Response to Reviewers

06.AGO.2021

To World Journal of Clinical Cases

Article Type: Case Report

Manuscript Title: Heart failure as an adverse effect of infliximab for Crohn's disease: A case report and review of literature

Dear Editor

Thank you for the opportunity to revise our manuscript. We are delighted that the journal has welcomed a revision. Based on the suggestions of the reviewer, we have modified the original manuscript. Our responses to the reviewer concerns, and the subsequent modifications made to the manuscript are listed below on a point-by-point basis.

The authors would like to thank the reviewer for their careful and constructive comments.

Sincerely Yours,

Thais Gagno Grillo

Department of Internal Medicine, São Paulo State University (Unesp), Medical School, Botucatu 18618687, Brazil.

Tel.: +5514 38801171. Fax: +55 14 38801667

Email: thaisgagno@gmail.com

Comments from the Reviewer:

Reviewer #1:

Specific Comments to Authors: The authors report a case of a patient who develops new heart failure approximately 6 months after commencing infliximab for Crohn's disease treatment. It is a well presented case. This is a well recognized complication of anti-TNF therapy but important for clinicians to be cognizant of when commencing anti-TNF therapy and the report provides a good overview of the topic.
I have the following suggestions:
1 - for the resected specimen, can you please provide histological findings such as the presence of granulomas or chronic inflammation
Response: Histological findings were added. Figure 4 showing the histological findings were added.

2 - did the patient have any prior echocardiograms? Is it considered that the patients heart failure was entirely due to anti-TNF therapy or due to underlying hypertensive cardiomyopathy that was worsened by anti-TNF therapy?
Response: The patient had no previous echocardiogram. We believe that the reported patient probably had asymptomatic prior cardiac structural damage, related to the presence of risk factors such as diabetes mellitus and arterial hypertension, characterizing stage B of the AHA/ACC classification. With exposure to infliximab, especially after dose optimization to 10mg/kg, HF decompensation could be observed. Thus, we could assume that exposure to infliximab was the main causal factor related to the onset of acute HF in this patient, who probably had previous structural heart disease. This information has been added to the text (discussion).

3 - do the authors propose any specific changes that their case and assessment of literature should be considered at higher risk of heart failure and what screening would be suggested?
Response: Yes, we have written some recommendations based on specific consensus. "We recommend for patients in AHA/ACC stage A who are indicated to use infliximab: 1) Pre-treatment basal BNP dosage; 2) Strict control of associated comorbidities such as diabetes mellitus, arterial hypertension, and coronary artery disease; 3) Close monitoring of signs and

symptoms of HF after starting treatment with infliximab; 4) Infliximab concentration monitoring and dose correction according to the therapeutic target. The recommendations for patients in stage B of the AHA/ACC are: 1) Pretreatment echocardiography in patients with baseline BNP levels above the reference value for outpatients. 2) If echocardiography (current or previous < 5 years) is normal or with minimal change, the recommendations are the same for patients in stage A of the AHA/ACC, as detailed above. 3) If echocardiography (current or previous) shows signs of structural and/or functional heart disease, it is recommended to start infliximab after adequate control of comorbidities, and introduction and dose adjustment of beta-blockers and angiotensin converting enzyme inhibitors or angiotensin receptor blockers. In addition, it is recommended to avoid other medications that potentially cause HF decompensation, use dose of 5mg/kg for infliximab, other specialties medical monitoring, and strictly monitor signs and symptoms of HF. We also emphasize the need for further studies on this topic." This information has been added to the text (discussion).

Minor points: Treatment section, first sentence

4 - Opted for infliximab suspension, and furosemide was introduced. Please revise the grammar of this sentence.

Response: The suggested sentence was revised. Thank you for your considerations.

Reviewer #2:

Specific Comments to Authors: The manuscript is well, concisely and coherently organized and presented.

Response: The authors would like to thank the reviewer**.**

4 LANGUAGE POLISHING REQUIREMENTS FOR REVISED MANUSCRIPTS SUBMITTED BY AUTHORS WHO ARE NON-NATIVE SPEAKERS OF ENGLISH

Response: A revised manuscript was provided.

5 ABBREVIATIONS

In general, do not use non-standard abbreviations, unless they appear at least two times in the text preceding the first usage/definition. Certain commonly used abbreviations, such as DNA, RNA, HIV, LD50, PCR, HBV, ECG, WBC, RBC, CT, ESR, CSF, IgG, ELISA, PBS, ATP, EDTA, and mAb, do not need to be defined and can be used directly.
The basic rules on abbreviations are provided here:

(1) Title: Abbreviations are not permitted. Please spell out any abbreviation in the title.
Response: There are no abbreviations in the title.

(2) Running title: Abbreviations are permitted. Also, please shorten the running title to no more than 6 words.
Response: The running title was shortened.

(3) Abstract: Abbreviations must be defined upon first appearance in the Abstract.
Response: Abbreviations have been defined upon first appearance.

(4) Key Words: Abbreviations must be defined upon first appearance in the Key Words.
Response: Abbreviation has been defined.

(5) Core Tip: Abbreviations must be defined upon first appearance in the Core Tip. Example 1: Hepatocellular carcinoma (HCC). Example 2: Helicobacter pylori (H. pylori)
Response: Abbreviations have been defined upon first appearance.

(6) Main Text: Abbreviations must be defined upon first appearance in the Main Text.
Response: Abbreviations have been defined upon first appearance.

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(8) Figures: Abbreviations are not allowed in the Figure title. For the Figure Legend text, abbreviations are allowed but must be defined upon first appearance in the text. Example 1: A: Hepatocellular carcinoma (HCC) biopsy sample; B: HCC-adjacent tissue sample. For any abbreviation that appears in the Figure itself but is not included in the Figure Legend textual description, it will be defined (separated by semicolons) at the end of the figure legend. Example 2: BMI: Body mass index; US: Ultrasound.
Response: There are no abbreviations in the Figures.

