Reviews questions and answers

Reviewer #1:

Scientific Quality: Grade C (Good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Accept (General priority)
Specific Comments to Authors: You have submitted an interesting manuscript.
(1) However, you mentioned in the comments that "this is the first reported patient with colonic involvement with IgG4-RD.", but there seems to have been a few reports in the past (PMID; 21240062, 19047846), please confirm.
Answer: Thank you for your suggestion. We added and cited the papers about IgG4-RD involved intestine.

(2) I have three questions about this manuscript. First, he had a history of allergic rhinitis, did he have sinusitis?
Answer: Thank you for your question. He did not have sinusitis. We supplemented this history.

(3) Also, did PET-CT show increased radioactive uptake in the pancreas?
Answer: Thank you for your question. There was no radioactive uptake in the pancreas. We supplemented this result.

(4) Finally, how many points can this case score on the IgG4-RD classification criteria?
Answer: Thank you for your question. The case score was 42. We supplemented this result.

Reviewer #2:

Scientific Quality: Grade D (Fair)
Language Quality: Grade B (Minor language polishing)
Conclusion: Major revision
Specific Comments to Authors: Review of manuscript "IgG4-related disease in the sigmoid colon in a patient with severe colonic fibrosis and obstruction: A case report" submitted to WJG. Overall: This is very rare and interesting case relevant and important from the clinical point of view.
Comments: Comment 1: In the introduction section the authors wrote: "Additionally, the imaging features of IgG4-RD are as follows: a diffusely enlarged pancreas surrounded by capsule-like edema ('sausage-shaped' pancreas) (Figure 2a) and the anterolateral aorta wrapped by soft tissue in the case of retroperitoneal fibrosis (Figure 2b). If this is your patient then the whole case should be described in different manner, it is not just IgG4 in colon but case of patient with IgG4-related pancreatitis (autoimmune pancreatitis type 1), IgG4-related aortitis, retroperitoneal fibrosis and

even involvement of colon (and probably urinary bladder) – did I understand right? Why you concentrated only at colon not mentioning other organ involvement?

Answer: Thank you for your comment. Figure 2 was cited from a published paper to illustrate CT and MRI about IgG4-RD. We supplemented the result of our patient below.

Comment 2: In the introduction section the authors wrote the sentence that is difficult to understand: "Since IgG4-RD is a multi-organ disease, and it can easily be confused with malignancies, infections, or other conditions." – is there something missing in this sentence? – it should be re-write/edit.

Answer: Thank you for your comment. We have rewritten this sentence.

Comment 3: In the introduction section the authors wrote: "It is also characterized by slow disease progression and irreversible organ dysfunction It is also characterized by slow disease progression and irreversible organ dysfunction." – which organ you mean when you mention "irreversible"?

Answer: Thank you for your comment. We have rewritten this sentence and citations.

Comment 4: In case-presentation authors wrote History of past illness including a 30-year-old history of hepatitis B that is already mentioned in the previous sub-section.

Answer: Thank you for your comment. We have rewritten and revised this part.

Comment 5: Data on smoking and alcohol consumption in personal history are missing as well as data on bowel movements/stool habits and stool consistency (any diarrhea in history?)

Answer: Thank you for your comment. We have added this history in the revised paper.

Comment 6: In history of present illness authors wrote that "Patient went to the urology department where prostatic hyperplasia was considered" - this is very interesting information – is histopathology analysis available (IgG4 in prostate or bladder?) Did they perform cystoscopy?

Answer: Thank you for your comment. The patient did not get cystoscopy and histopathology in the urology department. We have added this history in the revised paper.

Comment 7: Laboratory analysis: how you explained anemia? Did you check blood in stool?

Answer: Thank you for your comment. The patient had a positive fecal occult blood test. We have added this result in the revised paper.

Comment 8: Imaging: Authors wrote "We scanned the pancreas by CT and magnetic resonance imaging (Figure 5), and found an enlarged pancreas, which was similar to the 'sausage-shaped' pancreas finding in IgG4-RD." – that means that patient had autoimmune pancreatitis type 1. Did you perform amylase and lipase in serum? In

"initial diagnosis" you are not mentioning pancreatitis, vasculitis (aortitis), retroperitoneal fibrosis.

Answer: Thank you for your comment. The patient really had pancreas involved by CT and MRI. So we have revised the diagnosis in the revised paper.

Comment 9: Further diagnostic work-up: Authors wrote: "immunohistochemistry showed more IgG4-positive cells in the diseased tissues than that in normal tissue, and the ratio of IgG4/IgG was about 60%." - how many cells were there, can you be more specific? - it is very important to know. In European guidelines on IgG4 related autoimmune pancreatitis (AIP) criteria for AIP histology are as followed: For the diagnosis of AIP, the number of IgG4+ plasma cells should exceed 50 cells/high-power field (HPF) in surgical specimens and 10 cells/HPF in biopsy samples. In addition, the IgG4/IgG ratio should be more than 40%. Which diagnostic criteria for histology did you use?

