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Prof. Jin-Lei Wang
Editor-in-Chief
Baishideng Publishing Group Inc
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Dear Prof Wang,

RE: Manuscript No: 77035
Type 2 Autoimmune Pancreatitis Associated with Severe Ulcerative Colitis: A Case Series

We thank the reviewers for their time and comments. We have taken the feedback on board in this revised manuscript.

The three cases reported were not typical presentations of autoimmune pancreatitis, and the motivation to publish this series is to highlight the heterogenous and poorly defined characteristics of pancreatitis in the setting of inflammatory bowel disease. While the guidelines have been followed on the most part, the workup was based on real-life clinical practice and tailored to each patient's individual case and to what was relevant to their care. For example, where typical changes on baseline imaging (e.g. mass lesions) were not seen, repeat imaging 2 weeks later on steroids to rule out malignancy was not relevant, especially where multiple baseline investigations had been performed to rule out malignancy. The duration of steroid therapy in these cases was based on the recommended initial treatment dosages and weaning regimen as suggested in the "International consensus for the treatment of autoimmune pancreatitis" by Okazaki et al for treatment, rather than based on the recommended steroid trial. Additionally, as noted by Okazaki et al 'The Korean prospective study suggested estimation of " a two weeks steroid trial" was the most appropriate to differentiate AIP from pancreas cancer in difficult cases after non conclusive complete workup. Therefore, in cases of poor response to steroid, re-evaluation of the diagnosis including pancreatic cancer is needed.' (1) Whereas, in our cases through multi-modal evaluation pancreatic cancer had been confidently excluded as we will discuss further. Also of note a response to steroids is defined as rapid (<2 week) radiologically demonstrable resolution OR marked improvement in manifestations, with our assessment of improvement based on the latter. (2)

We have included a point-by-point response to the reviewers' comments below:

1. Rapid 2-week steroid taper and re-evaluation by imaging and CA19.9 to exclude cancer:
    a. Case 1 – This patient presented with a bile duct stricture, and imaging by CT and MRI did not show any pancreatic mass lesion, only biliary dilatation. Thus, repeating CT/MRI early was not thought to be clinically useful. Only the PET/CT scan demonstrated diffuse change. Cancer was felt to be confidently excluded by multimodal evaluation with ERCP/brushings, EUS with contrast and CT/MRI. Baseline CA19.9 was 47kU/L, this was not repeated. Initial steroid response was seen with improved symptoms and liver enzymes, therefore the decision was made to complete initial 8 week course of steroids before repeating the PET/CT. This was also in part due to the patient living >500km from the tertiary centre making early repeat imaging challenging
    b. Case 2 – This patient also presented with distal bile duct stricture. While MRI suggested pancreatic mass lesion, EUS soon after did not confirm this but rather diffuse change throughout the pancreas. He was having multiple ERCPs for stent exchange with brushings, cholangioscopy with biopsy and thus there was a high level of confidence that cancer was excluded. Repeat imaging was done by EUS and MRI 8 weeks later, with the time-frame again partly due to the practicalities of the patient living in a rural location, but also it was deemed a sufficient amount of time for the changes to resolve.
    c. Case 3 – For this patient there was a very low clinical suspicion of cancer given presentations with acute pancreatitis, therefore imaging was not repeated after 2 weeks. Response to steroids was evaluated by serial lipase, liver function tests and clinical assessment of abdominal pain. Given partial response, completing the therapy was justified.

2. Has CA19.9 been tested in case 1 and case 3? And why hasn't it been re-evaluated (in all three cases) after 2 weeks of steroid trial, as suggested by the Guideline?

The CA19.9 were not consistently performed and repeated in these cases. In case 2 baseline and several repeated measures were carried out. The manuscript has been updated accordingly. In case 1, baseline CA19.9 was performed, though not repeated. In the final case, CA19.9 was not performed given the initial presentations were with acute pancreatitis and imaging was not concerning for malignancy. In retrospect these should have been performed.

The manuscript has been updated, and a comment has been added to the discussion to clarify the steroid trial should generally be conducted with baseline imaging and CA19.9 that is repeated after 2 weeks

3. I would suggest to re-arrange Table 1 to reach higher clarity. Why don't Authors cite more precisely the ICDC tables 3 and 5?

A second table has been added to more clearly present the diagnostic criteria.

4. Can Authors provide histologic images of patient 3?

The histology for patient 3 has been retrieved and an image included as figure 4.

Again we thank the reviewers for their comments and we hope they find the revised manuscript addresses their feedback. If further clarification is required please feel free to contact me.

Kind Regards,

Dr. Simon Ghaly MB.BS, FRACP, PhD
Inflammatory Bowel Disease Clinical Lead
Staff Specialist
Gastroenterology

References

1. Okazaki K, Chari ST, Frulloni L, Lerch MM, Kamisawa T, Kawa S, et al. International consensus for the treatment of autoimmune pancreatitis. Pancreatology. 2017 Jan 1;17(1):1–6.

2. Shimosegawa T, Chari ST, Frulloni L, Kamisawa T, Kawa S, Mino-Kenudson M, et al. International consensus diagnostic criteria for autoimmune pancreatitis: guidelines of the International Association of Pancreatology. Pancreas. 2011 Apr;40(3):352–8.