Renal haemosiderosis: an unusual presentation of acute renal failure in a patient following heart valve prosthesis

Sir,
Heart valve replacement can be complicated by endocarditis, arrhythmias, embolic disease and traumatic intravascular haemolysis due to destruction of erythrocytes. Acute renal failure (ARF) is common shortly after the operation, but is very rare during the later rehabilitation phase. We present a patient with an aortic valve replacement complicated by ARF due to renal haemosiderosis with concurrent urinary tract infection during the rehabilitation period after discharge.

Case. The patient had an aortic valve replacement twice with a mechanical St Jude Medical prosthesis at the age of 48 because of destructive bacterial endocarditis. Eighteen years later and 1 month prior to admission to our clinic, a haemolytic anaemia was diagnosed due to a paravalvular leak of the mechanical prosthesis leading to intra-vascular haemolysis. The serum creatinine at this time was 112 µmol/l. The mechanical aortic valve was replaced by a Shellhigh Composite Xenograft Bioprosthesis and he was transferred to a rehabilitation clinic.

His creatinine at entry into the rehabilitation clinic was 124 µmol/l with a normal urine microscopy. Ten days later, he suddenly developed a fever with an increase of C-reactive protein but without an elevated white blood cell count, despite a shift to the left. Urinalysis showed the presence of leukocytes with microhaematuria. Subsequently, therapy with ciprofloxacin 250 mg b.i.d. was initiated because of the presence of Escherichia coli in the urine culture. Blood cultures remained negative. Despite the antibiotic treatment, renal function deteriorated further and the patient was transferred to our institution for the evaluation and treatment of ARF.

At admission, the patient was in poor general condition, but haemodynamically stable with a blood pressure of 140/80 mmHg. Urine output was almost zero, the serum creatinine increased to 730 µmol/l with a urea of 41.4 mmol/l and a potassium of 5.6 mmol/l. There were no obvious signs of ongoing haemolysis even in the blood screen, but the haemoglobin level was only 91 g/l. Thus, three consequent sessions of acute haemodialysis were performed. In addition, the patient received ceftriaxone for the previously documented urinary tract infection.

A kidney biopsy was performed 3 days after admission (Figure 1). The biopsy showed marked tubular and interstitial haemosiderosis with tubular damage, slight chronic tubulo-interstitial inflammation and fibrosis. There were no signs of either acute tubular necrosis or acute tubulo-interstitial nephritis, glomerulonephritis or cholesterol emboli. Prussian blue staining demonstrated heavy haemosiderin accumulation mostly within proximal and distal tubular cells.

Following the initial series of haemodialysis, the patient’s serum creatinine spontaneously improved and returned to 117 µmol/l on day 9 after admission. To potentially reduce oxidative stress by chronic iron deposits, treatment with acetylcysteine 200 mg b.i.d. was initiated. Two years after the episode of ARF, the patient remains in excellent health with well-preserved kidney function.

Renal haemosiderosis is a well-known complication of intravascular haemolytic anaemia, as for example in cases of traumatic vascular haemolytic anaemia complicating a heart valve operation or in paroxysmal nocturnal haemoglobinuria (PNH) [1,2]. To date, renal haemosiderosis has been studied mostly in patients with PNH. Yet only a few patients with PNH and renal haemosiderosis present with ARF [3]. Of the seven PNH patients with ARF described, three had concomitantly a urinary tract infection caused by E. coli. All patients underwent complete recovery of their renal function much like our patient. Only one post-mortem study investigated the clinical and morphological implications of renal haemosiderosis in patients with a heart valve prosthesis without known haemolytic anaemia [4]. From a total of 33 patients, 17 patients had variable degrees of renal haemosiderin deposits. Prior to death, the episodes of renal failure following valve replacement were more pronounced...
in patients with intra-renal haemosiderin deposits than in subjects without deposits. The frequency of cardiac failure was not different. Therefore, we postulate a probable link between renal haemosiderosis, possibly aggravated by co-existing urinary infection, and late ARF in patients with heart valve replacement, as was the case in our patient.

The pathophysiological mechanism of this association, however, is unclear. The mechanism of iron deposition in intravascular haemolysis is well known [5]. The role of haemosiderin in acute renal toxicity remains controversial. Ferrous iron catalyses the Fenton reaction, which leads to generation of the highly reactive cytotoxic hydroxyl radicals. Furthermore, it has also been shown that lipid peroxidation of polyunsaturated fatty acids occurs in the kidneys of experimental animals with iron overload. Peroxidatic alterations of the polyunsaturated fatty acids of membrane phospholipids can result in specific abnormalities of organelle function leading to cell injury or cell death [6].

Since a pathogenetic role for such reactive oxygen species could not be excluded, we attempted a novel medical treatment for renal haemosiderosis. In analogy to contrast media-induced renal failure [7], we administered N-acetylcysteine to the patient.

Conflict of interest statement. None declared.

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Non-oliguric acute renal failure and abortion induced by metamizol overdose

Sir,

Metamizol is a non-narcotic, analgesic and anti-pyretic pyrazolone derivative which belongs to the non-steroidal anti-inflammatory class of drugs. This drug is used in Germany, Spain and Italy, and in many South American countries. It is prohibited in other countries because of its capacity to induce agranulocytosis and aplastic anaemia. In addition to its effects on bone marrow, metamizol may also cause cutaneous reactions, allergic idiosyncratic reactions such as bronchospasm, anaphylactic shock, toxic epidermal

Fig. 1. The epithelial cells of the proximal tubules (left) show a variable height and are often packed with brown granules. The interstitium is broadened with collagenous fibres and a slight leukocytic infiltrate, focally with the brown pigment (lower centre). The glomerulus has a normal structure. Inset: the brown pigment is coarse granular (left), prussian blue-positive (right) and situated in the cytoplasm of the proximal tubule (haematoxylin–eosin and prussian blue (inset on the right side) (bar 50 µm and inset 10 µm).