gross proliferation of half of the placenta (figure). A number of echo-free zones in the placenta and multiple cysts of the ovaries were seen. The appearance was consistent with that of a hydatidiform mole coexistent with a live fetus. The amniotic fluid AFP concentration was normal at 8·5 mg/l. After discussion with the patient pregnancy was terminated by giving intra-amniotic prostaglandin $F_2\alpha$. The placenta was grossly abnormal with the characteristic features of hydatidiform mole. The female fetus had no abnormality. The histological appearance of the placenta was consistent with hydatidiform mole. The postoperative course was unremarkable and plasma human chorionic gonadotrophin concentrations have been under 25 IU/l since six weeks after abortion.

Comment

Raised maternal serum AFP concentrations in hydatidiform mole are extremely uncommon, since the major source of maternal AFP is the fetal liver.[4] Nevertheless, evidence of AFP synthesis by abnormal trophoblastic tissue has been reported.[5] The normal amniotic fluid AFP concentration in the presence of a normal fetus when the maternal serum AFP concentration was grossly raised was an unexpected finding in our case. Although the reason for the raised maternal concentration is unclear there are two likely explanations. Firstly, the altered permeability of the molar tissue may allow increased diffusion of AFP into the maternal circulation. Secondly, abnormal synthesis of AFP by molar tissue cannot be excluded in this patient.

This case report not only adds yet another abnormality of pregnancy, albeit rare, that may be detected by routine AFP screening but also emphasises the mandatory complementary role of ultrasound. If ultrasound examination had not been performed, since the amniotic fluid AFP concentration was normal the gross abnormality would have been missed.



Transverse echogram of pelvis showing abnormal placental proliferation (PP) encroaching on fetus (F). Normal placenta (P) area is well delineated from abnormal placental proliferation with cystic areas (C). Both ovaries have multiple cysts (O).

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Addiction to Distalgesic (dextropropoxyphene)

Distalgesic is a proprietary preparation containing dextropropoxyphene 32·5 mg and paracetamol 325 mg per tablet. It is widely prescribed for mild to moderately severe pain. Both components are effective analgesics by mouth. Dextropropoxyphene was introduced in 1957 as a substitute for codeine. Five other proprietary preparations containing dextropropoxyphene are now available in the United Kingdom. Dextropropoxyphene is similar in structure to methadone. It is a centrally acting drug without antipyretic or anti-inflammatory