Interesting Case

Biopsy-proven anuric acute tubular necrosis associated with vancomycin and one dose of aminoside

Harry Sokol, Cécile Vigneau, Eric Maury, Bertrand Guidet and Georges Offenstadt

Service de réanimation médicale, Hôpital St Antoine, Paris

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Introduction

We present the first report of a biopsy-proven acute tubular necrosis (ATN) secondary to vancomycin and a single dose of aminoside.

Case

A 71-year-old woman with a history of hypertension and restrictive chronic respiratory failure was admitted to our intensive care unit (ICU) for dyspnoea. She had been on levofloxacin for 3 weeks for pneumonia, and had purulent expectoration, fever (38.5°C) and pulmonary crepitations, but no signs of haemodynamic failure or hypersensitivity. Antibiotherapy was initiated empirically, with piperacillin, tazobactam and amikacin (10 mg/kg once), and after 48 hours also vancomycin (2 g/day), based on a blood culture positive for meticillin resistant Staphylococcus aureus. After 3 days, her laboratory tests showed: serum creatinine, 396 μmol/l (75 μmol/l at admission); no hypereosinophilia, vancomycin residual blood level 47.8 mg/l (normal 20 to 30 mg/l). A renal echography ruled out an obstructive uropathy. Urine tests suggested an organic acute renal failure (ARF) (natriuresis/kaliuresis <1 without diuretics). A renal biopsy after 26 days of anuria showed severe ATN. There were neither glomerular nor interstitial lesions, suggesting that her kidneys previously had been normal. Two months later she was still anuric.

Discussion

In ICUs, the main cause of ARF is ATN secondary to septic or non-septic shock [1]. Our patient, however, did not have any signs of shock or dehydration and did not receive any diuretics. Moreover she did not have a history of renal failure. The second cause of ARF is drug toxicity [1]. Aminoglycosides are known to be nephrotoxic, inducing ARF in ~10% of cases [2]. However, nephrotoxicity occurs after several days, is related to the cumulative dose, and only exceptionally causes terminal renal failure—with its typical histological lesion being ATN that regresses within 3 weeks [3]. Our patient received only a single injection of amikacin (10 mg/kg), yet was still anuric after 2 months. Both of these facts strongly suggest that amikacin was not the sole culprit in her ATN. Vancomycin also is a nephrotoxic drug [4]. After a hypersensitivity reaction it usually induces no anuria but a moderate elevation of serum creatinine associated with tubulointerstitial infiltration but never ATN [5,6]. The combination of vancomycin and aminoglycoside is nephrotoxic in 20–28% of cases [6]. However, most of the patients described have had other factors contributing to their ARF, such as sepsis, anaesthesia or other nephrotoxic drugs, but above all, they have had prolonged vancomycin and aminoglycoside therapy (>15 days) with a high cumulative dose [2]. Furthermore, there are no cases in the literature of biopsy-documented ATN attributed to this combination. Our patient had no other nephrotoxic factors, a very short course of antibiotherapy and a low cumulative dose of vancomycin (6.5 g in 3 days) and amikacin (one injection of 1 g).

After 2 months, our patient’s renal function did not recover. Most cases of ATN, especially those resulting from drug toxicity, improve after 3 weeks, even if return to normal renal function takes months [2]. One explanation could be that our patient’s pluripotent bone marrow-derived stem cells were depressed. Recently, Gupta et al. [7] showed that this type of cell contributes to the tubular regeneration that follows...
ATN. Thus, if the bone marrow is disabled, tubular regeneration may be impaired. Our patient’s liver biopsy showed extramedullary haematopoesis, an indirect sign of medullary dysfunction. Therefore, medullary dysfunction could in part explain the exceptionally prolonged anuria of our patient after vancomycin and a single dose of aminoside.

Conflict of interest statement. None declared.

References


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