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**Primary Sclerosing Cholangitis and Autoimmune Hepatitis
Overlap Syndrome associated to Inflammatory Bowel Disease:
Case Report and Systematic Review**

Authors: Vinícius Remus Ballotin, Lucas Goldmann Bigarella, Floriano Riva,
Georgia Onzi, Raul Angelo Balbinot, Silvana Sartori Balbinot, Jonathan Soldera.

Response to Reviewers

Reviewer 1

Dear authors; This review is informative. But, table 2 is too long. This table should be shortened before publication.

We thank you for the input and the opportunity for improving our manuscript. We have moved the Table 2 to appendix/supplementary material, since there is no way we can possibly shorten it, as it is a description of each systematically reviewed case, and there are 108 cases. The summarized data of the cases will be available in the main file in the Table 1.

Reviewer 2

This article report a Case of Primary Sclerosing Cholangitis and Autoimmune Hepatitis Overlap Syndrome associated to Inflammatory Bowel Disease and Systematic Review on the disease. The result is helpful for clinical practice. I have a little suggestions:

We appreciate your input on our paper and we hope we can solve all of the three suggestions accordingly.

1) *In the paragraph of abstract, it should add the content of the case.*

We have added a brief summary of the case report in the abstract section, as suggested.

2) *In the study, there is no data that need to analyze using "the t-test, chi-squared and Wilcoxon test".*

We had done the analysis, but felt it would add little, since there are no direct comparisons. A descriptive approach was used. I believe this description of the statistical analysis is residual of a previous version of the paper. It has been suppressed.

3) *In the last summary, authors suggest "In more severe cases, liver transplantation can be performed." please give the clinical evidence or reference.*

We have added a reference for this sentence, and expanded further the idea in this sentence.

Reviewer 3

The manuscript (02731847) entitled "Primary Sclerosing Cholangitis and Autoimmune Hepatitis Overlap Syndrome associated to Inflammatory Bowel Disease: Case Report and Systematic Review" is by Ballotin et al. This is a case report and systematic review. The authors reported a case of a female patient with Autoimmune Hepatitis (AIH) and Primary Sclerosing Cholangitis (PSC) Overlap Syndrome associated to Ulcerative colitis and to systematically review the available cases of AIH and PSC overlap syndrome. They analyzed, 108 cases reported in 44 references. They concluded that PSC and AIH overlap syndrome is generally associated to inflammatory bowel disease and is associated to a low mortality and a good response to treatment.

We are grateful for your input and we hope to clarify the comments of the reviewer, to improve our manuscript.

Main comments

1. *Some language editing is needed. For example, in the second paragraph on page 6/53, "gamma-glutyl transferase.." should be "glutamy!".*

We have reviewed the text of the whole manuscript and we hope it is improved accordingly.

2. *Please define abbreviation before using them. For example, "GGT" was not define in this manuscript.*

We have reviewed the abbreviations and corrected such shortcomings.

3. *Please discuss and evaluate the treatment strategies that help the patients the most if possible.*

We have added a paragraph in the text about treatments used and response to it.

Response to Editors

We thank you for the input and the opportunity for improving our manuscript. We hope we have corrected every shortcoming accordingly, as we state below.

1. I have sent attached the .pptx file which has the text of the PRISMA flowchart.
2. In the final pages of the paper, we have added the article highlights.
3. We have provided a PMID number for every citation that has it. If the citation does not have it, we have sent a supplementary file with the first page of these citations as requested.
4. We have defined the article in the first page of the manuscript as a systematic review.

