Clarithromycin-induced granulomatous tubulointerstitial nephritis

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Acute interstitial nephritis is an important cause of acute renal dysfunction, accounting for up to 15% of patients hospitalized for acute renal dysfunction. Drug-induced interstitial nephritis represents 4% of all cases studied histologically, with an estimated frequency of 8% [1]. We present a case of granulomatous interstitial nephritis in a 38-year-old woman prescribed clarithromycin for pharyngitis.

A 38-year-old woman was admitted with a history of abnormal renal function. She was seen by her GP with a history of sore throat and nasal discharge for which she was started on a course of clarithromycin. Whilst on these medications, she developed fever, night sweats, headache, rash and mouth ulcers. A subsequent blood test, done because of her worsening symptoms, revealed deranged renal function, following which she was referred to the hospital. Her past medical history included reactive arthritis requiring a short period of methotrexate more than 2 years previously but this was currently quiescent. She denied any drug allergy but was on clarithromycin and homeopathic medication (transfer factor: an immuno-modulating drug). On examination she was apyrexial, tachycardic (pulse 103 bpm) and had a blood pressure of 152/92. General and systemic examination was unremarkable. Investigations revealed: urine analysis pH-5.0, leucocytes <10/mm³, and few squamous cells; no blood or protein was detected; haemoglobin 10.2 g/dl, white cell count 9.2 × 10⁹/l (Neu-8.47, Eos-nil), platelets 513 × 10⁹/l, erythrocyte Sedimentation Rate (ESR) 136; sodium 137 mmol/l, potassium 4.4 mmol/l, bicarbonate 20 mmol/l, urea 17.3 mmol/l, creatinine 654 µmol/l, calcium 2.56 mmol/l, phosphate 1.38 mmol/l, albumin 30 g/l and C-reactive protein (CRP) 84. Autoantibody screen, Anti-glomerular basement membrane (GBM) and anti-neutrophilic Cytoplasmic Antibody (ANCA) were negative. Ultrasound of kidneys was normal. Subsequent renal biopsy showed diffuse inflammatory cell infiltrate within the interstitium, comprising of lymphocytes, plasma cells and numerous eosinophils with non-caseating epithelioid granuloma. A diagnosis of Tubulointerstitial Nephritis (TIN) was made, all medication was stopped and the patient was started on a short course of oral steroids, following which she made a complete recovery.

Drug-induced acute tubulointerstitial nephritis is an inflammatory process involving the tubules, the space between the tubules and the glomeruli. It is mediated by T-cell hypersensitivity reaction and cytotoxic T-cell injury. Renal biopsy is the gold standard for diagnosis. Stopping the suspected medication forms the main component of treatment, with most patients recovering rapidly on withdrawal of the offending drug. Corticosteroid and immunosuppressants, in cases where there is no significant improvement in the renal function, may be of value. Recovery is more rapid in those individuals who have been exposed to the drug for <2 weeks, in comparison to those who have taken the suspected medication for more than 3 weeks.

Epithelioid and non-caseating giant-cell granulomas are found in some cases, especially those in which acute interstitial nephritis is secondary to drugs [2]. Granulomatous TIN has been described with drugs like fluoroquinolines and lamotrigine [3,4]. There has been one report of granulomatous reaction in a patient on a combination of dihydrocodeine, amoxicillin, erythromycin and phenylpropanalamine [5]. Other reported cases of granulomatous TIN are seen in infections (tuberculosis), Wegener’s granulomatosis and in sarcoidosis. Idiopathic granulomatous TIN in the absence of features of extra-renal sarcoid has also been described, but these patients may have associated features of hypercalcaemia and raised serum angiotensin converting enzyme [6,7], which were absent in our patient.

In our case, the patient was on both clarithromycin and homeopathic medication, which was discontinued immediately after the initial diagnosis was made.
Since the symptoms began after starting clarithromycin, we believe it to be the offending medication in this case. We did notice the fact that this patient was also on a homeopathic medication during the same period and questioned if it had any role to play in the aforementioned pathogenesis. But on further enquiry, we were informed that she had been on this medication for some time prior to her current event. Furthermore, the initial blood test performed by her GP before the commencement of antibiotics did not show any evidence of deranged renal function. Detailed search for any significant side effects with the use of these medications has not been described. Clarithromycin has been reported previously as an aetiological factor in TIN. However, to the best of our knowledge, no reports of a granulomatous reaction to clarithromycin have been published. Since we excluded other causes of granulomatous tubulointerstitial nephritis, such as infections and sarcoid, we present this unique case.

Conflict of interest statement. None declared.

References


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