Rifampicin-Induced Minimal Change Disease Is Improved after Cessation of Rifampicin without Steroid Therapy

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INTRODUCTION

Rifampicin is one of the standard drugs used to treat tuberculosis, however, has been reported to induce some adverse renal effects.¹-¹⁰ The most frequent form of nephrotoxicity is a syndrome consisting of acute renal failure with pathological findings of tubular necrosis, while other forms of nephrotoxicity include interstitial nephritis with or without mild glomerular lesions, rapidly progressive glomerulonephritis and light chain proteinuria.² Rifampicin-associated nephrotic syndrome has been published, including cases of rifampicin-induced minimal change disease (MCD).⁴,⁷,⁹ Generally, MCD is treated with glucocorticoids,¹¹,¹² and rifampicin-induced MCD was treated with a steroid in a previous case.⁹ Herein, however, we report a patient with MCD after rifampicin treatment, which was improved after rifampicin cessation without undergoing steroid therapy.

CASE REPORT

There are several reports to demonstrate that rifampicin, a major anti-tuberculosis agent, is associated with some adverse renal effects, with a few cases of rifampicin-induced minimal change disease (MCD). In the present case, a 68-year-old female presented with nausea, vomiting, foamy urine, general weakness and edema. She had been taking rifampicin for 4 weeks due to pleural tuberculosis. The patient had no proteinuria before the anti-tuberculosis agents were started, but urine tests upon admission showed heavy proteinuria with a 24-h urinary protein of 9.2 g/day, and serum creatinine, albumin, and total cholesterol levels were 1.36 mg/dL, 2.40 g/dL, and 283 mg/dL, respectively. MCD was diagnosed, and the patient achieved complete remission after cessation of rifampicin without undergoing steroid therapy.

Key Words: Minimal change disease, rifampicin, steroid
Antinuclear antibody and P-anti-neutrophil cytoplasmic antibody (ANCA) and C-ANCA were all negative with normal serum complement levels.

According to a renal biopsy, MCD was present with focal thinning of the glomerular basement membrane (Fig. 1A). Non-sclerotic glomeruli were normocellular without mesangial expansion, and the tubules showed minimal atrophy and mild focal tubular injury. Additionally, the interstitium was widened by minimal fibrosis, and no depositions of immunoglobulins or complement components were observed in the glomeruli. Electron microscopy showed the podocyte foot processes to be diffusely effaced (Fig. 1B).

Due to toxic hepatitis, rifampicin and isoniazid were discontinued, but ethambutol hydrochloride and pyrazinamide were maintained. Moxifloxacin was added after 1 week, and isoniazid was added after 2 weeks. The pleural tuberculosis was well controlled with isoniazid, ethambutol hydrochloride, and moxifloxacin thereafter.

When her diagnosis was confirmed to be MCD, we determined to use steroid therapy at first. However, she was afraid of adverse effects of steroid treatment and asked us to observe closely. Moreover, we found out that heavy proteinuria was developed after using anti-tuberculosis agents. In addition, hepatitis also occurred after anti-tuberculosis agents started, and then we had to stop rifampicin and isoniazid agents. Fortunately, she improved spontaneously without steroid use only after quitting rifampicin. Therefore, we observed and followed up continuously. Her nausea, vomiting, and general edema improved and her body weight recovered from 68 kg to 63 kg at 3 weeks after rifampicin discontinuation, and a random urine protein-to-creatinine ratio was 0.14 at 8 weeks (Fig. 2). Furthermore, her serum albumin and cholesterol levels were shown to be 3.9 g/dL and

![Fig. 1.](image-url)
er medications except for daily 10 mg of amlodipine. We found out that heavy proteinuria developed after using anti-tuberculosis agents. Fortunately, her proteinuria was improved after discontinuation of rifampicin and isoniazid. In addition, we added isoniazid except for rifampicin, but MCD did not recur. Taken together, the use of rifampicin seems to have resulted in developing MCD mostly in this case.

Although there are no definite mechanisms offered for rifampicin-induced MCD, a hypersensitivity mechanism has been suggested in many drug-induced MCD cases. For example, drug exposure can result in the release of permselectivity promoting factors from activated inflammatory or immune cells, causing MCD. Another possible mechanism of MCD is via direct toxin effects on glomerular epithelial cells, resulting in abnormal permeability and effacement of the foot processes.

Neugarten, et al. reported the first case of rifampicin-induced nephrotic syndrome, and described the patient as having acute interstitial nephritis with heavy proteinuria and effacement of the glomerular epithelial cells. They suggested that cell-mediated and humoral immune responses to the rifampicin treatment could develop, and Tada, et al. suggested that endothelial injury resulting from rifampicin-induced hemolysis and thrombocytopenia seems to play a role in the development of nephrotic syndrome. In our case, there was no electron-dense glomerular deposits or immune complex glomerulonephritis to suggest a humoral immune mechanism. Additionally, there was no hemolysis or thrombocytopenia. Thus, we surmised that, rifampicin-induced MCD in this case, might have originated from direct toxin effects.

In many cases, withdrawal of the offending drugs can lead to a full recovery, and glucocorticoids may hasten the return of renal function and ameliorate proteinuria. In one rifampicin-induced MCD case, the MCD was improved after oral administration of prednisolone and the cessation of rifampicin. We simply terminated the rifampicin instead of initiating steroid therapy, and the patient recovered from heavy proteinuria, edema and hypoalbuminemia thereafter. Although additional studies are required, simply discontinuing rifampicin may improve the rifampicin-induced MCD without the need for steroid therapy.

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