Reviewer's report

Title: Anti-Outer membrane protein C and anti-glycoprotein 2 antibodies in inflammatory bowel disease and their association with complicated forms of Crohn's disease

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Reviewer: Antonio Di Sabatino

Reviewer's report:

Aim of Kohoutova et al. in this study is to assess relationship between serum anti-OmpC IgA, anti-GP2 IgG and anti-GP2 IgA antibodies with IBD and their association with complicated forms of Crohn’s disease. This manuscript shows that serum anti-OmpC IgA antibodies are higher in IBD patients compared to controls, whereas serum anti-GP2 IgG and anti-GP2 IgA antibodies are increased only in Crohn’s disease patients compared to controls. Moreover, Kohoutova et al. demonstrate that in Crohn’s disease anti-OmpC IgA are higher in B2 and in B2+B3 phenotypes than in B1, whereas anti-GP2 IgA are higher in B2+B3 and B3 phenotypes compared to B1. The paper also describes a significant difference in anti-OmpC IgA between Crohn’s disease patients with or without surgery and a significant difference in anti-GP2 IgA between Crohn’s disease patients with or without extraintestinal manifestations. On this basis, Kohoutova et al. depict an association between anti-OmpC IgA and IBD, an association between anti-GP2 (IgA and IgG) and Crohn’s disease and higher levels of anti-OmpC IgA and anti-GP2 IgA in complicated forms of Crohn’s disease. The topic is interesting but the manuscript should be improved addressing the following issues.

Major criticisms:

1. In the results the Authors state there is a significant difference in anti-GP2 IgA between Crohn’s disease patients with or without extraintestinal manifestations, p=0.05. How did they find significant difference if p=0.05 rather than p<0.05? It does not seem plausible to be typing mistake, since they repeat “p=0.05” both in abstract (page 2, line 29) and in results (page 6, line 7). Please clarify it.

2. Please add sensitivity, specificity, negative and positive predictive values of serum anti-OmpC IgA, anti-GP2 IgG and anti-GP2 IgA antibodies in all groups. Could you add them both in Table 1 and in “Results” sections?

3. From page 5, line 30 to page 6, line 4: on the basis of values of Crohn’s disease patients with surgery, they look to be approximately the sum of B2 patients with B3 patients, as I expect. Therefore, if I am right, please remove this analysis, as it is already described in Table 2.

4. Page 6, line 8-11: Since anti-GP2 IgA are higher in Crohn’s disease patients with immunosuppressive therapy, please specify if these patients are responder
or not. If there are both subgroups (responder and not responder) please split them and, accordingly, compare them with the group of Crohn’s disease patients without any treatment or treated with 5-aminosalicylates only. Moreover, please compare the other antibodies (anti-OmpC IgA and anti-GP2 IgG) between these three groups of Crohn’s disease patients.

5. Page 20, line 20-22: you cannot declare that anti-OmpC and anti-GP2 antibodies are useful to identify Crohn’s disease patients, who are more likely to develop complicated forms of disease. In order to be state it, you should have a follow-up of Crohn’s disease patients from diagnosis to complication development in association with measurement of these antibodies, which – on the other hand - are increased once patients already have the complication (B2 and/or B3 phenotypes).

Minor criticisms:

1. In the methods of abstract please delete number of men, women and age for each group recruited in the study, since this information is reported in the “Methods” section afterwards.

2. In the methods of abstract please write which antibodies are tested in patients’ sera.

3. The introduction is very short, only 178 words. Please expand it with major comments on papers cited (in particular from Reference 8 to 16) and with some observations regarding anti-OmpC and anti-GP2 antibodies, their target and what it is known about these antibodies in IBD.

4. In the “Methods” section please type a title of any method used in the study, for instance “Patients”, “ELISA”, “Statistical analysis” and so on.

5. In the “Methods” section please add duration disease and what treatments the patients are on at the time of blood withdrawal.

6. Please calculate whether in UC patients there is a correlation between anti-OmpC IgA and anti-GP2 IgA values in UC patients, between anti-GP2 IgG and anti-OmpC IgA values, between anti-GP2 IgG and anti-GP2 IgA as well as you did in CD patients (Page 5, line 1-3).

7. What are the extraintestinal manifestations of Crohn’s disease patients enrolled in this study? Please specify them in “Methods” section.

8. Page 6, line 7: Please compare the other antibodies (anti-OmpC IgA and anti-GP2 IgG) between Crohn’s disease patients with or without extraintestinal manifestations.

9. Page 7, line 15-16: please remove this statement, since Crohn’s disease patients with surgery look to be approximately the sum of B2 patients with B3 patients.

10. Page 8, line 11-12: please specify that even if the anti-GP2 IgA antibodies
are higher in Crohn’s disease patients with extraintestinal manifestations, there is not significant difference.

11. Graph 1 legend: please associate asterisk with p<0.001, as described in “Results” sections.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests