Author’s response to reviews

Title: Probiotics and infective endocarditis in patients with Hereditary Hemorrhagic Telangiectasia: a clinical case and a review of the literature

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Reza Ghotaslou (Reviewer 1)

1. How you concluded that prophylaxis with antibiotics before nasal packings in patients with HHT can be effective in preventing serious infections?

We agree that the final sentence is too strong. Actually, our statement is not supported by evidences from the literature; however, we think prophylaxis should be advisable for patients with this disease considering the reported high risk of infection following this procedure. Therefore, we changed the sentence as follows: “… antibiotic prophylaxis should be considered.”

2. The methodology employed by the authors was not straightforward, why you did not tested aminoglycoside MIC as a drug of choice against probiotic sepsis?

Susceptibility to aminoglycosides was assessed by disk diffusion. E-test was not used because it was unavailable at the time of the study. We added in the text that the isolate was susceptible to gentamicin, line 139 pag 4

3. Why you did not describe clinical manifestations and mortality rate?

We think that in the case report we described all the clinical manifestation. Regarding the mortality rate, I suppose that the reviewer referred to infective endocarditis in HHT. Based on data reported in table 3, the mortality rate was 16% (1/6). This was added in the text at line 285 pag 12
4. Minor Essential Revisions, The language in the manuscript needs improving. According with the reviewer’s suggestion the English text was improved.

5. The format of tables 2 and 3 is not correct, they are so small font. According with the reviewer’s suggestion, we enlarged the font

6. The title is not informative, please change it. The title was changed as follows: “Probiotics and infective endocarditis in patients with Hereditary Hemorrhagic Telangiectasia: a clinical case and a review of the literature”

7. Did you search any database about probiotics and endocarditis? In a review of 12 electronic databases, the authors evidenced no increased risk; however, rare adverse events were difficult to assess. (Hempel S et al. Evid Rep Technol Assess 2011; 200: 1-645). We think that this information is of limited utility for our manuscript and we decided not to include into the txt.

8. For definitive diagnosis of endocarditis where is your criteria? Duke's criteria were used (a statement was added in the text)

9. What dose difference between infective endocarditis and subacute bacterial endocarditis? In our knowledge, the dose of antibiotics is similar in acute and subacute infective endocarditis.

10. Did your patient have other predisposing factors as cardiac diseases? The patient had an aortic bioprosthesis implanted in 2015; we describe this in lines 105-106 pag 3; he had no other predisposing factors

11. your final sentence” Finally, we suggest that these patients avoid use of probiotics” seems is not absolutely correct, because probiotics is so important for health! In such patients how can the physicians avoid inappropriate use of probiotics? We agree with the suggestion of the reviewer and we deleted the last sentence.

12. Reference 3 has not published yet. According with the reviewer suggestion, we deleted the reference 3 and added the hyperlink in the text

13. Figure 1 delete.
A figure with a schematic representation of clinical events (timeline) was requested by the editor, but it is not essential and can be discarded. We also deleted tab 1.

Federico Pea (reviewer 2)

- In the description of the case there are some events that are not described in the right temporal sequence (i.e. lines 104-115). Please amend.

We amended the text (lines 114-116 pag 4)

- Treatment included a combination of amoxi/cav and gentamycin. However from the antibiogram, it appears that the susceptibility to GM was not tested. Please comment.

Susceptibility to aminoglycosides was assessed by disk diffusion. E-test was not used because it was unavailable at the time of the study. We added in the text that the isolate was susceptible to gentamicin, line 139 pag 4

- The section devoted to microbiology should be moved to supplementary material.

according to the reviewer’s suggestion the section devoted to microbiology was moved to supplementary material.

- The discussion is too long and not completely focused on the findings. The Ms. would greatly benefit from a consistent shortening of this section. For example, the concepts stated in the first paragraph have just been included in the introduction and may be deleted (lines 211-257). Conversely, it would be more interesting discussing more in depth the pathogenetic mechanisms of IE caused by L. rhamnosus and the exp model of IE (especially the work of Vankerckhoven V JMM 2007). In regarg to treatment options, it would be interesting discussing the study of Salminen et al. CID 2006 (Clin Infect Dis. 2006 Mar 1;42(5):e35-44. Lactobacillus bacteremia, species identification, and antimicrobial susceptibility of 85 blood isolates. Salminen MK1, Rautelin H, Tynkkynen S, Poussa T, Saxelin M, Valtonen V, Järvinen A.)

We agree with the suggestions of the reviewer and we modified the text accordingly.