ANSWERING REVIEWERS

January 24, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: ESPS Ms NO. 15395-Review.doc).

Title: FULMINANT ULCERATIVE COLITIS IN A HEALTHY PREGNANT WOMAN

Author: Rossana Orabona, Adriana Valcamonico, Marianna Salemme, Stefania Manenti, Guido Alberto Massimo Tiberio, Tiziana Frusca

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 15395

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

(1) BRIEF DESCRIPTION AND GENERAL COMMENTS This case report describes the onset of ulcerative colitis (UC) complicated by toxic megacolon in a 25 year old pregnant patient. A Caesarean section was performed and the colitis was managed conservatively. SECTIONS-SPECIFIC COMMENTS: Abstract: it should be cited in the abstract how was managed the colitis, for instance the fact that endoscopic decompression played an important role. We have added a sentence about it in the abstract. Background: absolute lack of references. I think the reader would be interested in how often UC presents for the first time during pregnancy. Has UC any particular aspect during pregnancy? Is there any special consideration the clinician must have for UC management in a pregnant women? Thanks to your advice, we have better specified UC characteristics and management during pregnancy. Do we really need to know all the people who managed this lady during her in-hospital stay? I think is probably enough to know that it was a multidisciplinary team. We have deleted all the clinicians involved. CASE PRESENTATION: - too long and too many details about laboratory data. We have resumed it. - No mention at the TrueLove criteria for the acute colitis. The colitis was severe according to the cited criteria. Thanks to your suggestion, it's now specified in the text. - medical treatment: amikacin + vancomycin+ metronidazole+meropenem. Could the authors please specify if this regimen is in keeping with the current guidelines? Current guidelines underline that oral or intravenous antibiotics in acute colitis have shown no consistent benefit in addition to conventional therapy. However, our patient was administered such antibiotic therapy until we were able to exclude a co-existing enteric infection with Cl. difficile. - CT scan shows that the colon is gas filled in every patient. The reader would prefer comments on the CT scan findings that would suggest the presence of an acute surgical pathology. We have revised CT scan description according to your suggestions. - How were all the endoscopic decompressions planned? It was planned in the surgery room at the presence of obstetricians and colorectal surgeons. The planning of endoscopic decompression is now present in the text. Did the authors performed any investigation to guide their treatment? This case was managed by a multidisciplinary team which included surgeons and gastroenterologists expert in IBD, according to current guidelines. -destiny of the baby? A paragraph about it has been added. The baby survived without complications. DISCUSSION - I would like to read some considerations on the balance between medical treatment alone, endoscopic decompression (risks related for the baby and the

mother) and surgery, in terms of risks for the baby and risks for the mother. Thank you for this comment. We have added a paragraph about it. - Is there any clinical sign that should recommend immediate surgery? Although current guidelines describe toxic megacolon as an indication of emergency surgery, endoscopic decompression together with medical treatment and intensive monitoring should be considered as the first step in the management of severe UC complicated by toxic megacolon if clinical conditions early improve. Vice versa the presence of signs including perforation, abscess, ischemia, thrombosis (which were not present in our patient) and/or the lack of response to conservative therapy imply to proceed to surgery. - Do you routinely manage toxic megacolon medically and endoscopically? Generally we evaluate case by case the initial strategy in the management of toxic megacolon on the basis of clinical, biochemical and radiological data. - Toxic megacolon is an indication for emergency surgery in UC. I understand that your treatment was successful, but I am wondering what are the true advantages of your management and if the actual learning point should be "if the patient does not improve immediately proceed to surgery". Yes, the message of our case report is that severe UC complicated by toxic megacolon occurring during pregnancy should be managed medically and endoscopically. However, if patient's clinical condition does not early improve emergency surgery is mandatory. The principal advantage of a conservative management during pregnancy is to let the baby reach an appropriate gestational age to survive. Secondly, prevent the mother from an emergency colectomy during gravidic sepsis.

(2) This is a case report of severe ulcerative colitis developed in the third trimester of pregnancy and the patient and child were saved by various methods without colon excision. There are some suggestive information in this paper, but needs to be revised as mentioned below. 1, The pictures of colonoscopy and pathology need be shown if possible. We have added pictures about both colonoscopy and histopathology. 2, Classical English words (foetal, haemoglobin, sierology, faeces, etc) are used in some sentences. They had better to be changed to modern English for easy reading. We modified those words according to your suggestion, thank you. 3, p3,line 8: What dose "A.A." mean? It meant fantasy name/surname of the patient. We have deleted it. 4, p4,line 16: "CS" might be an abbreviation for "cesarean section". If so, "CS" needs to be changed to "cesarean section (CS)". Yes, it means caserean section. We apologize for the mistake and we have corrected it. 5, The references of 5 and 14 are not presented appropriately. Please revise them as follows. 5 Korelitz BI. Inflammatory bowel disease and pregnancy. Gastroenterol Clin North Am 1998;24:213-22. 14 van der Woude CJ, Kolacek S, Dotan I, Oresland T, Vermeire S, Munkholm P, Mahadevan U, Mackillop L, Dignass A; European Crohn's Colitis Organisation (ECCO).European evidenced-based consensus on reproduction in inflammatory bowel disease. J Crohns Colitis. 2010; 4:493-510. We have revised them according to your suggestion. Thank you.

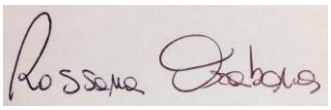
(3) Orabona et al showed a fulminant ulcerative colitis (UC) in a healthy pregnant woman. They reported that medical therapy and intensive care consented to the survival of both the mother and the baby and prevented the woman from an emergency pancolectomy. Although the case written in this paper is clinically interesting, the author should address the following points. 1. In this report, it is critical that the diagnosis of UC was correctly done in the patient. Thus, the authors should demonstrate both the pictures of colonoscopy and the histological findings of the rectal biopsy in the patient. In addition, the authors should show the history of bloody stool in the patient. Thank you. We have improved the manuscript according to your advice. Now pictures of colonoscopy and histology are embedded in it. In addition we have better described the patient's history of bloody stool. 2. With regard to the medical therapy, it is very important how much dose of drug was used for the therapy. Thus, the authors should show the doses of prednisolone and mesalazine used in the patient. We apologize for this mistake. We have added the doses of both drugs. 3. The authors should show the result of the examination for cytomegalovirus infection of the patient, if it was performed. Yes, CMV infection analysis were performed and we have reported them according to your suggestion.

3 References and typesetting were corrected

Finally, I would like to inform the reviewers that two Authors (Marianna Salemme and Stefania Manenti) have been added to the Authors' list because of their important contribution regarding the description of histopathologic diagnosis and the elaboration of Figure 3.

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

Sincerely yours,



Rossana ORABONA, MD
Dept. of Obstetrics and Gynecology
University of Brescia
Piazzale Spedali Civili 1
25123 Brescia, Italy
E-mail: oraroxy@libero.it