Author's response to reviews

Title: Polytetrafluoroethylene fume-induced pulmonary edema: a case report and comprehensive literature review

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Author's response to reviews: see over
Dear Professor Kidd,

Re: Revised version of the manuscript #ID 1826935669153157: “Polytetrafluoroethylene fume-induced pulmonary edema: a case report and comprehensive literature review”.

My coauthors and I thank you for considering our manuscript for publication in the *Journal of Medical Case Reports*. We very much appreciate the time spent on the manuscript by the reviewers and their invaluable comments and suggestions; we have incorporated these into the revised version. The reviewers have clearly identified the vulnerable points in our manuscript, enabled us to present new results and discussion, and greatly increased its scientific value. Our point-by-point responses to their comments are attached.

In the revised (R1) version of the manuscript, changes to the previous version have been highlighted in blue font. We hope these revisions render the revised manuscript suitable for publication in the *Journal of Medical Case Reports*.

The authors would like to inform you that because of the comprehensive literature review, the number of the references listed slightly exceeds the maximum reference limit recommended for this type of publication in your journal.

Once again, thank you very much for your time and consideration. We look forward to hearing from you at your earliest convenience.

Yours sincerely,

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Response to reviewers’ comments

Reviewer #1 (Dr Koichi Fukunaga)

Thank you very much for your time and helpful suggestions. We agree with your advice. Changes addressing your comment have been incorporated into the revised (R1) version of the manuscript.

It is well known although rare, that pulmonary edema induced by chemical agent is treated with NPPV before intubation and/or neutrophil elastase inhibitor in clinical.

Thank you for this comment. We understood your concern. As you indicate, our original manuscript may not have contained sufficiently novel information regarding the treatment of polytetrafluoroethylene (PTFE) fume-induced pulmonary edema. The other reviewer was also concerned about the usefulness of a neutrophil elastase inhibitor. Consequently, we have deleted or toned down the relevant descriptions concerning PTFE.

Instead, we have focused on the other important point in the R1 version. We sought to determine the radiological features of PTFE-induced pulmonary edema. Two chest radiologists (authors KK and TT) independently reviewed all of the CT images from the reported cases (including our case), and made significant findings. Our new results have been included in revised Table 2, as well as in the text of the R1 version of the manuscript. We hope these revisions meet with your expectations. Please re-evaluate the validity of our R1 version of the manuscript.

Reviewer #2 (Dr Dominick Shaw)

We were pleased to see your positive comments. Thank you for your time and valuable suggestions. We have thoroughly amended our manuscript based on your advice.

Nice report

Thank you very much for evaluating our manuscript positively.

the value of administration of the neutrophil elastase inhibitor is overstated.
the literature review reveals most patients survive (at least those published) with supportive treatment only.
there needs to be a lot more evidence that the neutrophil inhibitor had an effect; if there is none the statements around the drug need to be toned down.
We appreciate your comments. As you indicate, we have overstated the value of the neutrophil elastase inhibitor. We found pathological consistency between PTFE fume-induced pulmonary edema and the exudative phase of the acute respiratory distress syndrome (ARDS); there was marked neutrophil migration into the alveoli with alveolar edema. Although one study has suggested the clinical usefulness of Siverestat in this etiology [1], another double-blind placebo controlled trial did not [2]. We are aware that the clinical usefulness of neutrophil elastase inhibitor is still controversial. The other reviewer also stated concerns related to this matter. Therefore, we have deleted or toned down the corresponding descriptions.

Your valuable advice enabled us to focus on another important point, namely that the radiological features of PTFE fume-induced pulmonary edema have not been determined so far. Thus, we conducted the first radiological review of PTFE fume-induced pulmonary edema in the R1 manuscript with the assistance of two chest radiologists. Our survey revealed that the CT findings of bilateral ground-glass opacity or patchy consolidation with clear peripheral area sparing could be used to distinguish this disease. We also noted that the lesions were likely to distribute in a dorsally dominant manner. These plausible explanations for these characteristics are also discussed in the R1 manuscript. Once again, thank you for your comment, which clearly indicated the vulnerability of our manuscript.

Other changes

1. Systematic inflammatory response syndrome (SIRS)
We noted the occurrence of SIRS; and flu-like symptoms such as fever and chill frequently accompanied PTFE fume-induced pulmonary edema. We believe the essential etiology of PTFE fume-induced pulmonary edema is inflammatory pulmonary vascular hyperpermeability. Flu-like symptoms and SIRS are likely to be associated with the pulmonary inflammation response to the PTFE fumes. These revisions have been incorporated into the R1 text and Table 1.

2. Authorship changes
After discussion and mutual agreement, we have added two authors (KK and TT; both are chest radiologists who reviewed all of the CT images, and critically revised the manuscript) and made corresponding changes to the R1 title page.

3. Keywords alteration
Keywords listed in the R1 title page have been changed to be consistent with these revisions.
4. Update of the reference list
We have added several new references (references 19, 21, 23 and 24) to reinforce our work and/or provide updated information.

5. Title alterations
The title has been changed to be consistent with these revisions.

References