Answer: Thank you for your comment. We added this data and figures in the revised paper. We used the 2019 ACR/EULAR IgG4-RD criteria.

Comment 10: Authors wrote that "Immunology-related blood indices (Table 1, Table 2) showed that the IgG4 level was 1.830 g/L, which was significantly high (for IgG4-RD, the cut-off value is >1.35 g/L)." I do not agree that this is significantly high because IgG4 serum levels seem to have diagnostic value when the level is higher than four times the upper level of normal, which is the case in only a minority of patients. I agree that this elevation is important but suggest to re-write it in milder form without word "significant".

Answer: Thank you for your comment. According your suggestions, we have re-written and revised this part.

Comment 11: What was the result of final histopathology after the surgical resection? This is the crucial information.

Answer: Thank you for your comment. We have added some figures about IHC of MMU1, IgGs, IgG4.

Comment 12: What exactly was removed with surgery? Did you remove part of urinary bladder? Surgery should be described in more details. Was there IgG4 in urinary bladder too? Retroperitoneal mass?

Answer: Thank you for your comment. We have re-written and revised this part about the operation details.

Comment 13: Are authors sure that this is the first reported patient of IgG4 in intestine? I found more articles on this topic. Ciccone F, Ciccone A, Di Ruscio M, et al. IgG4-related disease mimicking Crohn's disease: A case report and review of literature. Dig Dis Sci 2018; 63: 1072–1086. Bilal M, Gulati A and Clarke K. Immunoglobulin G4 IgG4)-associated pouchitis - Part of IgG4 related disease? A case series and review of the literature. Dig Liver Dis 2016; 48: 817–819. Obiorah I, Hussain A, Palese C, et al. IgG4-related disease involving

the esophagus: A clinicopathological study. Dis Esophagus 2017; 30: 1–7. Notohara K, et al. Gastrointestinal manifestation of immunoglobulin G4-related disease: clarification through a multicenter survey. J Gastroenterol 2018; 53:845–853. Topal F, et al. The prevalence of IgG4-positive plasma cell infiltrates in inflammatory bowel disease patients without autoimmune pancreatitis. Turk J Gastroenterol 2014; 25: 558–562. Notohara K, Kamisawa T, Uchida K, et al. Clinicopathological features of Type 2 autoimmune pancreatitis in Japan: Results of a multicenter survey. Pancreas 2015; 44: 1072–1077. Choi S.B, Lim CH, Cha MG, et al. IgG4-related disease of the rectum. Ann Surg Treat Res 2016; 90:292–295. Fujita K, Naganuma M, Saito E, et al. Histologically confirmed IgG4-related small intestinal lesions diagnosed via double balloon enteroscopy. Dig Dis Sci 2012; 57: 3303–3306. Harada A, Torisu T, Sakuma T, et al. A case of duodenal bulb involvement of immunoglobulin G4 related disease complicated by ulcerative colitis. Dig Liver Dis 2018; 50: 515. Watanabe A, Goto T, Kamo H, et al. Resection of lesions in the ileum of patients with IgG4-related disease may ameliorate disease progression without steroid administration. Surg Case Rep 2018; 4: 148. Abe A, Manabe T, Takizawa N, et al. IgG4-related sclerosing mesenteritis causing bowel obstruction: A case report. Surg Case Rep 2016; 2: 120. Comtesse S, Friemel J, Fankhauser R, et al. Enterocolic lymphocytic phlebitis of the cecal pole and appendix vermiformis with increase of IgG4-positive plasma cells. Virchows Arch 2014; 464: 113–116. Kim HS, Kang WK and Chung DJ. Appendiceal immunoglobulin G4-related disease mimicking appendiceal tumor or appendicitis: A case report. Korean J Radiol 2016; 17: 56–58. Hiyoshi Y, Oki E, Zaitsu Y, et al. IgG4-related disease of the ileocecal region mimicking malignancy: A case report. Int J Surg Case Rep 2014; 5: 669–672.

Answer: Thank you for your suggestion. We added and cited the papers about IgG4-RD involved intestine.

Reviewer #3:

Scientific Quality: Grade C (Good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Minor revision
Specific Comments to Authors:

1.There is repetition of information in history of present illness, history of past illness and personal and family history.

Answer: Thank you for your comment. We have re-written and revised this part.

2.Please indicate the location of the lesion on the figure 3 to 5.

Answer: Thank you for your comment. We have revised this part according to your suggestions.

3.There is no mention of the patient's treatment other than surgery in the part of treatment.

Answer: Thank you for your comment. We have added the operation details and revised this part.

4.Follow up has not been provided.

Answer: Thank you for your comment. We have added the follow-up informations and revised this part.