

February 16, 2015

Ya-Juan Ma
Editor-in-Chief
World Journal of Gastroenterology

Dear Professor Ma,

Please find enclosed the edited manuscript in Word format (file name: 16221-review.doc).

Title: Endovascular Treatment of Post-Laparoscopic Pancreatectomy Splenic Arteriovenous Fistula with Splenic Vein Aneurysm

Author: Tatsuo Ueda, Satoru Murata, Akira Yamamoto, Jin Tamai, Yuko Kobayashi, Chiaki Hiranuma, Hiroshi Yoshida, Shin-ichiro Kumita

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 16221

The manuscript has been improved according to the reviewer's suggestions:

1 The format has been updated.

2 Revisions were performed according to the reviewer's suggestions.

(1) To Reviewer 02998176

Thank you for your important comments. According to your comments, we have revised our manuscript as follows.

Comments by Reviewer 02998176

This case presentation by Ueda and colleagues describes a splenic arterio-venous fistula, which was detected three months after a spleen preserving laparoscopic distal pancreatectomy. Splenic arterio-venous malformations are a very rare entity and therefore physicians generally have limited personal experience with the various treatment options. Here the authors describe a case in which an arterio-venous fistula caused a rapidly progressing venous aneurysm so that treatment appeared imminent. From a surgical point, a surgical intervention appeared difficult given the localization, the time after primary surgery and the potential collateral damage of an open procedure. Naturally, an interventional approach appears logical and is described in this case presentation. While, embolization and stenting of the splenic artery are well described interventional treatment options, in this case the rapid size progression of the splenic vein aneurysm was most likely driven by a distal occlusion of the splenic vein near the SMV-confluens. With this reversal of venous flow in the splenic vein it was unpredictable if interventional occlusion of the arterio-venous fistula would be sufficient for a long-term control of the

ectatic splenic vein. The authors decided to embolize the draining vein as well. Apparently, this treatment was successful since the patient was doing well three months after the intervention without any signs of AV-fistula or aneurysm. The case is concisely described and sufficiently illustrated with high quality images. There is a short discussion in which the authors explain the context of the case and describe previous interventional approaches to the clinical problem. The reference section is in line with the journal's, the language and grammar are without obvious mistakes and the manuscript is easy to follow. The authors claim that this is the first report of an AV-fistula occurring after laparoscopic distal pancreatectomy. However, the laparoscopic form of surgery seems of rather reduced importance in this case. The strategy to address the splenic vein aneurysm in the context of distal occlusion of the draining vein appears interesting to the readership. In order to understand the long-term results in this case better, the manuscript would benefit if the authors would elaborate more on the venous blood flow in this case and the consequences of the embolization on blood flow: 1. With an occlusion of the distal splenic vein, the venous drainage of spleen and pancreas can be deviated through the coronary gastric vein back into the portal system or through esophageal varices into the SVC bypassing the liver. It would be interesting how the venous blood flow had evolved in this case. And if the embolization of the draining vein had any influence on this. 2. Likewise the embolization of the splenic artery can cause hypoperfusion of the spleen if the blood flow is not compensated through the short gastric vessels. The authors should therefore also comment on the perfusion of the spleen during the three month follow up. The patient remained hospitalized for 6 days following the endovascular intervention. This LOS seems rather long for a 40-year old patient. Could the authors please comment on the post-interventional course of the patient more in detail? In summary, this is a case presentation of a rare condition, with which the readership might not have ample personal experience and is therefore worth reporting.

1. With an occlusion of the distal splenic vein, the venous drainage of spleen and pancreas can be deviated through the coronary gastric vein back into the portal system or through esophageal varices into the SVC bypassing the liver. It would be interesting how the venous blood flow had evolved in this case. And if the embolization of the draining vein had any influence on this.

Response:

Before the endovascular treatment, the venous blood from the splenic vein aneurysm flowed into the portal system through the right gastric vein that had developed as collateral vessels. After the endovascular treatment, the path of the collateral vessels was unchanged, and the collateral vessels in the splenic hilum had shrunk.

2. Likewise the embolization of the splenic artery can cause hypoperfusion of the spleen if the blood flow is not compensated through the short gastric vessels. The authors should therefor also comment on the perfusion of the spleen during the three month follow up.

Response:

We evaluated the perfusion of the spleen via CT 4 days and 3 months after the endovascular treatment. Therefore, we added a sentence on Page 5, Lines 14–16 (underlined) as follows.

