Case Report

Acute renal cortical necrosis caused by an antifibrinolytic drug (tranexamic acid)

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Introduction

Two synthetic derivatives of the amino acid lysine, aminocaproic acid and tranexamic acid, have antifibrinolytic activity in humans and frequently are used to reduce bleeding in a variety of clinical conditions [1]. The main risk involved with the use of these drugs is that thrombotic complications will result from the inhibition of fibrinolysis, which is a natural mechanism of defence against the formation of a thrombus. Thromboembolic complications after aminocaproic acid administration, including pulmonary emboli, peripheral gangrene and major arteriovenous occlusion of extremities, coronary and gastrointestinal tract vasculature, have been described previously [2–4]. We describe a case of tranexamic acid-induced acute renal cortical necrosis with glomerular thrombosis.

Case

A 37-year-old man was transferred to the renal unit due to acute anuria and azotaemia. He had a history of treated pulmonary tuberculosis ~15 years previously with sequelae of pulmonary bronchiectasis. He had been well until 9 days earlier, when he developed a moderate amount of haemoptysis. He was admitted to the department of chest surgery and treated with the recommended dose of intravenous tranexamic acid (3 g/day) for 5 days. At admission, his blood pressure and renal function were normal (BUN 18 mg/dl, serum creatinine 0.9 mg/dl, no proteinuria, no haematuria). After admission, the amount of haemoptysis was decreased and his clinical course was stable. However, 6 days later, he suddenly developed anuria and azotaemia (BUN 68 mg/dl, serum creatinine 6.9 mg/dl). His coagulation profile was normal (bleeding time 3 min, prothrombin time 13.1 s, partial thromboplastin time 35 s, fibrin split products 10 µg/ml, fibrinogen 550 mg/dl, protein C 50%, protein S 87%). No schistocytes was found on a peripheral blood smear. FANA, ANCA and cryoglobulin were all negative. Renal duplex sonogram and cardiac echocardiogram showed normal findings.

To investigate the aetiology of acute renal failure (ARF), renal biopsy was performed 11 days after admission. Light microscopy showed infarction, with fibrin thrombi in intraglomerular capillaries and arterioles (Figure 1). There was no specific immunofluorescent deposit on the glomerulus. Electron microscopy could not delineate any glomerular and vascular structure. CT scans showed lack of enhancement of the renal cortex with enhancement of the renal medulla (Figure 2).

He was treated with haemodialysis for 2 weeks following diagnosis of acute renal cortical necrosis. His renal function slowly improved and he was discharged 3 weeks later with stable renal function (24 h urine 1800 ml, serum creatinine 3.6 mg/dl).

Discussion

Acute renal cortical necrosis represents a relatively rare cause of ARF in which a diffuse necrosis of renal cortical structure is observed histologically [5]. Even though some cases of partial recovery have now been observed, as in our patient, most patients developing acute renal cortical necrosis had been known to undergo a severe renal ischaemic insult with non-reversible loss of renal function [5]. Complications of late pregnancy (abruptio placentae and septic abortion) are responsible for acute renal cortical necrosis in > 50% of all reported cases [6]. The various non-obstetric causes include sepsis with disseminated intravascular coagulation, severe hypotension and microangiopathic haemolytic anaemia [5].
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Fig. 1. Renal biopsy specimen showing thrombosis of intraglomerular capillary and arteriole (Masson-Trichrome stain, ×300).

Fig. 2. Contrast enhanced CT scans showed lack of enhancement of the renal cortex (arrows) with enhancement of the renal medulla.

There have been two reports of glomerular capillary thrombosis and cortical necrosis caused by aminocaproic acid [7,8]. In those cases, acute renal cortical necrosis occurred in hypotensive elderly patients, which were risk factors for ischaemic renal insult. However, in the present case, acute renal cortical necrosis developed in the absence of such risk factors for ischaemic ARF.

The normal bleeding time, prothrombin time and partial thromboplastin time seemed to rule out sepsis with disseminated intravascular coagulation as a primary cause of cortical necrosis. We also could not find any evidence of microangiopathic haemolytic anaemia, such as schistocytes and reticulocytosis, in a peripheral blood smear. Normal levels of protein C, protein S and negative FANA, ANCA and cryoglobulin tests also ruled out other secondary causes of glomerular thrombosis and ARF.

Antifibrinolytic drugs have been known to exert variable effects on the kidney. Hruby et al. [9] reported
beneficial effects of aminocaproic acid as a protease inhibitor in experimental anti-GBM nephritis in the rat. They did not find any appreciable deposition of fibrin thrombi in glomeruli of nephritic rats. However, antifibrinolytic drugs traditionally were regarded as pronephritic due to their interference with degradation of fibrin. Foster et al. [10] reported post-infectious crescentic glomerulonephritis with thrombi formation which seemed to be exacerbated by concomitant tranexamic acid therapy. Our experience also clearly indicates that antifibrinolytic drugs can produce acute renal cortical necrosis in an otherwise normal kidney and we must be aware of this potentially dangerous complication of this drug.

References


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