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Case report - Persistent pyrexia and acute kidney injury related to severe drug-related granulomatous tubule-interstitial nephritis secondary to ciprofloxacin.

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Background
Acute interstitial nephritis (AIN) is estimated to be the cause for acute kidney injury (AKI) in 15-20% cases [1] and drugs are thought to account for 70% of those. The presence of granulomatous tubulo-interstitial nephritis however is rare occurring in approximately 0.5-0.9% of kidney biopsies [2]. The findings of granulomas have been linked with infections or antibiotics such as vancomycin, ciprofloxacin, nitrofurantoin, penicillin and cephalosporins[2].
Case report
A 50 year old Caucasian female with a past medical history of polymyalgia rheumatica, hypothyroidism and anxiety presented to the emergency department following a recent diarrhoeal illness. She was confused, hypotensive and found to have an acute kidney injury (AKI stage 3, creatinine 326 mmol/l from a baseline creatinine of 54mmol/l). She required a HDU admission for inotropic support and was subsequently transferred to the renal unit. Blood and urine cultures were positive for E. coli. Despite treatment with IV Tazocin (piperacillin with tazobactam) for 10 days and then oral ciprofloxacin she continued to have intermittent episodes of pyrexia (39 degrees Celsius) with raised inflammatory markers (c-reactive protein (CRP) >200) and an AKI (creatinine 140mmol/l). There was no significant eosinophil levels detected at any point during her admission.
Over the next 3 weeks she remained pyrexial with no significant improvement in her blood results but remained clinically well apart from her high temperatures. Her CT imaging was reported to show “severe inflammation of both kidneys with small (non-drainable) focal collections bilaterally” and the ultrasound showed bulky enlarged kidneys measuring 13cm each.
A Positron Emission Tomography with CT (PET- CT) was requested to look for other sources of infection which might explain her persistent pyrexia and CRP. It revealed striking, bilateral increased renal cortical activity but no evidence of an alternative source of infection/inflammation.
Her renal biopsy had appearances of severe granulomatous tubulo-interstitial inflammation with white cell casts. The differential diagnosis of these appearances lies between infection (although no microorganisms are demonstrated on special stains) and a severe drug-related tubulo-interstitial nephritis. The degree of chronic damage was difficult to assess in the context of such severe acute changes but there was felt to be at least mild chronic tubulo-interstitial damage.
Microbiology testing of the biopsy sample did not reveal any organisms and 16S rDNA PCR testing was negative suggesting no active bacterial infection despite repeated temperatures above 38 degrees Celsius and CRP above 100. The decision was therefore taken to stop antibiotic treatment and start treatment with corticosteroids.
Outcome
Following the initiation of steroid therapy, her inflammatory markers and renal function started to improve and her pyrexia resolved within 72 hours.
Conclusion
Renal biopsy was critical in establishing the diagnosis and adjusting management. However it is often difficult to distinguish if the appearances are related to the underlying infection itself or the antibiotics used to treat the infection. Previous case reports and clinical experience suggest that in drug related

granulomatous interstitial nephritis the removal of the offending agent and initiation of corticosteroid therapy usually results in improvement in renal function.