Renal involvement in Cogan’s syndrome

Sir,

Nephrologists are accustomed to managing patients with systemic vasculitis. However, some of the rarer vasculitides may be primarily non-renal in their target organ damage and present with a long prodrome. We would like to briefly discuss one such syndrome that may not be well known to the general nephrological community.

Our patient presented aged 32 when, with no risk factors for coronary atheroma, he sustained a myocardial infarction. Aged 40, he presented with fever, bilateral uveitis and renal impairment (serum creatinine 420 mmol/l). Inflammatory markers and autoimmune profile including ANA, ANCA and anti-GBM antibody were normal. Renal biopsy revealed a diffuse proliferative glomerulonephritis with mesangial hypercellularity, irregular granular deposits of C3 in both the mesangium and capillary loops but no features of vasculitis or crescents. He was treated with a course of antibiotics that coincided with the resolution of his symptoms. His serum creatinine improved to 180 mmol/l and remained stable. Over the next 12 years he developed left hemiparesis; bilateral sensorineural deafness needing a cochlear implant; a second myocardial infarction with ventricular arrhythmia needing coronary stenting and an implantable cardioverter defibrillator.

Aged 52, he presented with bilateral pleural effusion, a widespread scaly erythematous rash and generalized lymphadenopathy. CRP was 64 mg/l (N < 10) and the serum creatinine 270 mmol/l. Pleural fluid was haemorrhagic showing only inflammatory cells. Echocardiography revealed severe left ventricular dysfunction. Skin and lymph node biopsy revealed leukocytoclastic vasculitis and dermatopathic lymphadenopathy, respectively.

This clinical presentation was consistent with a diagnosis of Cogan’s syndrome (CS). He was commenced on intravenous methyl prednisolone (0.5 g for 3 days), followed by oral prednisolone (1 mg/kg/day) and oral cyclophosphamide (2 mg/kg/day). Azathioprine was substituted for the cyclophosphamide at 3 months. There was significant clinical improvement returning to his baseline physical function at 6 months although still restricted by his cardiac disease. His serum creatinine had stabilized at 220 mmol/l after 6 months of treatment.

CS is a rare multisystem disease of unknown cause predominantly affecting young adults. Recent studies suggest an autoimmune process directed against the Cogan’s peptide, which is homologous to autoantigens such as Connexin 26 and DEP-1/CD148 on the sensory epithelia of inner ear and endothelial cells, as well as other antigens such as SSA/Ro, lamin, ladinin, kinesin and calcineurin [1,2].

CS comprises the association of inflammatory eye disease and audiovestibular dysfunction. However, firm diagnostic criteria have not been established. The audiovestibular disturbance presents with Meniere’s-like illness and progressive sensorineural deafness which is irreversible in ~50–85% of the patients. The eye signs include interstitial keratitis, scleritis, episcleritis and uveitis [3–5].

Systemic manifestations are seen in ~72% of cases and are usually non-specific but may include lymphadenopathy, hepatosplenomegaly, aortitis, coronary arteritis, pleuritis and pulmonary nodules [3,5]. A systemic vasculitis may occur in ~10% of cases usually affecting medium-sized vessels although any sized vessel may be affected [6].

Renal disease is poorly described in the literature. In a review of 78 cases, 14 had abnormal urinalysis, and three had renal impairment. Histopathological findings were available in seven of these patients and were abnormal in five patients. The abnormal findings included glomerulopathy, renal vasculitis, gross cortical scarring and renal infarction [5]. Corticosteroids are used topically for ocular inflammation and systemically for ear manifestations. Treatment of the

cardiovascular manifestations is similar to that of systemic necrotizing vasculitis [7]. Early diagnosis and treatment can significantly reduce morbidity and mortality. Therefore we feel that nephrologists should consider this rare condition in the differential diagnosis of patients presenting with ocular–auditory and renal symptoms.

Conflict of interest statement. There is no conflict of interest to be declared by any of the authors.


