Rifampicin Allergy Leading to Acute Renal Shutdown

Abstract

Rifampicin is a widely used drug to treat tuberculosis and leprosy. Its toxicity is predominantly hepatic and immunoallergic in character. While hepatic toxicity is dose-related, the immunoallergic effects are unpredictable and usually associated with intermittent therapy. These immunoallergic effects may be minor (a cutaneous, gastrointestinal, or influenza-like syndrome) or major (hemolytic anemia, shock, or acute renal failure). Herein, we report a case of rifampicin allergy in a patient who was on intermittent once monthly rifampicin therapy for neuritic leprosy and was on his 4th month of treatment. Rifampicin exposure led to sudden shock and acute renal failure, which eventually required hemodialysis support. The patient made a complete recovery over the subsequent days and his renal function returned to normal over the next 3 weeks. He continues his multidrug therapy of leprosy without rifampicin.

Keywords: *Acute renal failure, adverse drug reaction, leprosy, rifampicin*

Ranjith Jeyasekharan, Ninoo George[1]

Departments of General Medicine and [1]Nephrology, Dr. Jeyasekharan Hospital and Nursing Home, Nagercoil, Tamil Nadu, India

Introduction

Rifampicin is a widely used drug to treat tuberculosis and leprosy. Its toxicity is predominantly hepatic and immunoallergic in character. The hepatotoxicity is dose-related, while the immunoallergic effects are unpredictable and usually associated with intermittent therapy. These immunoallergic effects may be minor (a cutaneous, gastrointestinal, or influenza-like syndrome) or major (hemolytic anemia, shock, or acute renal failure).[1,2] Herein, we report a case of rifampicin allergy in a patient who was on intermittent once monthly rifampicin therapy for neuritic leprosy and was on his 4th month of treatment.

Case Report

A 30-year-old male developed a claw hand associated with ulnar nerve thickening and was subsequently diagnosed with neuritic-type leprosy 4 months ago. He was initiated on triple-drug therapy for leprosy with dapsone 100 g OD, clofazimine 50 mg OD, and once monthly 600 mg rifampicin. For the last 3 months, on the day of consumption of rifampicin, the patient had experienced minor allergic reactions such as fever and petechial rash. However, on intake of the 4th monthly dose of rifampicin, the patient experienced giddiness after an hour, with recurrent episodes of vomiting. On presenting to the hospital, he was drowsy and in severe shock with a blood pressure of 80/60 mmHg. His heart rate was 112/min, oxygen saturation was 98%, and respiratory rate was 24/min. He was immediately resuscitated with intravenous fluids and inotropic support. Blood investigations revealed jaundice and mild renal dysfunction. Over the next 48 h, the renal function continued to deteriorate and the patient went into complete anuric renal shutdown. Jaundice had completely resolved by then. Rifampicin anaphylaxis was suspected.

Rifampicin was stopped; while dapsone and clofazimine treatment were continued. Hemodialysis was initiated in view of volume overload and anuria due to acute tubular necrosis (ATN). Anuria was noted from 3rd to 9th day. The patient required intermittent hemodialytic support, with hemodialysis 7 times during the hospital stay. From 10th day of the hospital, his urine output showed gradual improvement and eventually normalized on 21st day. Hemodialysis support was withdrawn after 2 weeks and his renal function continued to improve [Figures 1-3]. He made a full recovery and reached a nadir creatinine of 1.3 mg/dl on follow-up. A renal biopsy was not performed in view of spontaneous clinical recovery.

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Address for correspondence:
Dr. Ninoo George, Kottar-Parvathipuram Road, Weavers Colony, Nagercoil - 629 003, Tamil Nadu, India.
E-mail: ninoogeorge@gmail.com

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Discussion

Mycobacterium leprae, acid-fast bacilli, an intracellular parasite with a preference for Schwann cells and skin, causes leprosy. The condition is extremely incapacitating, and in certain cases, systemic involvement has been reported.[3] The World Health Organization (WHO) advised the use of dapsone, rifampicin, and clofazimine as part of multidrug therapy (MDT) against leprosy in 1981. Rifampicin is the most important anti-leprosy medicine of the three, and it is used in both paucibacillary and multibacillary patients' regimens.

