

Dear Editors,

Thank you for giving us the opportunity to submit a revised draft of our manuscript titled **Small Bowel Perforation from a Migrated Biliary Stent: A Case Report and Review of Literature** to *World Journal of Gastrointestinal Endoscopy (WJGE)*. We appreciate the time and effort that you and the reviewers have dedicated to providing your valuable feedback on our manuscript.

As a result of these reviewer comments, we have made major revisions to the manuscript, and improved it substantially. Various portions of the manuscript have been clarified, while others have been expanded significantly. We have also added an additional 25 cases to our table as a result of a more systematic literature search as suggested by a reviewer.

Please see below our responses to the specific comments. We have included the reviewer comments in bold, with our responses in unbolded text. The changes in the manuscript corresponding to each comment has been included in each response in italics.

Reviewer #1:

1. The aim of presenting this case report should be clearly stated in the introduction and the abstract. What should the reader expect from reading through?

We have clarified this by adding the following statements to the manuscript. In the abstract we have added:

“This case presentation reports on the unusual finding of two migrated biliary stents, with one causing perforation. In addition we review the relevant literature on migrated stents.”

And in the introduction we added:

“Herein we report a case of a patient with multiple comorbidities and surgical interventions, who presents with two migrated biliary stents, one of which was perforating through the small bowel. Both stents were removed uneventfully with laparotomy and a single small bowel resection.”

2. Case presentation: please be more concise and less descriptive when presenting the patient’s history.

The case presentation has been significantly edited to be more concise.

3. Did the authors consider to perform an endoscopic stent retrieval using enteroscopy followed by endoscopic management of the perforation? If no, why? Any particular explication or risk factor that they took into account to make their decision?

We have edited the manuscript to include our thinking on why we did not consider an endoscopic approach. The following statement was added:

“Given that in our case the bowel perforation was in a mid-jejunal loop, the endoscopic approach was less feasible. In addition there was already significant inflammation seen around the bowel on CT scan, and we were concerned that an endoscopic mucosal repair would not hold. As such, we proceeded directly to surgery.”

4. Define the origin of the benign biliary stricture as well as the type of stent used.

The biliary stricture was eventually determined to be stone related, and this has been clarified in the manuscript. We have also included the timeline of her ERCP interventions, as well as what stents were used.

“She had been seen previously for a biliary stricture and underwent a diagnostic ERCP in October 2019, at which time a stent (7 French 7cm single external and single internal flap) was placed. A second ERCP was done in February 2020, at which time choledocholithiasis was noted, and a new stent was placed (8.5 French 7cm). The original stent was not seen at that time. In August 2020 she went for another ERCP at which time she had a normal cholangiogram, and the stent was not seen at that time.”

5. Discussion. Please extend your discussion to include all available modalities to treat stent-induced perforation. Endoscopic management (through-the-scope clip or over-the-scope clip) has been shown to be effective as shown in a recently published case series. Consider including it in your references. (Lateral duodenal wall perforation due to plastic biliary stent migration: a case series of endoscopic closure. PMID: 32355873 PMCID: PMC7165006 DOI: 10.1055/a-1123-7782).

We have edited the manuscript to include in our discussion the more recent literature on endoscopic management, including the above mentioned reference. included a poadded the following sentence in the discussion:

“An early growing body of literature describes endoscopic techniques for treatment of bowel perforation from migrated stent, but the majority focus on duodenal perforation or distal large bowel perforation. Bureau et al. recently described a case series of six patients with lateral duodenal wall perforation from displaced plastic biliary stent that were treated with over-the-scope clip^[11].”

6. Discussion. When should the surgical approach be preferred as the initial modality of treatment?

Obviously, it's a case-by-case decision, but as we mentioned in response to number 3, we have edited the manuscript to include our reasoning for why we proceeded directly to surgery.

7. Discussion. What about stent recall policy? Was there one in the hospital where the stent was placed? Was the patient called back to remove/replace the stent? If not, emphasize on the importance of recall registry as highlighted in the ESGE ERCP Quality Indicators paper.

There is a stent recall policy. The patient was brought back for a followup ERCP to remove the stent. However, the stent wasn't seen at that time, and was felt to have passed. The authors were not involved in the care of this patient at that time, but we think further imaging might have been helpful. A statement to this affect has been added to the manuscript:

"In general, most institutions have policies in place to make sure all stent patients are called back for stent removal, including our own. At the last ERCP there was a normal cholangiogram and the stent was no longer in place. It was felt to have migrated, but without symptoms the impression was that it had completely passed through and eliminated from the GI tract safely. In retrospect an X-ray or further imaging at that time would have been helpful."

