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 meningism. 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 angiitis 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 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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Nephrology and Internal Medicine Departments
Hospital de Terrassa
Barcelona
Spain
Email: smetgeshemo@csdt.es
Rosa Borrallo
Xavier de las Cuevas


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