Rifampicin has been linked to cutaneous eruptions, thrombocytopenic purpura, hepatitis, a flu-like syndrome, hemolytic anemia, shock, respiratory insufficiency, and acute renal failure. Clinical symptoms such as dizziness, chills, fevers, lumbar pain, abdominal discomfort, myalgias, and nausea appear ½h to 2 h after consuming rifampicin. Complement fixation can lead red blood cells to emit pyrogens, which could explain why people have fevers and flu-like symptoms.[4,5]

Renal anomalies caused by leprosy-specific treatment have been documented, notwithstanding their rarity. ATN, interstitial nephritis, and papillary necrosis have all been reported to cause acute kidney injury (AKI) in leprosy patients. AKI is a rare but serious consequence that can result in permanent kidney damage and can force therapy to be interrupted. The most common presenting symptoms at the onset of AKI were skin rash and gastrointestinal disturbance, followed by fever and arthralgia. Typical laboratory results include hypoalbuminemia, eosinophilia, anemia, elevated serum creatinine serum and uric acid level, proteinuria, sterile leukocyturia, and hematuria.[6,7]

Ambiguity exists about the exact etiopathogenic pathway of rifampin-induced AKI, with several researchers suggesting either a Type II or Type III hypersensitivity reaction. Anti-rifampin antibodies generate immunological complexes deposited in renal arteries, the glomerular endothelium, and the interstitial area leading to two pathological processes. Immune complexes deposited in the arteries produce vascular constriction and tubular ischemia, resulting in ATN, whereas immune complexes deposited in the interstitial area cause acute interstitial nephritis.[7]

Although WHO states that no adverse reactions have been noted on monthly administration, many researchers state otherwise.[4] Various studies have been conducted to assess the side effects of MDT in leprosy patients.

A retrospective, descriptive Brazilian study analyzed the side effects of MDT in 194 leprosy patients. It found that 24 patients on rifampicin exhibited side effects of hypersensitivity and hepatic abnormalities; with the drug being discontinued in five patients.[4]

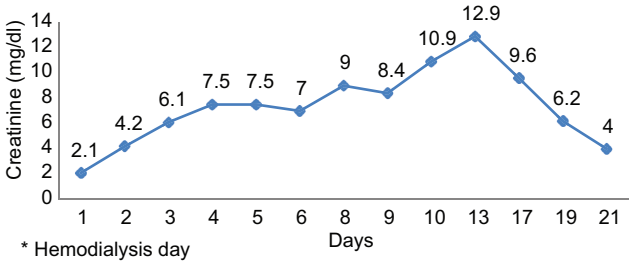

Figure 1: Creatinine level during hospital stay

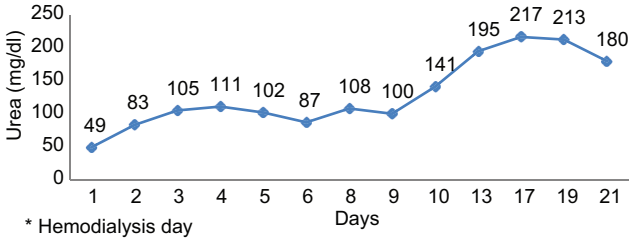

Figure 2: Blood urea level during hospital stay

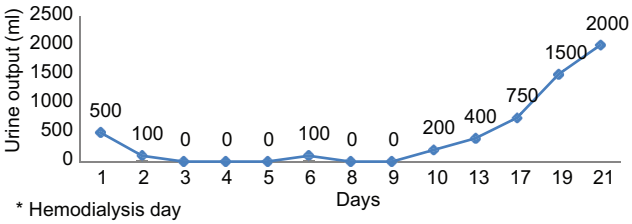

Figure 3: Urine output level during the hospital stay

A prospective and descriptive study done in Jagdalpur, India, assessed the adverse effects of MDT in 176 leprosy patients between 2006 and 2008. Seventy-nine patients exhibited adverse reactions, of which 8 were attributed to rifampicin. The rifampicin-associated adverse reactions were hepatic abnormalities, hemolytic anemia, abdominal syndrome, skin reaction, flu-like syndrome, and leukopenia. The drug was stopped in two patients.[8]

A retrospective analytical epidemiological study conducted at Uberlandia aimed to determine MDT's adverse effects studied charts of 187 patients treated with MDT from January 1995 to May 2000. Among the 113 side effects noted, 7 (6.2%) were attributed to rifampicin.[9]

A study of 25 patients who developed acute renal failure subsequent to rifampicin therapy revealed that the presenting symptoms were gastrointestinal and flu-like within 4 h (median) of drug ingestion. All subjects showed oliguria and required dialysis. Serum creatinine levels returned to the baseline level of 1.5 mg/dL in all patients by 7 weeks.[10]

Reports of acute renal injury in individuals taking rifampicin for the first time are less reported in the literature. Studies indicate that more than 80% of patients with AKI recover within 120 days. Furthermore, these

situations carry a mortality rate of 1.6%. Therefore, in the 3 to 4 months following the onset of AKI, vigilant monitoring is recommended to avoid further kidney impairment.[6,7]

Conclusion

This case reports a rare case of hypersensitivity to a monthly dose of rifampicin in a leprosy patient. This case report also highlights the importance of recognizing the adverse effects of rifampicin. The patient developed a hypersensitivity reaction to the anti-leprosy drug and reached a state of a medical emergency. Symptom awareness led to prompt treatment and thus proved life-saving. Hence, it is pertinent to include rifampicin hypersensitivity reactions in the differential diagnosis if any unanticipated symptoms arise after its introduction.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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