(9) Tables: Abbreviations are not allowed in the Table title. For the Table itself, please verify all abbreviations used in tables are defined (separated by semicolons) directly underneath the table. Example 1: BMI: Body mass index; US: Ultrasound.

Response: There is no Table in the manuscript.

6 EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor:

1 Scientific quality: The manuscript is a case report of patient who develops new heart failure approximately 6 months after commencing infliximab for Crohn's disease treatment. The topic is within the scope of the WJCC. (1) Classification: Grade C, Grade C. (2) Summary of the Peer-Review Report: this is a well-presented case, it presented a good overview of the topic.

Please clarify that patients heart failure was entirely due to anti-TNF therapy or due to underlying hypertensive cardiomyopathy that was worsened by anti-TNF therapy?

Please provide histological findings such as the presence of granulomas or chronic inflammation.

Response: These items were answered above.

(3) Format: There are 3 figures; (4) References: A total of 31 references are cited, with no reference published in the last 3 years; (5) Self-cited references: There are no self-cited references. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations (i.e. those that are most closely related to the topic of the manuscript) and remove all other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated; and (6) References recommendations: The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially references published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation:

Classification: Grade B, Grade C. Certificate from Editage was issued. 3 Academic norms and rules: Authors provided Non-Native Speakers of English Editing Certificate. CARE Checklist–2016. Signed Informed Consent Form(s) or Document(s). No academic misconduct was found in the Google/Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The topic has not previously been published in the WJCC. 5 Issues raised:

(1) Core-tip audio is missing;
Response: Core-tip audio was provided.

(2) Please update manuscript format per journal guidelines;
Response: The manuscript was updated.

(3) Please provide Copyright License Agreement and *Conflict-of-Interest Disclosure Form;
Response: The Copyright License Agreement was provided.

(4) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.
Response: Ok, original pictures were provided.

(2) Company editor-in-chief:

1 Scientific quality: The manuscript is a case report of patient who develops new heart failure approximately 6 months after commencing infliximab for Crohn's disease treatment. The topic is within the scope of the WJCC. (1) Classification: Grade C, Grade C. (2) Summary of the Peer-Review Report: this is a well-presented case, it presented a good overview of the topic. Please clarify that patients heart failure was entirely due to anti-TNF therapy or due to underlying hypertensive cardiomyopathy that was worsened by anti-TNF therapy? lPease provide histological findings such as the presence of granulomas or chronic inflammation. (3) Format: There are 3 figures; (4) References: A total of 31 references are cited, with no reference published in the last 3 years; (5) Self-cited references: There are no self-cited references. The self-

referencing rates should be less than 10%. Please keep the reasonable self-citations (i.e. those that are most closely related to the topic of the manuscript) and remove all other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated; and (6) References recommendations: The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially references published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com. The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately. 2 Language evaluation: Classification: Grade B, Grade C. Certificate from Editage was issued. 3 Academic norms and rules: Authors provided Non-Native Speakers of English Editing Certificate. CARE Checklist–2016. Signed Informed Consent Form(s) or Document(s). No academic misconduct was found in the Google/Bing search. 4 Supplementary comments: This is an unsolicited manuscript. The topic has not previously been published in the WJCC. 5 Issues raised: (1) Core-tip audio is missing; (2) Please update manuscript format per journal guidelines; (3) Please provide Copyright License Agreement and *Conflict-of-Interest Disclosure Form; (4) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. 6 Re-Review: Not required. 7 Recommendation: Conditional acceptance.

Response: The issues were answered above.

7 STEPS FOR SUBMITTING THE REVISED MANUSCRIPT

Step 5: Footnotes and Figure Legends

(1) Requirements for Figures: Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file, and submit as "69783-Figures.pptx" on the system. The figures should be uploaded to the file destination of "Image File".

Response: Ok, the Figures were provided.

Step 6: Automatically Generate Full-Text Files

Authors cannot replace and upload the "Manuscript File" separately. Since we only accept a manuscript file that is automatically generated, please download the "Full Text File" or click "Preview" to ensure all the contents of the manuscript automatically generated by the system are correct and meet the requirements of the journal. If you find that there is content that needs to be modified in the Full-Text File, please return to the corresponding step(s), modify and update the content, and save. At this point, you then have to click the "Save & Continue" button in Step 5 and the F6Publishing system will automatically regenerate the Full-Text File, and it will be automatically stored.

Step 7: Upload the Revision Files

For all required accompanying documents (listed below), you can begin the uploading process via the F6Publishing system. Then, please download all the uploaded documents to ensure all of them are correct.

(1) 69783-Answering Reviewers
(2) 69783-Audio Core Tip
(3) 69783-Conflict-of-Interest Disclosure Form
(4) 69783-Copyright License Agreement
(5) 69783-Approved Grant Application Form(s) or Funding Agency Copy of any Approval Document(s)
(6) 69783-Signed Informed Consent Form(s) or Document(s)
(7) 69783-Non-Native Speakers of English Editing Certificate
(8) 69783-Video
(9) 69783-Image File
(10) 69783-Table File
(11) 69783-CARE Checklist–2016
(12) 69783-Supplementary Material

9 CONFLICT-OF-INTEREST DISCLOSURE FORM

Please click and download the fillable ICMJE Form for Disclosure of Potential Conflicts of Interest (PDF), and fill it in. The Corresponding Author is responsible for filling out this form. Once filled out completely, the Conflict-of-Interest Disclosure Form should be uploaded to the file destination of 'Conflict-of-Interest Disclosure Form'.