Rapid deterioration of renal function in a long-term allograft recipient with recurrent IgA nephritis—is it the only cause?

Keywords: allograft dysfunction; cholesterol emboli; renal transplantation; tachycardic episodes

Case

A 74-year-old renal transplant patient was admitted with an acute rise in blood pressure, tachycardic episodes and increase in S-creatinine. Renal transplantation had occurred 25 years previously. The original renal disease was mesangio-proliferative glomerulonephritis. Renal transplant function was stable over 25 years, until the last check-up 4 weeks ago (S-creatinine 1.5 mg/dl) and immunosuppressive treatment consisted of low-dose steroids for the previous 5 years. Blood pressure was adequately controlled with β-blocker, calcium-antagonists and diuretics. The most recent history revealed a common cold with rhinitis followed by rising macrohaematuria and an increase in proteinuria. On admission, the patient was in good health (height 175 cm, body weight 74 kg), temperature was regular, blood pressure elevated with 210/100 mmHg, heart rate 100/min and only minor peripheral oedema. Cardiovascular, abdominal and neurological examination was normal.

Pathological laboratory findings were an S-creatinine of 2.41 mg/dl, uric acid 8.4 mg/dl, haemoglobin 11.4 g/dl, C-reactive protein 69 mg/l; all other parameters were normal including electrolytes and differential blood count. Urine dipstick showed three-times positive protein and erythrocytes. Urine microscopy revealed dysmorphic erythrocytes (25 erythrocytes per high-power field), and erythrocyte casts; 24 h proteinuria was 3.8 g. Electrocardiogram and chest X-ray revealed no specific pathological findings. A colour Doppler ultrasound of the transplanted kidney showed regular arterial and venous perfusion, resistance indices were in normal level and there were no signs of a renal artery stenosis.

To further clarify the cause of the acute deterioration of transplant function, a renal transplant biopsy was performed. The renal allograft biopsy showed the given images (Figures 1 and 2).

Question

- What is the diagnosis?
The renal biopsy showed recurrence of IgA-glomerulonephritis, with mesangial enlargement and IgA and C3 deposits in immunohistology and concomitant cholesterol embolism. SV40 staining and C4d were negative. Surprisingly, the biopsy revealed significant cholesterol embolism. Peripheral eosinophil count and complement level were normal. Since no invasive angiography had previously been done, a native pelvic CT for evaluation of aortic, iliac or renal transplant arterial calcification was performed. This showed severe vascular calcification of the aorta, the main allograft artery and the large pelvic arteries (Figure 3).

The rapid deterioration of renal function is most probably due to the cholesterol embolism and less likely due to the recurrent IgA-GN. The patient was treated with antihypertensives, including ACE-inhibitors, statins and aspirin therapy. At discharge, blood pressure was 130/80 mmHg, heart rate 64/min, S-creatinine was 2.40 mg/dl and diuresis was normal.

Despite intensive treatment for cardiovascular risk factors, the patient was back on haemodialysis 1 year later.

**Comment**

Cholesterol atheroembolic disease is a multisystem disorder generally involving the skin, muscle, kidneys, gastrointestinal tract and central nervous system. It is characterized by the occlusion of small arteries, with cholesterol emboli deriving from the aorta and the larger arteries. It is a well-known cause of acute renal failure in native kidneys, especially after angiography or other vessel intervention, with a poor prognosis resulting in chronic renal failure or death [1]. The high blood flow and the proximity of the kidney transplant to the abdominal aorta and pelvic arteries make them a potential target for cholesterol embolism. Cholesterol embolism of the renal allograft may arise from

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**Fig. 1.** (A) Glomerulus with mild mesangial expansion (Masson trichrome stain, original magnification 160×). (B) Diffuse mesangial deposition of IgA (direct immunofluorescence, original magnification 160×).

**Fig. 2.** Interlobular artery with complete obliteration of the lumen by cholesterol clefts (Masson trichrome stain, original magnification 100×).

**Fig. 3.** Native CT-scan of patient 1 with diffuse vascular calcification of the recipient’s pelvic arteries and the allograft renal artery.
either donor or recipient vessels and causes a varying degree of renal functional impairment: from moderate loss of renal function to severe renal failure with oligo-anuria [2].

The histological diagnosis of cholesterol atheroembolic renal disease is based on the presence of characteristic intraluminal biconvex needle-shaped clefts in the small arterial blood vessels, typically 150–200 μm in diameter. They are classically seen in arcuate and interlobular arteries, and less commonly in glomerular arterioles. Initially, an incomplete occlusion of the affected vessel with perivascular accumulation of inflammatory cells can be observed, whereas later, the vessels are occluded from intimal hyperplasia and perivascular fibrosis and concomitant glomerular and interstitial scarring. The pathological lesions may be overlooked, since cholesterol embolisms are often single and small. Superficial, smaller vessels might contain a lower burden of emboli than larger arteries of the renal medulla. As arcuate and interlobular arteries are often involved, superficial biopsies, without arteries, might show only non-specific changes of renal function, which may be accompanied by rather unspecific symptoms (e.g. fever, myalgic pain, hypertension), the inconsistent presence of eosinophilia, eosinophiluria and hypocomplementaemia or clinical signs suggestive of small vessel obstruction [2,3].

In transplant patients, the systemic signs and symptoms of cholesterol embolization are rarely seen, and therefore cholesterol embolism may be an unrecognized cause of renal graft dysfunction [2,4].

There are two different clinical courses of cholesterol embolism in the renal allograft. In one case, the cholesterol embolism occurs early after transplantation, usually associated with initial non-function. This cholesterol embolism occurs before or during organ procurement, or during the anastomosis with atheromatous recipient vessels. The late cholesterol embolization originates from the recipient’s arterial vessels; it may be spontaneous, or caused by plaque rupture with systemic anticoagulation treatment, or more frequently, it is associated with the traditional predisposing factors [5–7].

In an overview of the literature, graft dysfunction and subsequent graft loss are common in patients with cholesterol embolism of donor origin [8]. The earliest description of the disease is by Cosio et al. [3], who found cholesterol embolism in a nephrectomized allograft of a patient suffering from acute oligo-anuria in the immediate post-operative period. It may become more prevalent, as donors of increasing age and recipients with advanced atherosclerosis are accepted for transplantation. In the case of recipient origin, the number of patients with loss of allograft function was less, for example 4 out of 13 patients [9].

As no effective treatment for cholesterol embolism is available, prevention is most important. Clinical awareness, careful evaluation of donors and recipients, cautious organ procurement and implementation of intra-operative allograft biopsies prior to transplantation allow for early detection and prevention of this complication. In renal allograft recipients, underlying risk factors for atherosclerosis should be strictly controlled and non-invasive diagnostic procedures should be preferred.

Conflict of interest statement. None declared.

References


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