Author's response to reviews

Title: Inhaled tobramycin solution-associated recurrent eosinophilia and severe persistent bronchospasm in a patient with cystic fibrosis: a case report

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Author’s response to reviews:

Dear Dr. da-Silva,

We very much appreciate the reviewers’ constructive suggestions, and the opportunity to clarify the case presentation in our manuscript.

Our responses to the reviewers' comments follow:

Reviewer 1

1. The Naranjo scale is not longer mentioned in the abstract.
2. Homozygous was replaced by homozygosity.
3. The rationale for cromolyn and dornase alfa now is provided in the manuscript.
4. The information regarding the serum level was deleted.
5. Our rationale for initiation of chronic aminoglycoside inhalation therapy is provided during the two occasions when there was no concurrent positive Pseudomonas culture.
6. It has been clarified that the eosinophilia developed during treatment with intravenous tobramycin during the hospitalization.
7. Bronchoscopy should have been considered, and this is addressed in the discussion section.
8. Prior to ordering a sinus biopsy, it seemed prudent to ensure that the patient had CT evidence of sinus disease. (As the reviewer states, sinus disease is present in "almost all" patients with CF, which is an acknowledgement that on rare occasions patients do not have sinus disease.)
9. When the patient was 6.5 years old, the prednisone was tapered slowly after the patient had received systemic steroid therapy for a year. (The prednisone was not decreased when the patient was between 6 and 6.5 years old, because his clinical improvement at the time was thought to be related to the systemic steroid therapy rather than discontinuation of the TSI.)
10. ABPA is discussed as a potential diagnosis in the discussion.
11. The validation of the Naranjo scale is provided in the discussion.
12. The dose response paragraph has been deleted.
13. It is clarified that the idea of intra-cellular tobramycin accumulation is based on in vitro data, and that it is only possible that this is related to our patient's response.

Reviewer 2

1. We do not have data regarding airway eosinophilia, and mention in the discussion that the patient might have benefited from such a measurement.
2. When there was no baseline airway obstruction, there was no evidence of bronchodilator responsiveness. This observation has been added to the results section. An airway challenge test was never performed.

Thank you very much for your consideration.

Sincerely,

Ran D. Anbar, MD