Reply to the reviewers

Providence, RI, October 10, 2018

Dear Editor-in-Chief,

Enclosed please find a revised version of our manuscript, "Gangrenous Cholecystitis: A Silent but Potential Fatal Disease in Patients with Diabetic Neuropathy – A case report", that we would be grateful to have considered for publication in World Journal of Clinical Cases. We appreciate the opportunity to submit a revised version of the manuscript. We have addressed the concerns raised in the comments provided in the following point-by-point manner:

1. Reviewer 1: 03465354

Comment 1: My only recommendation for this manuscript is in the Introduction section the authors to revise the definition of diabetes mellitus.

Reply 1: We edited the definition of diabetes mellitus

2. Reviewer 2: 02945812

Comment 1: what is the relationship between neuropathy and cholecystitis among diabetic patients?

Reply 1: This is a great question. There is no direct relationship between diabetic neuropathy and cholecystitis. However, during cholecystitis, one of the coordinal symptoms is right upper quadrant abdominal pain. In patients with neuropathy, their ability to experience pain is impaired and therefore, just as we describe in this case, he presented with asymptomatic cholecystitis.

Comment 2: Mention the duration of diabetes

Reply 2: We have now mentioned the duration of the patient's diabetes.

Comment 3: Not clear. More elaborate neurological exam findings are to be given

Reply 3: We have now added the full neurological exam

Comment 4: Generic to be added.

Reply 4: We added the generic names of the medications.

Comment 5: what was the post op HPE reports?

Blood culture and this pus culture revealed what organism? whether that was typical of gangrenous cholecystitis?

Reply 5: The post op HPE report showed gangrenous gallbladder and yes, this was typical for the diagnosis. We never cultured the pus. The blood culture was negative and thus, the patient did not have bacteremia.

Comment 6/7: Add references

Reply 6/7: We added the references.

Comment 8: All are featurs of autonomic neuropathy. Clinically, no such feature is mentioned in this patient.

Reply 8: Correct, which is why this is a rare case.

Comment 9: not pertinent

Reply 9: Thank you for your comment. However, we do believe that this is reflect the disease and is a good teaching point for the reader. Therefore, we kept it. However, if you truly insist, we can remove this sentence.

Comment 10: Add features suggestive of severe neuropathy

Reply 10: We did in the clinical exam section.

Comment 11: Corrrect the spelling

Reply 11: Thank you for noticing this typo. We corrected it.

Comment 12: Few sentences regarding the etiopathogenesis GC in diabetes can be added

Reply 12: Great suggestion. We did add this in the discussion section.

3. Reviewer 3: 03460306

Comment 1: The authors emphasized the presence of diabetic neuropathy. However, they did not show any clinical diagnosis of diabetic neuropathy. Examinations of diabetic neuropathy such as deep tendon reflexes, vibratory sensation inspection, R-R interval, orthostatic hypotension and nerve conduction velocity should be assessed and described

Reply 1: Thank you for this comment. We added the full neurological exam which now reflect this.

Comment 2: The authors described this case as "long-standing" diabetes. However, duration of diabetes was not described. Also, the condition of other micro- and macroangiopathy (nephropathy, retinopathy and cardiovascular diseases) should be described.

Reply 2: We have now added the duration of the diabetes in this patient. We did mention in the beginning of the case that the patient had hyperlipidemia and hypertension. The rest of the information such as nephron- and retinopathy was not diagnosed in this patient.

Comment 3: Obesity is a risk factor of gall stone. Height, weight and BMI of this case should be describe

Reply 3: This is correct, however, unfortunately, we do not have information regarding the height and weight of the patient.

Comment 4: Why the authors conducted a HIDA scan? CT or MRI scan may be more informative.

Reply 4: in the U.S., the guidelines are to perform a HIDA scan and not an CT or MRI.

Comment 5: GC was confirmed by pathology? The pathological findings should be described

Reply 5: Yes, this was confirmed with histopathology and we have now added this sentence in the manuscript. Thanks for this comment.

Very respectfully,

Raman Mehrzad, MD, MHL Corresponding author