When the kidney catches a cold: an unusual cause of acute renal failure

Sir,

We report the case of a 51-year-old man with no medical history and no treatment who developed acute renal failure (ARF) after cold water immersion. He was admitted to hospital in August after nearly drowning in a lake while trying to save his dog which was drowning. When he got back to the shore, he was exhausted and fainted briefly. He was transported to the hospital in a warm ambulance. Arriving at the hospital 1 h later, he was conscious but sleepy; his rectal temperature was 35.8°C, his blood pressure 130/70 mmHg and there was no haemodynamic failure during the observation period. Physical examination showed no abnormality. Laboratory studies showed: serum creatinine, 141 µmol/l; urea, 6.8 mmol/l; C-reactive protein <5 mg/l; leukocytosis count, 18 000/mm³; aspartate aminotransferase, 31 U/l; alanine aminotransferase, 27 U/l; creatine phosphokinase (CPK), 135 U/l; ionogram and coagulation functions were normal. An arterial blood gas sample showed moderate metabolic acidosis and hypoxaemia (pH 7.33, HCO₃⁻ 16.6 mmol/l, PCO₂ 32.6 mmHg and PO₂ 60 mmHg). Electrocardiogram and chest radiography were normal. The patient was discharged after a 24 h observation period.

He was re-admitted 5 days later, complaining of being tired and anuric. Biological analysis revealed ARF (creatininaemia 1600 µmol/l, urea 38 mmol/l) with hyperkalaemia (6.1 mmol/l), hyperphosphataemia (3.12 mmol/l), normocalcaemia (2.27 mmol/l) and metabolic acidosis (pH 7.34, bicarbonates 18.4 mmol/l). There was no elevation of muscle and hepatic enzymes, no red or white blood count disorder; blood prostates and albumin were respectively 61 and 33.7 g/l, and proteinuria was 0.33 g/24 h. There was no infectious or immunological biological abnormality. Urinary analysis showed <1000 red blood cells/ml, 20 000 leukocytes/ml and aserter culture was sterile. Urinary ultrasonography was normal, and Doppler ultrasonography showed no stenosis of the renal arteries. The patient needed three sessions of dialysis over the succeeding 3 days and then renal function recovered spontaneously. Creatininaemia was 652 µmol/l 3 days after the last haemodialysis session, 125 µmol/l 10 days later and 90 µmol/l 7 weeks later. Given the clinical course of this ARF, no renal biopsy was performed and the diagnosis of acute tubular necrosis was retained.

ARF associated with severe hypothermia has been reported widely, but is usually the direct consequence of associated overt haemodynamic failure and/or rhabdomyolysis [1]. ARF related to cold water immersion has to our knowledge only been reported once, by Yoshitomi et al. [2], who described the case of a 27-year-old patient who developed histological acute tubular necrosis after nearly drowning in a lake, and then lying on the lake shore for 2 h while the external temperature was –5°C. Interestingly, in our case, the accident occurred in summer when the water temperature was not very cold, and our patient probably experienced only moderate hypothermia as assessed by his rectal temperature (35.8°C) upon arrival at the emergency room. Thus our observation illustrates that the association of prolonged water immersion with even moderate hypothermia can trigger acute tubular necrosis in a patient not particularly at risk of ARF. The mechanism responsible for the renal hypoperfusion is unclear. Water immersion increases venous return and thereby raises cardiac output, and natriuresis [3]. Conversely, removal from water acutely decreases cardiac output. Hypothermia may blunt or delay the normal haemodynamic response that allows maintenance of an adequate renal blood flow in this setting. In an animal experimental model, hypothermia, in contrast, has been shown to prevent ischaemia–reperfusion-induced renal injury [4]. Thus, rather than hypothermia per se, rewarming coincident with renal hypoperfusion after removal from water could be involved in the pathogenesis. Hypoxaemia associated with near drowning could have also played a role in the renal insufficient oxygen delivery. Whatever the mechanism involved, nephrologists should be aware of this rare cause of ARF.

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