8. Table. Please avoid all these abbreviations in Table's first line.

The table has been modified in order to remove the abbreviations.

9. Consider adding a sentence presenting the key words that were used for the literature search.

We thank the reviewer for this suggestion. We included the statement below describing our search strategy. Indeed this led to many more articles being including in the manuscript.

"We performed a systematic review of literature from 2000 until present 2020 for bowel perforation from migrated biliary stents and we found 81 cases (Table 1). Eligible articles were identified by a search of MEDLINE bibliographical database (last search: July 4th, 2021) using the following search algorithm: (("intestinal perforation"[MeSH Terms] OR ("intestinal"[All Fields] AND "perforation"[All Fields]) OR "intestinal perforation"[All Fields] OR ("bowel"[All Fields] AND "perforation"[All Fields]) OR "bowel perforation"[All Fields]) AND ("migrate"[All Fields] OR "migrated"[All Fields] OR "migrates"[All Fields] OR "migrating"[All

Fields] OR "migration"[All Fields] OR "migrational"[All Fields] OR "migrations"[All Fields] OR "migrator"[All Fields] OR "migrators"[All Fields]) AND "biliary"[All Fields] AND ("stents"[All Fields] OR "stentings"[All Fields] OR "stents"[MeSH Terms] OR "stents"[All Fields] OR "stent"[All Fields] OR "stented"[All Fields] OR "stenting"[All Fields])) AND (2000:2020[pdat]). Further search was performed in the references of related articles and relative articles with our topic were included. Manuscripts with full text available online were used and E-Videos, E-pictures and not English manuscripts were excluded. Cases were also excluded if there was not full text available online."

Reviewer #2:

1) Instead of writing year, it will be better to mention the duration. For example 2019 and 2020 may range from 1 day to 729 days. So, please mention duration in months or years.

We have edited the manuscript to include the month of each intervention so that the time frame would be more clear.

2. Clostridium Difficile- Clostridium difficile.

This was corrected in the manuscript.

3. The cause of biliary obstruction remains obscure

We have revised the manuscript to clarify that this was due to stones.

"A second ERCP was done in February 2020, at which time choledocholithiasis was noted."

4. What was the duration between first and second ERCP?

As per our response to question 1, the month of each intervention has been added, which makes the duration between interventions more obvious.

5. Patient suffered with active sepsis in the background of AIDS, Cirrhosis, prior laparotomy and ileorectal anastomosis. Why were vitals and lab parameters in the normal limit?

Although the patient presented with localized peritonitis, she was not septic as described. We have added to the manuscript our hypothesis as to why this was the case.

“Most patients with perforation will present with diffuse peritonitis and signs of sepsis. In our patient, we believe the amount of infection was limited by the perforation happening slowly over time, and her septic response was also blunted by her HIV with a low CD4 count.”

6. Could endoscopic removal of migrated stents be tried in this patient? Especially after total colectomy and ileo-rectal anastomosis, access to ileum becomes relatively easier. This could also have saved patient from laparotomy and risky procedure considering hostile abdomen due to prior surgeries.

We have revised the manuscript to include information on endoscopic techniques for removal. While we didn't think it was a good option in our case, it can definitely be used in other cases.

“An early growing body of literature describes endoscopic techniques for treatment of bowel perforation from migrated stent, but the majority focus on duodenal perforation or distal large bowel perforation. Bureau et al. recently described a case series of six patients with lateral duodenal wall perforation from displaced plastic biliary stent that were treated with over-the-scope clip ^[11]. Given that in our case the bowel perforation was in a mid-jejunal loop, the endoscopic approach was less feasible. In addition there was already significant inflammation seen around the bowel on CT scan, and we were concerned that an endoscopic mucosal repair would not hold. As such, we proceeded directly to surgery.”

7. Introduction and first two paragraphs of discussion are repetitive.

The manuscript has been modified to shorten the introduction, and keep more of the discussion in the later part of the manuscript.

8. The stent could have caused perforation in this patient could kinked and adhered small bowel. Reason for stent impaction and bowel perforation should have been elaborated in the discussion section.

