Exertion-induced rhabdomyolysis in a patient on statin therapy

Sir,

We describe a patient on long-term statin treatment who developed acute renal failure (ARF) from rhabdomyolysis following severe unaccustomed exertion. Reviewing the available literature, we did not find reports of exertion-induced rhabdomyolysis and ARF requiring dialysis while on statins.

A 57-year-old male, with hypertension and hyperlipidaemia (on ramipril 2.5 mg, atorvastatin 10 mg daily for several years), went trekking and described it as ‘the most exhausting exercise in recent times’. Coming downhill, he noticed thigh pain and took two doses of a non-steroidal anti-inflammatory drug (NSAID). On day 3, his urine output decreased; examination showed blood pressure 160/100 mmHg and clinical evidence of fluid overload. Investigations showed: blood urea 141 mg/dl, creatinine 9.4 mg/dl, potassium 6.4 mEq/l, mildly deranged liver functions, no proteinuria, and no urinary casts or urine eosinophils. Serum creatine kinase (CK) was elevated: 3389 IU/l (normal 38–174 IU/l), as was lactate dehydrogenase 469 U/l (140–300 U/l) and serum myoglobin 617 µg/l (5–85 µg/l); urine myoglobin was negative. Haemodialysis was performed for hyperkalaemia and volume overload. Previous medications were stopped. Urine output improved by the fourth day of hospitalization and renal functions started improving in 1 week. At 6 weeks, urea was 32 mg/dl and creatinine 1.0 mg/dl.

In this patient, treatment with statins and the development of rhabdomyolysis following exertion raises the possibility of an association between the two, either direct or indirect. Our patient had several factors predisposing to ARF, i.e. volume depletion, use of an angiotensin-converting enzyme inhibitor (ACEI) and an NSAID, and severe exertion that could by itself cause rhabdomyolysis. It is probable that treatment with statins amplified the muscle damage caused by intense exertion. We can only speculate as to whether he would have developed rhabdomyolysis if he was not taking statins.

In studies looking at statins and exertion-induced muscle damage, patients receiving lovastatin had 62–77% higher CK levels after exercise compared with those on placebo, showing that statins increase exercise-induced muscle injury [1]. In another study, several patients on statins showed a post-exercise rise in serum CK, although there was no difference in average CK levels compared with placebo [2]. A personal report documented an exercise-induced CK rise with atorvastatin; the symptoms and CK levels normalized on stopping statins and reappeared after switching to pravastatin [3]. Theories of statin-induced rhabdomyolysis include effects on muscle cholesterol synthesis and isoprenoid levels [4]. Statins inhibit GTP activation. Exercise may unmask the effects of statins on skeletal muscle because GTP-dependent protein kinase pathways are important in muscle recovery following exercise [4].

Based on the association noted, it needs to be considered whether statins should be withheld prior to engaging in ‘more than an accustomed range’ of physical exertion. Most statins have a short half-life and withholding the drug for 2 days would be reasonably intelligent to avoid its contribution to muscle injury [5].

Conflict of interest statement. None declared.

Acute nephropathy due to Salmonella typhimurium septicaemia

Sir,

Salmonella typhimurium (STM) is a non-typhoid salmonella which essentially entails intestinal infections. Extra-intestinal involvements such as septicaemia or renal lesions are uncommon in developed countries and mainly occur in frail people [1]. We describe a case of STM septicaemia with acute nephropathy in an elderly subject.

A 92-year-old man was hospitalized for epigastralgia; vomiting and fever of 40°C suddenly appeared. His medical history consisted of non insulin-dependent diabetes, deep-vein thrombosis, chronic respiratory insufficiency, mild chronic renal insufficiency, a pacemaker and chronic alcoholism. He had been treated by omeprazole, fluindione, furosemide, gliclazide, molsidomine, trinitrine, ramipril, and trimetazidine and sertraline. Except for a mild abdominal pain without contracture, the physical examination was normal and blood pressure was 110/80 mmHg. Initial biological screening showed moderate hyperuricemia, macrocytosis without anaemia, inflammatory syndrome (C-reactive protein (CRP) 98 mg/l, fibrinogen 5.5 g/l), renal insufficiency (serum creatinine 160 µmol/l, urea 16 mmol/l) and an increase of γ-glutamyltransferase (210 IU/l). A few hours after admission, profuse diarrhoea, dyspnoea and haemodynamic shock appeared. The second set of laboratory tests disclosed lactic acidosis (pH 7.10, moderate decrease of pCO₂ to 33 mmHg (normal: 35–45), reduction of serum

