Reviewer’s report

Title: A case of pleural effusion caused by Mycobacterium fortuitum and Mycobacterium mageritense coinfection

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Reviewer: Tavs Qvist

Reviewer's report:

Review "A case of pleural effusion caused by Mycobacterium fortuitum and Mycobacterium mageritense coinfection"

Hirabayashi and coauthors from the respected Kobe City Medical Center have written a case report on the successful management of a parapneumonic effusion from Mycobacterium fortuitum and Mycobacterium mageritense.

The case will interest readers particularly NTM clinicians and microbiologists and it is important that these cases be published in order for NTM management experiences to be shared.

The microbiological methods employed are sound and the manuscript is concise. It would benefit from a little English language editing, but is generally well-written. The chosen radiological images are good.

There are however some major and minor issues that need to be addressed

Major comments:

1. It is important to report if the patient was resampled from any sites, whether she became sputum or BAL negative (or was simply unable to produce). And how fast did her infection resolve. In the image texts it is simply written "after the treatment" - this should be specified - how many weeks into treatment? The length and content of the maintenance therapy is very important, and what was the status at the time of manuscript writing. Was she still on treatment? Is she considered cured?
She clearly fulfilled the ATS/IDSA criteria for NTM pulmonary disease when she presented and this should be mentioned. But did she also fulfill the criteria for being cured or is she still in treatment and is it in fact too early to say (which is okay - the timeline should just be clear). We would like to know the rationale behind the chosen therapy (which seems like reasonable choices and doses). But was it local guidelines or a multidisciplinary team decision based on clinical experience.

I'm not sure the concluding remark about "If the species cannot be identified, mycobacterial coinfection should be considered" is validated or backed up in guidelines.

In general the case needs to be placed better within the context of the existing literature. ATS/IDSA guidelines are correctly mentioned, but they predate some methods and I think the manuscript would benefit from referring to the new British Thoracic Society NTM guidelines by Haworth and Floto published in Thorax. It's section 8 contains evidence graded statements on diagnostics including MALDI-TOF (that are generally positive).

Minor comments:

Abstract Line 19: Grammar - remove the word "who" after "pegol".

Abstract line 42: "There are no previous report about the coinfection with two different mycobacterial species."

This sentence is not precise and contextually confusing. Pulmonary coinfection with NTM has been observed, for example in cystic fibrosis, although not that commonly. This point is correctly made later in the manuscript, but this sentence is too reductive. I agree that pleural effusion/infection with two rapid-growers is unreported. So the sentence should be reformulated with the words pleural effusion and "mycobacterial" should be changed to "non-tuberculous mycobacterial". Alternatively delete completely as the next sentence repeats the point about originality.
Concerning keywords: remember non-tuberculous is often spelled nontuberculous, "NTM" is relevant keyword too

Background page 4 line 15: "As a group of NTM, rapid-growing mycobacteria (RGM) contain Mycobacterium abscessus, M. chelonae, and M. fortuitum group species which include M. mageritense.

This sentence structure is too convoluted and uses passive voice - should be reworded.

Background page 4 line 18: Mycobacterium abscessus is a complex of 3 subspecies. Should be written as "Mycobacterium abscessus complex"

Case report page 4 line 56: 9 years ago should be changed to "9 years prior" or "earlier"

Page 5 line 18: A sentence on occupational exposure could be included after smoking.

Page 5 line 40: Was the thoracentesis performed as a diagnostic or therapeutic procedure (or both?) Was the 150 ml the entire effusion? Later on in the discussion, the importance of thoracentesis should probably be repeated - how important was this procedure therapeutically? Was it pus or clear fluid?

Page 5 line 50: Was a pH value obtained? The fluid cells counts are mentioned, but we lack some interpretation of the finding. In the discussion, the issue of (parapneumonic) effusion vs. empyema could be mentioned.

Page 5 line 56: Sentence structure problem. Should probably say: "Acid-fast bacilli were detected by Ziehl-Neelsen staining, but the species could not be identified by DNA-DNA hybridization or MALDI-TOF." Then the bit about drug susceptibility.
Remember MALDI-TOF cannot suggest or determine drug susceptibility - that part of the sentence should be changed. MALDI-TOF under the score cut-off might point in the direction of rapid growing mycobacteria", but really no susceptibility conclusions should be drawn from this.

Page 6 line 40: Was an initial loading dose of minocycline used?

Page 6 line 43: How long was maintenance therapy and with which compounds? How fast did it take for her fever / cough to resolve?

Page 7 line 1: "There are several reports of pulmonary infection or pleural effusion caused by NTM and MTC coinfection or M. avium and M. intracellulare coinfection."

This sentence is confusing for a number of reasons. It's the first time tuberculosis is mentioned, so the abbreviation should be written out, the use of "or" (twice) is not easy to understand. Remember also that M. avium is a complex (MAC) of which intracellulare is a part - so the phylogeny should be clear here.

Page 7 line 11: Yes, the mentioned contamination problem is relevant, although I wonder if the authors are thinking more about a airway "colonization" problem. If the patient's airways is infected with one NTM and simultaneously colonized by another, than the sputum culture might show both and not discriminate between the meaningful infection and the transient colonization. In this case report, certainly we are more likely to think that both rapid growers are significant. So I agree on that point, but I think the word "contamination" should be replaced with "colonization".

If the authors are in fact thinking about nosocomial or lab contamination, remember that even aseptic aspiration is subject to environmental exposure later in the lab as some procedures take place in the open and in vials that might have been exposed to tap water. The most common lab contaminant is a species such as M. gordonae, but others are also seen.

Page 7 line 21: I would leave out the words "in a rare occurrence" as the point has been made quite a few times.
Page 7 line 34: Grammar: "MALDI-TOF MS is one of the developing methods for identifying the mycobacteria" I would rephrase "developing methods", use NTM instead of mycobacteria and remove "the" before NTM. I would refer to the BTS guidelines here also and mentioned the context.

Best regards,

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Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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I am able to assess the statistics

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