We thank the reviewer for bringing this up. We agree with this thinking, and included it in the revised manuscript:

“Distally migrated stents usually pass through the bowel without any complication ^[1, 9]. In our case the patient had multiple previous laparotomies which led to adhesions, thereby making the bowel less mobile. This led to an increased likelihood that the stent would get impacted and not pass.”

9. Language editing is required to improve the quality of manuscript.

The manuscript has been re-edited by the senior author who is a native English speaker.

Reviewer #3:

1) Stent migration is not uncommon in clinical exercises. However, very few of them caused very serious complications, like perforation, including small bowel, large bowel and duodenum. For treatment, surgery is the priority in most of the hospitals. Furthermore, there are several types of plastic stents can be used in benign or malignant bile stricture. It will be better If the authors could describe which type of these stents tend to migrate.

The manuscript has been revised to include this information. In the case presentation we have added information about the type of stent:

“She had been seen previously for a biliary stricture and underwent a diagnostic ERCP in October 2019, at which time a plastic stent (7 French 7cm single external and single internal flap) was placed. A second ERCP was done in February 2020, at which time choledocholithiasis was noted, and a new plastic stent was placed (8.5 French 7cm).”

In the discussion we mention that plastic stents are the more likely stents to migrate, and included relevant references for this:

“Stent migration rate ranges from 5% to 10%, with the migration rates in plastic stents higher compared to others^[2, 7, 8]”

In addition, we found that in our literature review of migrated stents, the vast majority were plastic stents. This too, was incorporated into the manuscript.

“The majority of patients had a plastic stent (92.4%).”

Reviewer #4

Gastrointestinal perforation due to migration after the biliary plastic stent placement has already been reported and is not a new finding. You need to investigate the period from stenting to perforation in detail.

The timeline between stenting and presentation with perforation has been clarified in more detail in the manuscript:

“She had been seen previously for a biliary stricture and underwent a diagnostic ERCP in October 2019, at which time a plastic stent (7 French 7cm single external and single internal flap) was placed. A second ERCP was done in February 2020, at which time choledocholithiasis was noted, and a new plastic stent was placed (8.5 French 7cm). The original stent was not seen at that time. In August 2020 she went for another ERCP at which time she had a normal cholangiogram, and the stent was not seen at that time. She presented to our Emergency Department in November 2020.”

Reviewer #5

Congratulations to the authors. Excellent report. Congratulations on the literature review

Thank you!

Reviewer 1:

Unfortunately, intestinal perforation due to movement after biliary plastic stent placement has already been reported and is not a new finding.

Response:

We appreciate this comment. We feel this case is interesting because there were two stents, placed at separate times, both of which migrated into the small bowel. In addition, we have included an extensive literature review summarizing the other reports of perforation after migrated biliary stents.

Reviewer 2:

The authors have incorporated the suggested changes. The timeline of events have been clarified. Minor typographic errors have been highlighted in the attached file. Patient had cirrhosis and portal vein thrombosis. The ERCP and surgery is difficult in these circumstances. Was there evidence of portal biliopathy in this patient? What was the cause of biliary stricture in this patient? What was the finding on side viewing endoscopy? What precautions were taken to avoid hemorrhage during ERCP? What were the changes in bowel, liver and spleen at the time of surgical exploration? Many aspects of the case have been left open-ended. History of past illness need to be more detailed.

Answer:

We appreciate the reviewer's comments. We cannot see the attached file, but we have reviewed the manuscript to correct any remaining typographic errors. With regard to the cirrhosis and portal vein thrombosis, these were identified on imaging in the past, prior to the patient's presentation for this issue. She had a normal platelet count and a normal INR at that time. There was no issue with the ERCPs, and no evidence of biliopathy noted. We did not expand further on her cirrhosis in the manuscript in order not to confuse the presentation of the current issue, which is perforation after migration. We did expand the HPI significantly, in order to explain why she ended up getting an ERCP. This also explains the nature of the stricture, which we feel was likely due to choledocholithiasis. At the time of exploration there were extensive adhesions, and the bowel was cocooned in the abdomen, as mentioned in the manuscript. As a result, we did not explore the liver and the spleen, and only addressed the matter at hand, which was the perforation. A statement about this has been added to the manuscript in the "treatment" section.

Reviewer 3:

The manuscript can now be accepted.

Answer:

We thank the reviewers for their help in improving our manuscript to this point.