CASE REPORT

Anti Tuberculous Therapy Induced Acute Kidney Injury- A Case Report

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ABSTRACT

Anti- Tuberculous Therapy (ATT) is a combination of drugs used to treat tuberculosis, with Rifampicin forming the bedrock of therapy. It is a bactericidal drug with a relatively safe side effect profile. We present the case of a lady in her 50s, treated for Pulmonary tuberculosis 15 years ago, who came with complaints of hemoptysis x 5 episodes, loss of weight and appetite for 2 weeks. She was clinically diagnosed to have a tuberculosis reactivation and was empirically started on ATT, 5 days following which she developed pedal edema and decreased urine output. She was diagnosed to have an acute kidney injury (AKI) and initiated on dialysis. A renal biopsy was taken to identify the cause for renal failure and it revealed an acute tubular injury with pigment casts, probably secondary to intravascular hemolysis induced by Rifampicin. This case highlights the importance for physicians, especially in countries with a high tuberculosis burden, to have a good understanding of the adverse reactions associated with the use of ATT, no matter how uncommon they may be. This will facilitate faster recognition and more effective management of these patients, resulting in less long-term morbidity for these patients.

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INTRODUCTION

The tuberculosis burden in India is the highest in the world, including both infected and latent cases (1). Over the years a number of drugs have been used in the treatment of tuberculosis. The Anti- Tuberculous Therapy (ATT) is a combination of drugs used to treat tuberculosis, with rifampicin forming the bedrock of therapy. It is a bactericidal drug and is also used in the treatment of leprosy, brucellosis, and in meningococcal prophylaxis. The common side effects include hepatotoxicity, reddish pigmentation of urine, thrombocytopenia, a flu-like syndrome and rarely, acute kidney injury(AKI) and renal failure. It is believed that the rifampicin dependant immunoglobins (IgG and IgM), react with the I antigen (1) present on the erythrocyte surface as well as the epithelia of Henle's loop resulting in immune complex deposition and an AKI. Here is a case of rifampicin induced AKI in a patient started on ATT.

CASE REPORT

A 52 year old lady, treated for pulmonary tuberculosis 15 years ago (completed ATT x 6 months), came with complaints of hemoptysis x 5 episodes, loss of weight and appetite for 2 weeks. On examination, she was conscious, oriented and afebrile. She had no pallor, icterus or pedal oedema. Respiratory and other system examinations were unremarkable. A computerized tomography(CT) of the thorax was taken which showed tractional bronchiectasis. Fibreoptic bronchoscopy was attempted but the patient was not cooperative. She was clinically diagnosed to have a tuberculosis reactivation and was empirically started on ATT.

After 5 days of ATT, she complained of a sudden decrease in urine output and bilateral leg swelling. Her blood investigations (Table 1) revealed Hemoglobin: 9.5 g/dl, a total leukocyte count: 9,600/ cu.mm, Platelets: 60,000/ cu.mm, Urea: 62 mg/dl, Creatinine: 6.7 mg/dl, Total/Direct bilirubin: 5.2/1.8 mg/dl, AST: 300 IU/L, ALT: 55 IU/L and LDH: 1006 U/L. An ultrasonogram of the abdomen revealed normal sized kidneys with maintained corticomedullary differentiation, and increased renal cortical echoes. Her coagulation profile was within normal limits. Urine examination revealed protein +++, 3-5 RBCs/hpf, bile pigment and bile salts. Serial RFTs revealed worsening values and her urine output reduced to less than 30 ml/hr. She was diagnosed to have an AKI and was initiated on haemodialysis.

Renal biopsy (Fig. 1 and 2) was done and it showed acute tubular injury with pigment casts, probably intravascular hemolysis associated acute tubular injury. The tubular casts were positive for Haemoglobin immunostaining. The glomeruli were negative for all antisera tested: IgG, IgA, IgM, C3, C1q, kappa and lambda.

A total of 3 dialysis sessions were required. She improved (clinically and biochemically) and recovered complete kidney function by 7 days of drug withdrawal. Modified ATT without rifampicin was continued.

