Author's response to reviews

Title: A case of Mycobacterium goodii prosthetic valve endocarditis in a non-immunocompromised patient: use of the 16S rDNA technique for rapid diagnosis

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Version: 3 Date: 31 May 2012

Author's response to reviews: see over
To the editor,

In response to reviewer Jakko van Ingen, we have the following comments:

We regret all the factual errors in the manuscript. We have therefore included a mycobacteriologist, Dr Erik Sturegård, as a coauthor. Dr Sturegård is in fact responsible for our mycobacteriological laboratory and was involved in the diagnosis of this particular *M. goodii* strain.

#1 Our intention was not to review all slow and rapid growers, but mainly discuss *M. goodii* infections and endocarditis due to other NTM. We have deleted the 2nd sentence in “Background”.

#2 Rational for empirical treatment of suspected bacterial meningitis (p 4, l 19-) and suspected endocarditis (p 5, l. 7-8) are already stated. Cefotaxim was replaced by meropenem and gentamycin and ciprofloxacin were continued, all based on susceptibility pattern. This information is added and rephrased on p 5, bottom line and first line p 6. Later meropenem was replaced by ampicilllin (again based on lower MIC – added in p 6, l 10-11). The same rationale applies for tigecycline as already stated.

#3 We agree with the reviewer’s comment describing antibiotic susceptibility testing (AST) for NTM (including RGM) as an artform. The standard procedure for AST of RGMs at our mycobacterial lab is Etest on Mueller Hinton agar. We have a long experience interpreting these results and have seen good correlation with our results using Etest and results from other labs using micro titer plates with MH broth. We have clarified this in the manuscript (p.5, bottom).

#4 The mycobacterial laboratory consults the reference mentioned (Griffeth et al) at a regular basis. We chose, however, to expand the number of antibiotics tested in our AST. The reasons for this were twofold: i) we had no experience in handling invasive *M. goodi* infections and wanted to obtain as much information as possible. ii) There was only quite limited data available adding to our motivation of obtaining as much AST results as possible.

#5 First part of conclusion has been rephrased.

#6 Species identification of NTM’s can be difficult and the lack of a golden standard for identification is problematic. In our case we initially investigated the strain using 16S rDNA sequencing as the initial diagnosis was a slow growing Gram positive rod. Once the strain was sent to the mycobacterial laboratory additional analyses with line probe assay (Genotype® Mycobacterium CM/AS, HAIN Lifescience) was performed. In the Genotype® Mycobacterium AS assay the *M. smegmatis* can be differentiated from *M. goodi*. As both analyses showed *M. goodi* we felt confident that we had the correct identification to the species level. Moreover, the strain has demonstrated complete homology with *M. goodii* isolates in GenBank by sequence analysis of the 16S rRNA gene This is clarified in the manuscript (p.5, bottom)

#7 We realize that our discussion on clarithromycin susceptibility and the erm gene are less relevant for this case report, and a further clarifying discussion on this issue would require a lot of space. Therefore this section has been deleted (p 9, top).
We certainly agree that the clinical validity of breakpoints is scarce and that coherent data supporting the correlation between MIC´s and treatment outcome is lacking; we nevertheless felt it would be improper to ignore our MIC values when choosing drugs for antimicrobial treatment, as these drugs were commonly used in NTM treatment. We have added a comment on this issue (p 9, l 7-8).

We appreciate the information on treatment with tigecycline, and “NTM” is replaced by “M. goodii” (p 9, l 9).

“Increasingly” is removed. We are fully aware of specific blood-culture systems for mycobacteria which we certainly use when there is clinical suspicion of mycobacterial bloodstream infection. But one important message of this paper is that RGM can be detected in ordinary blood-culture systems. This information has been added on p 9, l 13-17.

Minor revisions:

1. 65 is replaced by more than 135 (p 7, l 10)
2. Ref 20 is excluded
3. “Atypical” replaced by “NTM” (p 8, l 11).
4. “Intermittent” replaced by “partial” (p 5, l 12).
5. Chest “X-ray” is replaced by chest “radiograph” (p4, l 22)
6. In Sweden betamethasone is used – dexamethasone is not available.
7. We realize we have confused “previously healthy” before the first valve replacement, and at the time of prosthetic valve endocarditis she was certainly not healthy. “Otherwise healthy patient” has been removed from background chapter.

In response to reviewer Bum-Joon Kim we have the following comments:

We believe we have responded also to this reviewer´s comments – see #6, reviewer van Ingen.

Comments to the editor:

We have rewritten the abstract according to your guidelines.

We have rewritten the section on informed consent.

Sincerely,

M.D., PhD. Göran Jönsson

Lund, 28:th of May 2012