Author's response to reviews

Title: Rifampin-associated tubulointerstitial nephritis and Fanconi syndrome presenting as hypokalemic paralysis

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Author's response to reviews: see over
Editor-in-Chief, BMC Nephrology

Thank you very much for the evaluation of our manuscript. We are returning a revised manuscript which incorporates many of the suggestions made by reviewers. A response to the referees’ suggestions has been listed one by one, and an index of change has been included. We hope that the comments of the referees are adequately addressed in the revised manuscript.

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Title: Rifampin-associated Tubulointerstitial Nephritis and Fanconi Syndrome Presenting as Hypokalemic Paralysis

**Major Changes**

1. Detailed description about re-exposure, interruption and compliance to rifampin
2. Addition of electrolyte data in Table 1
3. Additional description of IgA nephropathy

**Minor Changes**

1. Change in conclusion sentence
2. Additional description about hematuria and liver enzymes

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Reviewer: Thangamani Muthukumar

Minor essential revisions

1. Please provide information on how long the patient was treated with Rifampin-based therapy prior to the development of symptoms.

   I agree with your comment. The information on duration of rifampin therapy was important to comprehend this article. He had been treated with isoniazid 300 mg, rifampin 450 mg, and ethambutol 800 mg daily during past 2 months prior to the development of symptoms. We added this information in case presentation.

2. Based on the discussion section it appears that the patient was not on a interrupted regimen. How was his medication compliance? Did he skip taking any dose. Mention in the 'Case Presentation' section the nature of his dosing regimen and his compliance status.

   He had no history of prior exposure to rifampin or drug interruption, as you indicated. His compliance to antituberculosis antibiotics was good, and did not skip any dose of rifampin during 2 months of antituberculosis therapy. This information is critical to make this article interesting, because most patients with rifampin-associated acute tubulointerstitial nephritis had history of reintroduction on rifampin in previous reports. We clearly described his compliance and no exposure history of rifampin to the section of case presentation.

3. Please provide the urine electrolytes values in the table.

   I agree with your comment. Addition of data about urine electrolytes might provide more detailed information. We revised the Table 1 to include the values of urine electrolytes.
4. In Conclusion section (line 1), please change the sentence "rifampin can induce ATIN' to 'rifampin can be associated with ATIN.

I appreciate your comments. Your recommendation made conclusion more sensible. We changed the conclusive sentence as you indicated.
Reviewer: Rafique Moosa

Major

1. Please, indicate if patient had prior exposure to Rif. Most patient, have had previous exposure.

As you indicated, patients with rifampin-associated acute tubulointerstitial nephritis (ATIN) were frequently associated with interruption or reintroduction on regimen in previous reports. However, our patient had no history of prior exposure to rifampin or drug interruption. This finding is distinct difference from most reports on rifampin-associated ATIN. We clearly described no history of re-exposure or interruption on rifampin and his compliance to drug in case presentation.

2. What were the findings in dipsticks examination? Haematuria is a consistent finding with ATIN

I agree with your comment that hematuria is one of the findings associated with ATIN. In our patient, hematuria was detected in urinalysis at initial assessment and it disappeared at the three-month follow-up after rifampin withdrawal. We additionally described this information in case presentation.

3. The renal pathology is consistent with Ig A nephropathy. The authors should comment on this.

I agree with your comment. The deposits of immunoglobulin A (IgA) in the glomeruli and electron-dense deposits in the mesangial spaces supports the findings of IgA nephropathy. We added the comments about IgA nephropathy in case presentation and discussion.

Minor
1. If serum magnesium available, should be mentioned.

I agree with your comment. The normal concentration of magnesium is crucial for neuromuscular activity and magnesium deficiency is often seen with hypokalemia. In this patient, serum magnesium level was in normal range at initial assessment and follow-up. We added the value of serum magnesium level in Table 1.

2. Were liver enzymes

I agree with your comments that information about liver enzyme is necessary. In previous reports, the elevation of liver enzymes was often accompanied with rifampin-associated ATIN. However, liver enzyme levels of our patient were within the normal ranges. We additionally described the information about the liver enzymes in case presentation.