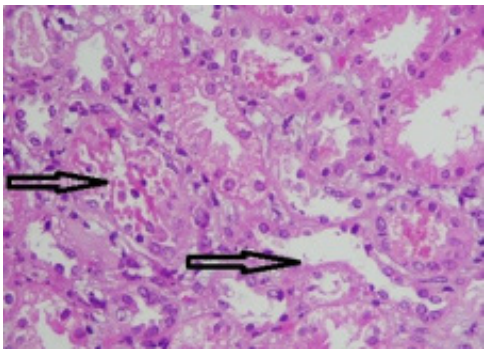

Fig. 1: The tubules show attenuated lining epithelium and loss of brush borders

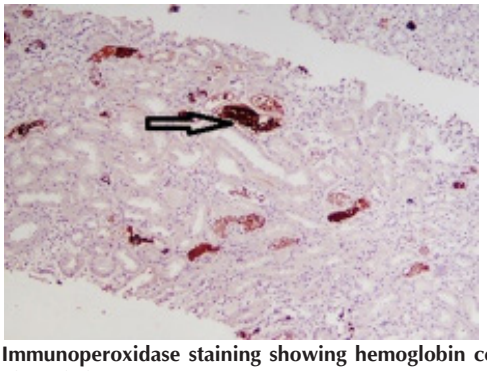

Fig. 2: Immunoperoxidase staining showing hemoglobin containing casts in the tubules

DISCUSSION

Rifampicin is a bactericidal drug used in the treatment of tuberculosis, as a mainstay in the Anti-Tuberculous Therapy (ATT). Other drugs used in ATT(first line) are isoniazid, pyrazinamide, and ethambutol. Isoniazid is a bactericidal drug to rapidly proliferating mycobacteria, the major side effects include hepatotoxicity and peripheral neuropathy. Pyrazinamide is a bacteriostatic drug. It is associated with hyperuricemia and gouty arthritis. Ethambutol is a bacteriostatic drug, and is associated with optic neuropathy.

Rifampicin is also used in the treatment of leprosy, in meningococcal prophylaxis, brucellosis etc. It acts by inhibiting the DNA dependant RNA polymerase. Acute kidney injury and acute renal failure have been reported rarely before. It usually occurs during intermittent therapy or after reintroduction of the drug after an extended period (2). Acute Interstitial nephritis (AIN) is the most common histological finding (3), however acute tubular necrosis (ATN) has been described as the predominant lesion by some investigators as well. Other rare patterns include acute cortical necrosis, crescentric glomerulonephritis, and papillary necrosis.

The exact mechanism of renal injury is still unknown. It is believed that the rifampicin dependant Immunoglobins (IgG and IgM), react with the I antigen (1) present on the erythrocyte surface as well as the epithelia of Henle's loop. A predominant AIN or ATN probably depends on the site of the resulting immune complex deposition (in the interstitium or the tubular epithelium respectively). It is believed that massive production of preformed antibodies occur on re-exposure to the antigen i.e, rifampicin and target cell damage is produced by complement activation. It is often associated with thrombocytopenia, hemolytic anemia, hepatitis, and flu-like symptoms. A study done by Ata F et al (4), found anti-rifampicin antibodies to be positive in 32% of cases with a rifampicin induced AKI.

Muthukumar et al conducted a study on 25 patients with rifampicin induced AKI (5). Among the twelve patients who underwent a renal biopsy, seven (58%) had features of AIN, one showed diffuse proliferative glomerulonephritis, and three had mesangial proliferation. Our patient however had an ATN on histopathological examination.

Another study conducted by Covic et al (3) found that among 60 patients with rifampicin induced AKI, 25% had associated hepatic injury as well. The most common laboratory abnormalities in these patients were anemia(93%), with features of marked hemolysis in 25% of the cases, leucocytosis(63%) and thrombocytopenia(50%). They showed that the more severe the anemia, the more frequent the presence of hemolysis and thrombocytopenia. Our patient had anemia with features of hemolysis, thrombocytopenia and hepatic injury as well.

Although quite rare, Rifampicin is the most likely anti tuberculous agent (3) to be implicated in renal injury. Early diagnosis and withdrawal of the drug is extremely

important to preserve renal function. Dialysis and other supportive measures may be required, as in our case.

CONCLUSION

Owing to the widespread prevalence of tuberculosis, ATT is a commonly prescribed regimen, especially in countries like India and other east Asian countries with a high tuberculosis burden. It is important for general physicians and thoracic medicine physicians to have a thorough understanding of all the major adverse reactions associated with the use of ATT, no matter how uncommon. Though uncommon, rifampicin induced Acute Kidney Injury (AKI), as in this case, must always be considered when dealing with a patient on ATT developing AKI. Early recognition and withdrawal of the drug is essential to preserve kidney function and prevent further complications.

No conflicts of interest to be declared.

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No specific acknowlegement to be made

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