Renal artery thrombosis with acute renal failure after withdrawal of angiotensin converting enzyme inhibitor: a case report

Sir,
Acute renal failure is a well known complication after treatment with angiotensin converting enzyme inhibitors (ACEIs) or angiotensin II antagonists [1,2] and usually resolves after rehydration and withdrawal of diuretics. Thrombosis of the renal arteries in association with acute renal failure during ACEI therapy is unusual and may be causally related to severe hypotension [3,4]. We report a case where an initial and reversible ACEI-induced acute renal failure was succeeded by another episode of acute renal failure due to bilateral renal artery occlusion and renal artery thrombosis after the withdrawal of ACEI.

Case. A 67-year-old man (a non-smoker) presented with untreated hypertension (blood pressure 194/118 mmHg left arm), normal serum creatinine (116 µmol/l, reference 60–125 µmol/l), systolic murmur over both carotid arteries and left subclavian artery, blood pressure somewhat lower on the right compared with the left arm, without symptoms of claudicatio intermittens or coronary disease. Anti-hypertensive combination therapy with irbesartan 150 mg and hydrochlorothiazide 12.5 mg once daily was insufficient
(the blood pressure was 174/100 mmHg) and an increase in serum creatinine (190 μmol/l) was noted after 3 months. The medication was changed to enalapril 20 mg and hydrochlorothiazide 12.5 mg once daily and diltiazem depottablets 180 mg once daily. Four weeks later he was admitted to the hospital with acute renal failure, anuria and clinical signs of dehydration. The blood pressure at admittance was 165/60 mmHg, serum creatinine 427 μmol/l, urea 40.4 mmol/l and serum potassium 8.8 mmol/l. Ultrasonography showed normal kidney size (10–11 cm) and normal parenchyma bilaterally, but the renal circulation was not evaluated. Antihypertensive drugs were withdrawn. Anti-coagulation was not prescribed. After rehydration and standard potassium lowering therapy, including two dialysis sessions, diuresis resumed as expected within 24 h. After 9 days serum creatinine was 297 μmol/l. No hypotension episodes were noticed, the lowest and highest blood pressures recorded in this period were 195/92 and 228/89 mmHg respectively.

On day 11 diuresis suddenly declined, and on day 12 the patient became anuric with symptoms of pulmonary oedema. The blood pressure was persistently elevated in the observation period (190–230/100–120 mmHg) and serum creatinine increased to 406 μmol/l. Renal angiography on day 13 showed bilateral renal artery occlusion, and successful blind recanalizing and stenting of the right renal artery was performed. Because of persistent hypertension, a second angiography was performed on day 24, and the left renal artery was successfully recanalized, dilated and stented. Contrast infusion showed a mobile thrombus distal to the stent (Figure 1). Subsequent thrombolysis with recombinant tissue plasminogen activator (rt-PA) was undertaken and anticoagulation was prescribed with heparin infusion for 24 h followed by triple therapy with dalciparin for 3 days, ticlidopidin for 3 weeks and long-term acetylsalicylic acid.

After the final procedure day 24 the blood pressure rapidly normalized, and was 163/81 mmHg at dismission day 33 on antihypertensive treatment with labetalol 200 mg three times daily and nifedipine depottablet 30 mg once daily. Serum creatinine at discharge from hospital was 147 μmol/l, and was 120 μmol/l and 123 μmol/l after 1.5 and 6 months, respectively. Contrast enhanced computed tomography at 6 months demonstrated bilateral open stents and normal parenchymal contrast distribution without any signs of renal infarction.

Comment. Renal artery thrombosis after the withdrawal of ACEIs has not been reported previously. Our patient experienced a sudden unexpected second anuric episode 11 days after ACEI withdrawal, and no hypotensive episodes that could have predisposed the patient to thrombosis preceded this event [5]. Since the patient had normal diuresis after initial rehydration and withdrawal of ACEI, at least one of the kidneys would be expected to have sufficient blood supply, although this was not shown by Doppler or angiography at that time. In addition, his blood pressure was persistently elevated after withdrawal of the ACEI and the patient developed pulmonary congestion after the second anuric episode, both observations indicating that the renin-angiotensin system was activated.

Although the relationship between ACEI withdrawal, stimulation of the renin-angiotensin-aldosterone system and the subsequent renal artery thrombosis is hypothetical, the subsequent demonstration of bilateral renal artery occlusion and left renal artery thrombus indicate a potentially deleterious change in the fibrinolytic balance when ACEIs are withdrawn in patients with activated renin-angiotensin systems. Haemodynamic changes associated with turbulence and a drop in renal perfusion pressure distal to the renal artery stenoses may also facilitate acute thrombosis. However, thrombosis is usually associated with episodes of systemic hypotension [3], which were not observed in our patient.

In vitro and in vivo data have supplied considerable evidence that angiotensin II has prothrombotic effects [5]. Angiotensin II and aldosterone have been shown to stimulate the expression of plasminogen activator inhibitor-1 (PAI-1), and treatment with ACEI reduces the PAI-1 activity [6]. ACEIs seem to exert their anti-thrombotic effects partly through inhibition of platelet aggregation and concurrent stimulation of the fibrinolytic pathway [7]. In addition, they appear to preserve the fibrinolytic balance in the recovery phase after an acute myocardial infarction [8]. Chabielska et al. [9] also demonstrated captopril and losartan to have direct antithrombotic effects in rats.

Fig. 1. Thrombus with peripheral dislocation in the left renal artery (arrow) after recanalizing and stenting of a central highgraded stenosis.
In conclusion, we speculate that during the stimulation of the renin-angiotensin system following ACEI withdrawal, the antifibrinolytic effects of angiotensin II and aldosterone may have facilitated acute thrombosis of a significant renal artery stenosis in the left kidney in our patient. When unexpected acute renal failure occurs the diagnosis and invasive endovascular reconstruction of renal artery occlusion may restore the kidney function up to 24 days after the anuric episode. Our observation also suggests that prophylactic anticoagulation should be given to patients with acute renal failure in association with critical renal artery stenosis.

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