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P430 -A rare renal complication of ceftazidime therapy

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We present the case of a 43 year-old lady with cystic fibrosis, diagnosed approximately 7 years previously. A month prior to this presentation, she had received a 2-week course of intravenous aztreonam and meropenem for an infective exacerbation of her cystic fibrosis. Her pulmonary function failed to improve and she was admitted electively to a local hospital for optimisation. On the day of admission, her creatinine was 40umol/L, and she was clinically asymptomatic. She was commenced on ceftazidime 3g TDS and meropenem 2g TDS the following morning, after which she developed a temperature of 39 deg C and felt unwell. Blood tests on day 3 showed a creatinine of 375umol/L, haemoglobin of 113g/L (from 123g/L), platelets 38 x10^9/L (from 222 x10^9/L) and a CRP of 154mg/L (from 67mg/L). Of note, eosinophils were 0.2 x10^9/L. Urine dip demonstrated 4+ blood and 2+ protein. Antibiotics were discontinued that afternoon. Blood pressure was normal and there were no systemic features of note. Her creatinine the next day had risen to 594umol/L, a renal tract ultrasound was normal, and she was transferred to our centre.

On transfer, her creatinine was 712umol/L, haemoglobin 97g/L, platelets 56 x10^9/L, haptoglobin 0.4g/L, LDH of 562U/L, bilirubin of 4umol/L, with a positive direct antiglobulin test. A blood film did not demonstrate any fragments. ADAMTS-13 activity was normal and immunology unremarkable. A renal biopsy was performed, demonstrating extensive acute tubular injury with tubules containing eosinophilic material, consistent with intravascular haemolysis. Glomeruli and blood vessels were normal. By the following day, creatinine had risen to 890umol/L, she remained oligoanuric, and was commenced on haemodialysis. Conversely, by this point, her markers of haemolysis and platelets had normalised. One week post-presentation, the patient remains oligoanuric and dialysis-dependent.

The clinical setting and biopsy results are in keeping with drug-induced haemolysis, most likely secondary to ceftazidime. The thrombocytopaenia led us to initially consider a microangiopathic haemolytic anaemia, but there was no evidence of this on the renal biopsy, and repeat review of her blood film demonstrated platelet clumping, thought to induce an artefactually low platelet count by the automated counter.

Haemolysis is a recognised, albeit rare, adverse effect of 3rd generation cephalosporins. To date, acute haemolytic reactions and acute kidney injury have only been reported in the paediatric literature. 3rd generation cephalosporins are thought to induce haemolysis through formation of immune complexes with red cell surface glycoproteins, generating a novel epitope targeted by anti-red cell antibodies. The resultant release of haem pigment leads to acute tubular necrosis through direct injury to renal tubular cells, renal vasoconstriction and intraluminal cast formation. Given the increased frequency of cephalosporin usage, it is important for nephrologists to be aware of this rare complication.