as well as a pauci-immune segmental necrotizing glomerulonephritis and mesenteric arteritis [5]. How infections produce ANCA is not clear but chronic suppurrative infections comprise mainly neutrophils, and the injection of rats with apoptotic (but not non-apoptotic) neutrophils generate ANCA [6]. Furthermore, infections themselves result in the surface expression of proteinase 3 and myeloperoxidase, and ANCA binds to these and activates the neutrophils resulting in a damaged vascular endothelium [7].

ANCA sometimes occur with malignancy or after antibiotics, but the temporal relationship in this patient is inconsistent with these as pathogenetic factors. The presence of arteriolitis in the initial renal biopsy, and the demonstration of an ischaemic bowel without atherosclerosis or embolism are more consistent with an overlap syndrome with polyarteritis nodosa rather than the diagnosis of microscopic polyangiitis alone.

Conflict of interest statement. None declared.

Department of Medicine (Austin Health/Northern Health) University of Melbourne
The Northern Hospital, Epping VIC 3076 Australia
Email: jasavige@unimelb.edu.au


doi:10.1093/ndt/gfl152

1996; 335: 16–20
1994; 120: 12–17
1996; 335: 16–20
1994; 95: 12–17
1994; 95: 12–17

Advance Access publication 24 July 2006

Pathological rupture of spleen in a haemodialysis patient due to tuberculosis

Sir,

A traumatic rupture of the spleen has been described as a condition with grave consequences, if unrecognized and untreated. The spleen can get ruptured in the following circumstances: due to trauma to a diseased spleen; trauma to a normal spleen; spontaneous rupture of a diseased spleen (pathological rupture) and spontaneous rupture of a normal spleen (spontaneous rupture) [1,2].

The true incidence of pathological rupture is unknown. A Medline search confirmed that 352 cases were reported between 1966 and 2000 [3]. The causes were wide-ranging, from infective, haematological, metabolic, drug-induced to iatrogenic.

Tuberculosis as a cause of pathological spleen rupture has been described in a few case reports [3]. No case report has been reported of a haemodialysis patient. We report a 27-year-old male patient with a diagnosis of hypertension, end-stage renal disease, on maintenance haemodialysis from August 2005, who developed sudden onset of pain in the abdomen, vomiting, and shock following a session of haemodialysis, in which heparin was also given. He had no prior complaints of fever, night sweats, chill, weight loss or anorexia. There was no other organomegaly or lymphadenopathy. A plain radiograph of the abdomen showed opacification of the left half, with relative paucity of bowel loops, due to fluid collection in the left half of the abdomen. A CT scan showed the presence of peri-splenic haematoma and blood collection in the abdominal cavity. The chest radiograph was normal. An emergency splenectomy was done along with a blood transfusion, as about 1.5 l of blood was evacuated from the abdominal cavity. A histopathological examination showed the presence of granulomas with Langerhans giant cells (Figure 1). Ziehl–Neelsen staining did not reveal any acid-fast bacilli. He was discharged on anti-tuberculous therapy, and made a speedy recovery.

Oedema of the spleen may occur in uraemia [4]. The rupture appears to be precipitated by uraemic coagulopathy and the use of heparin, coupled with tuberculosis infection. The tuberculous infection of the spleen has been reported in both immuno-competent and immuno-suppressed patients, albeit in the form of case reports [5]. It appears that there is no clear-cut way of diagnosing splenic tuberculosis other than a chance discovery on laparotomy and subsequent histopathological examination.

Conflict of interest statement. None declared.

Fig. 1. Granulomas with Langerhans giant cells.
Topiramate induces type 3 renal tubular acidosis by inhibiting renal carbonic anhydrase

Sir,

We report a case of mixed (type 3) renal tubular acidosis (RTA) associated with the anti-convulsant drug topiramate used for migraine prophylaxis. A 47-year-old woman treated with topiramate (150 mg/day) since 12 months for invalidating migraine was referred for a metabolic acidosis evidenced in a routine blood sampling. She complained of muscle weakness and bone pain. Clinical examination showed weight loss (−6 kg in 4 months) and joint sensitivity. Blood analyses confirmed a mild hyperchloremic metabolic acidosis (plasma HCO₃⁻ 19.0 mEq/l; plasma anion gap, 8 mEq/l) with hypokalaemia (3.2 mEq/l) and normal renal function. Plasma HCO₃⁻ before topiramate administration was normal. The urine pH was 6.0 with a positive urinary anion gap (UAG, +39 mEq/day), positive β₂-microglobulinuria (2.1 mg/l) and a low urinary citrate excretion (0.7 mM/24 h). Serology and auto-immune markers were negative. Echography showed no kidney calcifications. The hyperchloremic metabolic acidosis with normal glomerular filtration rate (GFR) and positive UAG indicates RTA, associated with both proximal (β₂-microglobulinuria) and distal (hypocitraturia) tubular dysfunction. The normal blood analyses before the introduction of topiramate suggests that these disorders result from tubular dysfunction caused by inhibition of carbonic anhydrase (CA).

Type II CA (CAII) plays an essential role in the reabsorption of ultrafiltered HCO₃⁻ by the proximal tubule (PT) and the net urinary acidification by α-type intercalated cells of the distal nephron (Figure 1). It also provides the H⁺ for extracellular acidification during bone resorption by osteoclasts. Deficiency in CAII, either inherited (marble brain diseases; OMIM #259730) or acquired (e.g. acetazolamide-induced), is associated with a mixed proximal and distal RTA (type 3 RTA), without evidence for generalized PT dysfunction [1,2]. Topiramate is a sulfamate-substituted monosaccharide that is structurally related to acetazolamide (Figure 1). As such, it inhibits CAII more effectively than other isoforms [3]. Long-term inhibition of CAII by topiramate may thus disturb the homeostasis of both the

---

Fig. 1. Role of CA isoforms in the kidney and structure of topiramate. (A) Pathways involved in HCO₃⁻ reabsorption and H⁺ secretion in PT cells and α-type intercalated cells of the collecting ducts, respectively. Cytosolic type II CA is distributed in both cell types. Note that PT cells also express type IV CA in the apical brush border and basolateral membrane. (B) Comparative structure of topiramate and acetazolamide. Both molecules present a sulfonamide group responsible for the inhibition of CA activity.