Title: Overlap syndrome (auto-immune hepatitis and primary sclerosing cholangitis) and membranous glomerulonephritis in a patient with ulcerative colitis. A case report and literature review.

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The manuscript has been improved according to the suggestions of reviewers:
1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

We would like to thank all reviewers for their careful consideration as well as for their helpful and productive comments, which helped to improve the overall quality of our manuscript.

Please find bellow the replies to the different comments by the reviewers.

1. The title of this case report should be revised to define the overlap syndrome.

The title has been changed accordingly to the reviewers request.

2. The abstract should provide some details of this case: concise clinical history of patient including the gender, diagnosis and treatment. As written, it is unclear what the take-home message is.

We would like to thank the reviewer for this helpful comment. The abstract has been changed to include more information, however as the treatment modality of this specific patient changed several times it is very difficult to abbreviate the whole clinical history of this patient

3. It is unclear how the diagnosis of UC was established in this patient and whether or not the patient was under any form of treatment.

This point has been added and clarified in the manuscript.

4. The details of the laboratory results including reference ranges for each test should be provided in Table 1. Reference of these could be made in the text.

The values have been added to the table.

5. Authors should define abbreviations of tests the first time these are mentioned in the document (MPO, PR-3, ANCA, CEA, a-FP, NRT, ERCP etc.). The used of SI units should follow standard abbreviations e.g. g/I should be revised to g/L.

Modifications have been made accordingly to the request.

6. The assumption is made that anti-nuclear antibodies (ANA) and anti-neutrophil cytoplasmic antibodies (ANCA) were determined by indirect immunofluorescence antibody (IFA) tests.

Thank you for this comment. This point has been added to the manuscript.

7. Results for ANCA, myeloperoxidase (MPO) and proteinase 3 (PR-3) should be revised: ANCA (pattern?) with PR-3 positive but MPO negative results.

Thank you very much for this comment. However the result mentioned in the manuscript are those, which were obtained for this patient. We checked several times. We can therefore not modify these results.

8. A table with the treatment history and response may be useful.

Thank you very much for this comment. We did not provide a table of the different treatment modalities and their response, as this should not be the main focus of the article. A comparison of the different treatment used in the same patient but at different points of his clinical history may raise some issues.

1. The over-lap syndromes in hepatology include other than PSC/AIH, particularly PBC/AIH. This should be mentioned in the abstract and in the Discussion.

Thank you for this comment. We clarified this point in the manuscript.

2. It is unclear to me if PSC was diagnosed in 2000 or during the diagnostic work-up in 2005

This has been added to the manuscript.

3. The comments in relation to the pathophysiology of glomerulonephritis in the last paragraph of the Discussion is irrelevant to this case.

Thank you for this comment. We would like to keep this paragraph as it may render the article more appealing to a wider audience.

4. Reference intervals should be added to Table 1.

Reference values have been added

1. The patient should be treated by 5-ASA for UC during the development of PSC-AIH and GN, the authors should mentioned possible dangerous effects of this drug in patients with hepatic failure and renal insufficiency. I think it is important to give information about this problem. The other important issue is 5-ASA alone may lead development of nephrotic syndrome (Avicenna J Med. 2012 Jan;2(1):9-11. doi: 10.4103/2231-0770.94804.) rather than association of GN and UC

Thank you for this comment. We included the reference in our discussion

2. Case presentation should better while normal ranges for all laboratory examination are necessary.

This has been added to the manuscript

3. Absence of PSC findings on liver biopsy are interesting while PSC do not respond to UDCA, transplantation is only one outcome for these patients.

It is noted in the manuscript that in cases of advanced diseases transplantation is a valid option. Currently the patient is doing fine on his current treatment and is closely monitored. Due to the organ shortage the criteria for transplantation are not yet met for our patient.

4. It is better to say when liver enzymes and IgG normalized while it is unnecessary to provide liver enzyme levels a one week after therapy.

Thank you for this comment. Due to local economical policies we cannot rely on continuous measurements of IgG titers in the close follow up and have to rely on liver

enzyme levels for close monitoring. We measured IgG on several occasion and included a small statement in the manuscript concerning the levels.

> 5. Discussion should be extensively revised because authors reviewed exiting literature regarding overlap syndrome and discussing this issue is not main point of the paper. It is enough to provide following sentence in the beginning of discussion about terminological confusion.''' The term overlap has been used for patients with features of both AIH and PSC. It is not clear whether PSC-AIH is a distinct autoimmune liver disorder or a variant of PSC or AIH. Several reports have suggested that overlap syndrome does not represent the co-existence of two different autoimmune liver diseases but involves "variants" of typical diseases. Some authors define PSC -AIH overlap as "PSC with hepatitis features," while others prefer the term "AIH with cholestatic features" (cjaza and position paper). Thereafter I suggest authors should mentioned co-existence of autoimmune liver disease with other non-hepatic autoimmune disorders and should apply mosaic of autoimmunity for their patient(please see ''Eur J Gastroenterol Hepatol. 2012 May;24(5):531-4. doi: 10.1097/MEG.0b013e328350f95b''.). In this study authors also described AIH-PBC overlap patients who had GN. The following of manuscript should be designed about co-existence of AIH and GN which association has been described in literature. This should be suggested by association of PSC or PBC with GN.(Clinical Journal of Gastroenterology,August 2012, Volume 5, Issue 4, pp 292-297)

Thank you very much for this suggestion. It is surely difficult to find a correct balance in the discussion of a paper. We believe however that the focus of this manuscript is the overlap syndrome and we believe that it's important to illustrate the reader the ongoing discussion and difficulties about it's definition, as well of it's composition. As this is a case report there is only so much that can me mentioned. Further aspects concerning the immunological entanglement of those diseases are a great topic for future publications.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the World Journal of Gastroenterology.

Sincerely yours,

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