Format for ANSWERING REVIEWERS

April 30, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 17483-review.doc).

Title: Jejunitis and Brown Bowel Syndrome associated with multifocal carcinogenesis of the small bowel

Author: Martin Raithel, Tilman T. Rau, Alexander F. Hagel, Heinz Albrecht, Thomas de Rossi, Thomas Kirchner, Eckhart G. Hahn

Name of Journal: *World Journal of Gastroenterology*

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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

(1) Reviewer 00057306:

We have now included some follow up data from transabdominal sonography and small bowel radiology in the paper. Unfortunately, CT-abdomen was not performed initially and was only made at a later stage when the disease showed progression to malignancy. The MRI finding at the time where small bowel stenosis became manifest is now included in the text. As suggested by this reviewer we do also not believe that the Brown Bowel Syndrome is clearly causal for the development of the malignancy, but the long lasting malabsorption and inflammation. However, as small bowel carcinogenesis is an as yet incompletely explored field, there is scarce data to confirm this strictly with already published literature. Therefore, we would like to add this case to gain more attention for the possible connection of long lasting malabsorption and inflammation in neoplasia induction. In addition, we have now included further literature observations from other investigators pointing in the same direction.

(2) Reviewer 02441672:

In our case report we conclude that there is evidence that local enteritis activity caused dysplasia and neoplastic transformation and finally the development of multifocal nests of small bowel adenocarcinoma may be seen as similar to the transformation process in chronic colitis. The Brown Bowel Syndrome which was associated and caused by the devastating malabsorption may have further influenced the malignant transformation.

1) Reynaert et al. (Am J Gastroenterol. 1994 May;89(5):812-3) also established a connection between long- term malabsorption and malignant transformation when they summarize: "We believe that vitamin E deficiency is responsible for the development of the Brown Bowel Syndrome and may be partially responsible for the high incidence of malignancy in patients with celiac sprue and chronic pancreatitis.".

2) There is also evidence pointing in the same direction in the work of Bergmann et al. (Oncol Rep. 2010

Dec;24(6):1535-9) who draws a connection between long term malabsorption, vitamin E deficiency and malignant transformation.

(3) Reviewer 00053417:

For the development of colorectal cancer the adenoma-carcinoma-sequence is well established, whereas for development of small bowel cancer little has been published. We present a case of longstanding malabsorption which finally presented with small bowel carcinogenesis and multifocal appearance at a given time point. We suppose the transformation into malignant disease is caused by molecular genetic changes in small bowel transformed throughout the longstanding period of malabsorption. Thus these adenocarcinomas could be suggested that they also parallel the molecular genetic changes which occur in colorectal carcinogenesis (Neugut A et al. Adenocarcinoma of the small bowel., Holzheimer RG, Mannick JA, editors. Munich: Zuckschwerdt; 2001.).

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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