Letters


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bicarbonate to 15 mmol/l (normal: 22–30) and increase of serum lactate to 523 mg/l (normal: 63–189), an increase of CRP to 198 mg/l, mild anaemia and aggravation of renal insufficiency (creatinine 429 μmol/l, urea 25 mmol/l). Serum total protein and albumin were in the normal range. Complement was normal. Urinalysis showed proteinuria 2.83 g/l, haematuria 6 × 10^6 red blood cells/ml without leukocytes or bacteria. The patient’s daily urine output was ~1.5–2.5 l. Blood and fecal cultures showed the same STM, but urinary culture was sterile. Abdominal ultrasonography showed normal morphology and height of the kidneys and urinary tract. The patient was treated with two antibiotics (ceftriaxone and ciprofloxacin), perfusion of macromolecular and sodium bicarbonate solutions, insulin, oxygen, an antipyretic and an antiemetic. Molsidomine and trinitrine were stopped. A few days later, clinical examination became normal and biological analysis revealed anterior values of creatinine and urea and disappearance of proteinuria and haematuria.

Septicaemia or extra-digestive involvements are exceptional in cases of STM infection. Immunosuppression, cancer, haemoglobinopathy, hepatic cirrhosis, gastric hypochlorhydria, past history of digestive surgery, malnutrition, previous antibiotic or anti diarrhoeic treatment, and extreme age contribute to its development [1]. Thus, in our case report the patient had risk factors because he was very old and possibly immunosuppressed owing to chronic alcoholism. Renal lesions which can be observed in the presence of STM infection are: abscess, acute pyelonephritis, tubulointerstitial nephritis, interstitial nephritis and glomerulonephritis [2,3]. In our report, pyelonephritis was excluded because urinary analysis and culture carried out before antibiotics were initiated did not reveal any infection. However, there were arguments for tubulointerstitial/interstitial nephritis and for glomerulonephritis in addition to haematuria and renal insufficiency found in the previous two cases. Therefore, the normality of complement and the very quick decrease of renal signs with the treatment of infection argue for acute tubulointerstitial/interstitial nephritis, whereas the absence of leukocytosis in urinalysis and the high rate of proteinuria, ~3 g/l, are noted in glomerulonephritis. However, proteinuria can be important in cases of tubulointerstitial/interstitial nephritis [4]. Only histopathological analysis of renal biopsy showing typical changes for tubulointerstitial/interstitial nephritis or for glomerulonephritis confirms the diagnosis [5,6]. Renal biopsy was not performed in this case because of its potential complications and the patient’s renal function tests spontaneously improved with antibiotic and symptomatic treatments of the infection.

To conclude, this report adds further information relating to rare cases of acute nephropathies due to STM infection published in the literature and should prompt the physician to consider it, particularly when renal signs are associated with intestinal symptoms, in order to make a suitable analysis and begin an appropriate treatment quickly.

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Incidental living donor nephrectomy: a unique expansion of the donor pool

Sir, Renal transplantation remains the most desirable form of treatment for patients with renal failure, yet the number of donors falls drastically short of the need. In 2002, there were 53,704 potential renal recipients in the United States and only 11,863 renal donors (see the 2003 Annual Report of the US Scientific Registry of Transplant Recipients and the Organ Procurement and Transplant Network: Transplant Data 1993–2002, available at http://www.optn.org/AR2003). In almost 50 years of clinical renal transplantation, the rate-limiting factor has been the availability of a suitable donor. The evolution of the donor pool has paralleled the elucidation of the phenomenon of allograft rejection, beginning with the unsuccessful use of cadaver donors to identical twin, living-related, cadaveric and, eventually, living non-related sources. Although there have been unique donor/recipient transplants in the past, this is believed to be the first reported case of planned incidental nephrectomy for transplantation [1].

Case. A 51-year-old female presented for evaluation of faecal vaginal discharge. Computerized tomography (CT) demonstrated a colovaginal fistula. The patient underwent uneventful sigmoid resection with fistula repair. She was readmitted 5 weeks post-operatively with a retroperitoneal abscess, which was drained percutaneously. Following recovery from adult respiratory distress syndrome, the patient was discharged. She returned 1 week later with increasing output from the abscess drain, which was determined to be urine. Retrograde pyelography demonstrated obstruction of the ureter at the level of the fourth lumbar vertebrae without evidence of extravasation. A drain study revealed a normal proximal ureter. Subsequent CT showed resolution of the abscess.

Options of repair were discussed with the patient, including primary uretero-ureterostomy, Boari flap, transureterostomy, nephrectomy with auto-transplantation, simple nephrectomy or simple nephrectomy with intention to donate the kidney. Because of previous complicated hospitalizations, she desired the route that would lead to the quickest resolution of her problem with the minimum of time and risk involved. She elected simple nephrectomy with intention to donate the kidney for transplantation. The organ transplant team at the University of Wisconsin in Madison was contacted and, after relating the patient’s history, it