ID: 02731847 Primary Sclerosing Cholangitis and Autoimmune Hepatitis Overlap Syndrome associated to Inflammatory Bowel Disease: Case Report and Systematic Review Authors: Vinicius Remus Ballotin, Lucas Goldmann Bigarella, Floriano Riva, Georgia Onzi, Raul Angelo Balbinot, Silvana Sartori Balbinot, Jonathan Soldera. Response to Reviewers Re-Review 1 Dear authors, there are some error in manuscript. In 'core tip' section you mentioned that 'She had negative auto-antibodies' but in case report section you report that 'She had a reagent antinuclear factor (1:640, with a homogeneous nuclear pattern)' You have to check manuscript for language. There are some spelling error. We thank you for the input and the opportunity for improving our manuscript. We have reviewed the sentence and the text of the whole manuscript and we hope it is improved accordingly. Re-Review 2 The author has modified the article. After reviewing it again, I agree the manuscript is qualified for publishing on the journal. We thank you for the input and the opportunity for improving our manuscript. Re-review 3 In the Research perspectives of Article highlights, please correct "ghly" in the first sentence. In addition, abbreviations like " Hb: hemoglobin. Ht: Hematocrit" may not be needed. These abbreviations do not help the readers and could not save space either. We thank you for the input and the opportunity for improving our manuscript. We have removed the abbreviations "Hb: hemoglobin and Ht: Hematocrit" from the manuscript and we reviewed the text of the whole manuscript and we hope it is improved accordingly. Reviewer 1 This article report a Case of Primary Sclerosing Cholangitis and Autoimmune Hepatitis Overlap Syndrome associated to Inflammatory Bowel Disease and Systematic Review on the disease. The result is helpful for clinical practice. I have a little suggestions: We appreciate your input on our paper and we hope we can solve all of the three suggestions accordingly. 1) In the paragraph of abstract, it should add the content of the case. We have added a brief summary of the case report in the abstract section, as suggested.2)In the study, there is no data that need to analyze using "the t-test, chi-squared and Wilcoxon test". We had done the analysis but felt it would

add little since there are no direct comparisons. A descriptive approach was used. I believe this description of the statistical analysis is residual of a previous version of the paper. It has been suppressed. 3) In the last summary, author suggest "In more severe cases, liver transplantation can be performed." please give the clinical evidence or reference. We have added references from the patients who performed liver transplantation, for this sentence, and expanded further the idea in this sentence. Reviewer 2 Dear authors; This review is informative. But, table 2 is too long. This table should be shortened before publication. We thank you for the input and the opportunity for improving our manuscript. We have moved the Table 2 to appendix/supplementary material, since there is no way we can shorten it, as it is a description of each systematically reviewed case, and there are 108 cases. The summarized data of the cases will be available in the main file in Table 1. Reviewer 3 The manuscript (02731847) entitled "Primary Sclerosing Cholangitis and Autoimmune Hepatitis Overlap Syndrome associated to Inflammatory Bowel Disease: Case Report and Systematic Review" is by Ballotin et al. This is a case report and systematic review. The authors reported a case of a female patient with Autoimmune Hepatitis (AIH) and Primary Sclerosing Cholangitis (PSC) Overlap Syndrome associated to Ulcerative colitis and to systematically review the available cases of AIH and PSC overlap syndrome. The analyzed, 108 cases reported in 44 references. They concluded that PSC and AIH overlap syndrome is generally associated to inflammatory bowel disease and is associated to a low mortality and a good response to treatment. We are grateful for your input and we hope to clarify the comments of the reviewer, to improve our manuscript. Main comments 1. Some language editing is needed. For example, in the second paragraph on page 6/53, "gamma-glutyl transferase.." should be "glutamyl". We have reviewed the text of the whole manuscript and we hope it is improved accordingly. 2. Please define abbreviation before using them. For example, "GGT" was not define in this manuscript. We have reviewed the abbreviations and corrected such shortcomings. 3. Please discuss and evaluate the treatment strategies that help the patients the most if possible. We have added a

paragraph in the text about treatments used and response to it. Response to Editors We thank you for the input and the opportunity for improving our manuscript. We hope we have corrected every shortcoming accordingly, as we state below.

1. We have set all figures and tables at the end of the text; 2. We have provided the decomposable figures and organized them into a PowerPoint file; We have prepared and arranged all figures into the PowerPoint file; We have avoided colors like red and green; 3. We have reviewed the manuscript according to the format of the template in the attachment.