There was a small splenic infarction on the CT scan 4 days after endovascular treatment; however, the infarction had almost disappeared by 3 months after endovascular treatment.

3. The patient remained hospitalized for 6 days following the endovascular intervention. This LOS seems rather long for a 40-year old patient. Could the authors please comment on the post-interventional course of the patient more in detail?

Response:

The patient remained hospitalized for 6 days following the endovascular intervention due to a slight fever on postoperative day 4. Therefore, we added a sentence regarding the post-interventional course of the patient on Page 5, Lines 10–11 (underlined) as follows.

The patient had a slight fever on postoperative day 4, and he received antibiotic medication for 3 days.

(2) To Reviewer 02551692

Thank you for your comments. We appreciate the critical comments and useful suggestions that have improved our manuscript considerably.

Comments by Reviewer 02551692

The work is interesting and the english language are clear and correct. It could be interesting to show the TC upper abdominal images of patients before laparoscopic pancreatectomy too. The splenic vein aneurysm and artero-venous fistula could be also the consequence of the vascular spleen dissection during laparoscopic pancreatectomy (expecially in spleen preserving technique). Moreover, have you made patient's abdominal ultrasonography (or TC) before 3th p.o. month? Did the patient have a pancreatic leakage after pancreatectomy? I agree (according to my experience and the data of Literature) on usefulness and safety (in expert hands) of endovascular treatment for this type of complication

expecially in cases of pancreatic region reoperations.

1. Have you made patient's abdominal ultrasonography (or TC) before 3th p.o. month?

Response:

A CT scan was performed 17 days after pancreatectomy, and the CT scan demonstrated no splenic arteriovenous fistula or dilated splenic vein at that time.

2. Did the patient have a pancreatic leakage after pancreatectomy?

Response:

There was no pancreatic leakage during the postoperative hospitalization.

(3) To Reviewer 00058328

Thank you for your important comments. According to your comments, we have revised our manuscript as follows.

Comments by Reviewer 00058328

This is a well-written and adequately documented report of a postoperative arteriovenous fistula, following laparoscopic distal pancreatic resection. The authors complete their report with a comprehensive review of relevant literature evidence. The subject of this case report is relevant to multiple disciplines, including surgeons, gastroenterologists, and interventional radiologists. The differential diagnosis, which might define the therapeutic approach, is of outmost importance. Some comments regarding the manuscript: 1. Perioperative data need to be provided: Was surgery uneventful? What was the postoperative course? How long was the length of stay? More importantly, why was the splenic vein ligated? 2. What was the indication for 3-month postoperative CT? 3. Why did the patient have to stay inpatient for 6 days after embolization? 4. How was splenic perfusion at control-CT 3 months after embolization? 5. 'Pathological diagnosis' under 'Comments' may be omitted.

1. Perioperative data need to be provided: Was surgery uneventful? What was the postoperative course? How long was the length of stay? More importantly, why was the splenic vein ligated?

Response:

As suggested, we added the perioperative data on Page 4, Lines 12–15 (underlined) as follows.

The surgery was performed uneventfully, and there were no complications such as bleeding, pancreatic leakage or infections during the hospitalization. The patient was discharged on postoperative day 7.

The surgeon did not ligate the splenic vein. However, the postoperative CT scan demonstrated splenic vein occlusion.

2. What was the indication for 3-month postoperative CT?

Response:

We usually perform postoperative CT scans at 3-months after laparoscopic pancreatectomy to evaluate late complications.

3. Why did the patient have to stay inpatient for 6 days after embolization?

Response:

The patient remained hospitalized for 6 days after embolization due to a slight fever on postoperative day

4. Therefore, we added a sentence on Page 5, Lines 10–11 (underlined) as follows.

The patient had a slight fever on postoperative day 4, and he received antibiotic medication for 3 days.

4. How was splenic perfusion at control-CT 3 months after embolization?

Response:

We evaluated the perfusion of the spleen via CT scan at 4 days and 3 months after endovascular treatment.

Therefore, we added a sentence on Page 5, Lines 14–16 (underlined) as follows.

There was a small splenic infarction on the CT scan 4 days after endovascular treatment; however, the infarction had almost disappeared by 3 months after endovascular treatment.

5. 'Pathological diagnosis' under 'Comments' may be omitted.

Response:

As suggested, we omitted 'Pathological diagnosis' under 'Comments'.

3 The references and typesetting were corrected.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

Tatsuo Ueda

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