Renal infarction due to combination of fibromuscular dysplasia and factor V Leiden mutation

Sir,

The clinical presentation of acute onset of nausea, vomiting and flank pain in combination with acute elevation of blood pressure should raise high suspicion of renal infarction. We describe a patient with these symptoms and signs who had renovascular disease due to an unusual origin.

A 37-year-old former healthy man was admitted to the hospital due to acute and severe pain in the right upper abdomen. He was a non-smoker and was not taking any regular medications. Physical examination revealed elevated blood pressure (180/100 mmHg) and diffuse abdominal tenderness. Chemistry at admission was unremarkable besides mild hypercholesterolaemia (219 mg/dl). Blood count, erythrocyte sedimentation rate and C-reactive protein were in the normal range.

Abdominal X-ray, ultrasound and gastroscopy were unremarkable. The pain was relieved by opioids only for a few hours, and repetition of laboratory examinations disclosed progressive elevation of lactate dehydrogenase, reaching a peak of 1180 U/l. Furthermore, creatinine was rising to 1.3 mg/dl and urinary protein excretion increased to 0.88 g in 24 h. Magnetic resonance (MR) imaging of the kidneys showed several infarcted areas of the right kidney. Due to the very rare nature of this disorder and the angiographic appearance of thrombotic occlusions of the intrarenal branches, a search for underlying thrombophilia was undertaken, using a second-generation coagulation assay to test for activated protein C (APC) resistance. A diagnosis of APC resistance could be established in our patient as the ratio was low and genotyping showed heterozygosity for the factor V Leiden mutation. Due to this diagnosis, aspirin was stopped and oral anticoagulation with phenprocoumon was initiated. In the following 3 months, the patient was asymptomatic. Serum creatinine and urinary protein excretion returned to normal values.

FMD is an uncommon, genetic non-inflammatory vascular disease affecting small to medium-sized vessels. Renal artery involvement is most common, leading to renovascular hypertension [1]. Progression of FMD to renal infarction is rare [2,3]. APC resistance represents the most common cause of hereditary thrombophilia. The major clinical manifestation is deep vein thrombosis [4]. An association between APC resistance and arterial thrombosis has not been well established.

To our knowledge, a combination of FMD and APC resistance, leading to renal infarction, has not been reported in the medical literature until now. Therapy consisting of blood pressure control and oral anticoagulation was successful in our patient. We conclude that this case report reminds us of the acute clinical presentation of FMD and that it might be of clinical relevance to investigate for APC resistance in patients with renal infarction.

Conflict of interest statement. None declared.

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**Fig. 1.** Selective angiogram of the right kidney showing mild stenotic and dilated lesions and thrombotic occlusions

The results of arteriography and the negative serological markers of vasculitis led to the diagnosis of FMD which had caused infarction of the right kidney. Due to the very rare nature of this disorder and the angiographic appearance of thrombotic occlusions of the intrarenal branches, a search for underlying thrombophilia was undertaken, using a second-generation coagulation assay to test for activated protein C (APC) resistance. A diagnosis of APC resistance could be established in our patient as the ratio was low and genotyping showed heterozygosity for the factor V Leiden mutation. Due to this diagnosis, aspirin was stopped and oral anticoagulation with phenprocoumon was initiated. In the following 3 months, the patient was asymptomatic. Serum creatinine and urinary protein excretion returned to normal values.

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Acute intratubular obstructive renal failure after ampicillin treatment

Sir,

Hospital acquired renal insufficiency has been increasing in frequency in recent years and now accounts for ~7.2% of patients admitted to the hospital for renal failure [1]. Its most common cause is a decrease in renal perfusion. Medications (mainly antibiotics) that variously produce nephrotoxicity also frequently cause renal failure during hospitalization [1].

We present a patient with *Listeria monocytogenes* meningitis treated with high doses of endovenous ampicillin, who developed microscopic crystalluria and acute renal failure with oliguria.

**Case.** A 79-year-old male was admitted to our hospital because of fever (39°C) and meningoencephalitis. He had hypertension for >10 years and was diabetic with diabetic retinopathy, but had normal renal function. On admission he was normotensive. His laboratory tests showed 15 900/mm³ white cells with 89% neutrophils, haemoglobin 16 g/100 ml, haematocrit 44.5%, and platelets 203 000. Blood urea was 60.1 mg/dl, creatinine 1.18 mg/dl, and he had proteinuria 1.5 g/day. Blood and urine cultures were negative. The analysis of the cerebrospinal fluid showed 300/mm³ white cells with 55% polymorphonuclears, and its culture was positive for *L. monocytogenes*. High doses of endovenous ampicillin (3 g/4 h) were given resulting in initial clinical improvement. On the third day after starting ampicillin, the patient had microscopic crystalluria and one episode of gross haematuria. During the following days, creatinine levels increased (6.2 mg/dl) and progressive oliguria developed. Abdominal ultrasonography showed enlarged kidneys with normal structure. At time, his mental status deteriorated, and he showed myoclonus, irritability and confusion. A cranial scan was normal, and an electroencephalogram showed diffuse slowing with paroxysms. Because of oligoanuria, renal failure and the neurologic symptoms of ampicillin overdose, a subclavian catheter was inserted and a 4-h session of haemodialysis was carried out. During the haemodialysis session, post-obstructive diuresis commenced (4500 cc in 18 h), and his neurologic state as well as renal function improved so no additional dialysis was needed. The antibiotic was administered in adjusted doses until completion of treatment. On the day he left the hospital, the patient had completely recovered from his meningitis and renal insufficiency (creatinine 1.3 mg/dl).

**Discussion.** Crystalluria has been observed after high doses of ampicillin [2]; and in renal failure, reducing its dose is recommended. The main adverse effects of penicillins are hypersensitivity reactions and rash. Less than 1% of cases have penicillin encephalopathy, seizures (mainly after large endovenous doses or in patients with renal dysfunction) and other haematological disorders. Semi-synthetic penicillins, can cause nephrotoxicity. Three distinct patterns of penicillin nephrotoxicity have been discerned: one consists of a spectrum of anergic and glomerulonephritic lesions, another one manifests as anaphylactic reactions and acute renal insufficiency with anuria after a single injection of penicillin, and the last one is acute interstitial nephritis in which the majority of patients recover renal function with discontinuation of therapy [3]. This third pattern is the most frequent, and several cases have been reported.

In our case, renal failure was mediated by a different process. The crystalluria observed after high doses of ampicillin caused renal failure by tubular obstruction. Overdose, dehydration and/or hypoalbuminaemia increase the unbound form of the drug. The free drug, which is ultrafiltered by glomeruli, can precipitate within the tubular lumina [4].

Dialysis lowered the plasma concentration of ampicillin (20–50%), reducing the drug to below toxic concentrations and, consequently, improving our patient’s mental status. It also reduced the intratubular level of ampicillin, which was immediately followed by polyuria and progressive improvement of renal parameters (creatinine, urea). The massive microscopic crystalluria associated with high doses of ampicillin, renal insufficiency and the evolution after only one haemodialysis of postobstructive polyuria and reversal of renal failure allow us to suggest that tubular obstruction produced by ampicillin crystals was the cause of renal failure in our patient. Crystalluria associated with the administration of drugs has been described, but it infrequently ends in renal failure. This phenomenon has been reported previously associated with other drugs [5,6], but in our review of the literature we did not find any case attributed to ampicillin.

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