

A Case of Acute Tubulointerstitial Nephritis Associated with Rifampin Therapy Presenting as Fanconi-like Syndrome

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Rifampin is a common drug used in the treatment of tuberculosis. During treatment for tuberculosis, patients require careful monitoring for adverse drug reactions. Among these reactions, hepatotoxicity is common and may be associated with isoniazid, rifampin or pyrazinamide treatment. Renal toxicity related to rifampin is a rare complication requiring switching to a different drug and extension of the treatment period.¹ Rifampin-induced acute kidney injury is associated with acute tubulointerstitial nephritis (AIN) and/or acute tubular necrosis (ATN).^{2,3} We report a case of rifampin-induced AIN presenting as Fanconi-like syndrome.

A 53-year-old man was admitted to the hospital because of renal dysfunction after receiving anti-tuberculosis treatment for one month. He had been treated with 300 mg of isoniazid, 450 mg of rifampin, 800 mg of ethambutol, and

1,000 mg of pyrazinamide daily one month prior. Physical examination revealed coarse and decreased breath sounds on the right lung field and no pretibial pitting edema. Laboratory tests showed a white blood cell count of 12,900/mm³ (eosinophil, 150/mm³), hemoglobin of 9.7 g/dL, platelets of 664,000/mm³, a blood urea nitrogen level of 40 mg/dL, serum creatinine of 4.23 mg/dL, total CO₂ of 11.8 mmol/L and serum glucose of 89 mg/dL. Serum Na⁺, K⁺, and Cl⁻ were 133, 2.9 and 104 mM, respectively. Total calcium and phosphorus levels were within the normal range. Fractional excretion of K⁺ was 64.1% (normal, 4-16%). Urinalysis revealed 2+ proteinuria, glycosuria, microscopic hematuria and sterile pyuria. The patient's urinary protein/creatinine ratio was 3,197 mg/g. Renal ultrasonography demonstrated that both kidneys had a normal size range and echogenicity. We suspected acute kidney injury associated

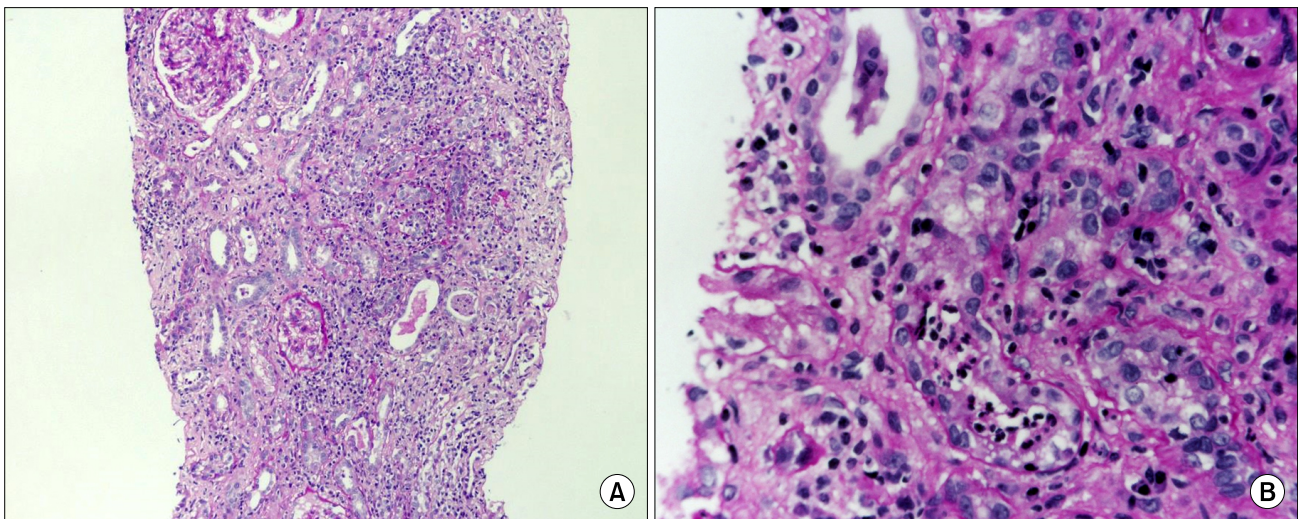


FIG. 1. Renal pathologic findings. Most glomeruli show slight mesangial matrix expansion with a mild increase in mesangial cells. The tubules show focal atrophy, degenerative changes and sloughing, with frequent infiltration of lymphocytes to form tubulitis. The interstitium is markedly widened by focal edema, fibrosis and diffuse infiltration of lymphocytes, plasma cells, neutrophils and macrophages. A small number of eosinophils are recognized (periodic acid-Schiff stain, A: original magnification $\times 100$, B: original magnification $\times 400$).

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Article History:

Received October 31, 2016

Revised December 1, 2016

Accepted December 5, 2016

with anti-tuberculosis medications. Therefore, we performed renal biopsy, which showed atrophic, degenerative changes and sloughing of tubules with lymphocyte infiltration. Focal edema and fibrosis of the interstitium, and diffuse infiltration of plasma cells, neutrophils, and macrophages were also observed. A small number of eosinophils were seen (Fig. 1). We changed out rifampin for levofloxacin and reduced the doses of ethambutol and pyrazinamide. Three months later, the patient's creatinine level was within the normal range. Pyuria and glycosuria had resolved and urinary protein/creatinine ratio was also decreased to 247 mg/g.

We report a case of rifampin-induced AIN presenting as Fanconi-like syndrome. This patient exhibited renal glycosuria, hypokalemia, and heavy proteinuria, leading to suspicion of proximal tubular dysfunction. The typical presentation of drug-induced AIN is similar to that of an allergic reaction such as skin rash, fever, and elevated eosinophils. This case did not include allergic symptoms and the patient had a normal eosinophil count. A definitive diagnosis of drug-induced AIN was made by renal biopsy. The primary treatment for rifampin-induced AIN is discontinuation of the causative drug and use of corticosteroids.⁴ Our patient successfully recovered renal function after switching from rifampin to levofloxacin. Because this patient had active pulmonary tuberculosis, we could not administer corticosteroid therapy.

In conclusion, this case demonstrates that rifampin therapy can induce acute kidney injury as a manifestation

of AIN and Fanconi-like syndrome. Clinicians should monitor renal function during rifampin-based therapy.

ACKNOWLEDGEMENTS

This work was supported by the National Research Foundation of Korea (NRF) funded by the Korean government (NRF-2015R1D1A3A03015653, to K.P.K).

CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Covic A, Goldsmith DJ, Segall L, Stoicescu C, Lungu S, Volovat C, et al. Rifampicin-induced acute renal failure: a series of 60 patients. *Nephrol Dial Transplant* 1998;13:924-9.
2. Nessi R, Bonoldi GL, Redaelli B, di Filippo G. Acute renal failure after rifampicin: a case report and survey of the literature. *Nephron* 1976;16:148-59.
3. Schubert C, Bates WD, Moosa MR. Acute tubulointerstitial nephritis related to antituberculous drug therapy. *Clin Nephrol* 2010;73:413-9.
4. Min HK, Kim EO, Lee SJ, Chang YK, Suh KS, Yang CW, et al. Rifampin-associated tubulointerstitial nephritis and Fanconi syndrome presenting as hypokalemic paralysis. *BMC Nephrol* 2013;14:13.