Author's response to reviews

Title: Giant uterine artery pseudoaneurysm after a missed miscarriage termination in a cesarean scar pregnancy

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Author's response to reviews: see over
Dear Editor:

Thank you very much for your consideration of our manuscript. We have made revisions according to the comments and suggestions of yourself and the reviewers. The paper has also been edited carefully by a native English-speaker.

In page 2 lines 33-38, we revised “The uterine artery pseudoaneurysm was detected on the next day by Doppler ultrasonography. It measured 71 × 44 × 39 mm. On day 10 after curettage, the pseudoaneurysm ruptured spontaneously and an emergency hysterectomy was performed.” to “A uterine artery pseudoaneurysm measuring 71 × 44 × 39 mm was detected the next day by Doppler ultrasonography. While waiting for admittance to an advanced institution to undergo embolization treatment, the pseudoaneurysm ruptured spontaneously. The subsequent severe hemorrhage necessitated hysterectomy.”

In page 2 lines 40-47, we changed “Conclusion” in the structured Abstract according to your comments as to “A delay in diagnosis of uterine artery pseudoaneurysms may result from a long period between the curettage and follow-up examination. Ultrasound and Doppler ultrasonography should be performed repeatedly at short intervals to rule out them, especially in cesarean scar pregnancies. For a giant uterine artery pseudoaneurysm, interventional embolization might be the first treatment choice. If time allows, intra-operative ligation of the feeding vessels should be attempted before any decision to perform a hysterectomy is made. However, hysterectomy remains a possibility when severe bleeding occurs.”
In page 3 line 70, the word “woman” was revised to “female patient”.

In page 3 lines 72-74, we revised the past obstetric history as: Four years ago she had a missed miscarriage at 9 weeks of gestation, which was managed by surgical curettage. Two years prior to presentation she had delivered a baby by elective cesarean.

In page 3 lines 74-75, we revise “She had been diagnosed as being pregnant at 40 days of gestational age, 20 days before presenting at the hospital” to “Twenty days before presenting at the hospital she had been diagnosed as 40 days pregnant”.

In page 3 line 77, we add “On presentation” in the beginning of the sentence.

In page 4 lines 93-94, “It was connected with an artery by a narrow neck in its posterior wall” was revised to “which was connected to an artery via a narrow neck in its posterior wall”.

In page 4 lines 96-104, we move the paragraph in “Discussion” in former version to the “Case Presentation” as: “The patient was examined by interventional radiologists; however, they lacked experience in treating such a giant lesion and thought that repeated treatment might be required. A persistently high serum β-hCG concentration suggested that there were retained chorionic villi present within the pseudoaneurysm. Thus, recanalization of the pseudoaneurysm by rapid recruitment of collateral vessels might occur even after arterial embolization. Repeated uterine curettage immediately after embolization, or methotrexate therapy, might decrease the likelihood of recanalization. Therefore, the patient sought admittance to an advanced institution for embolization treatment.”

In page 5 lines 104-106, we revised the sentences “At day 10 after curettage,
severe vaginal bleeding occurred suddenly and an emergency hysterectomy was performed.” to “However, while waiting to be admitted, massive bleeding occurred suddenly at day 10 and emergency surgery was performed.”

In page 5 lines 107-108, “A ruptured pseudoaneurysm measuring 60 × 70 × 50 mm in the cesarean scar position of the uterus was found during the operation (Fig 4).” was revised to “During the operation, a 60 × 70 × 50 mm pseudoaneurysm was located in the cesarean scar position (Fig. 4).”

In page 5 lines 108-112, we added the paragraph: “Ideally, the lesion would have been completely resected and the uterus repaired after ligation of the uterine artery feeding the pseudoaneurysm. However, the hemorrhage was immediately life threatening. Therefore, to stop the bleeding quickly and save the patient’s life a hysterectomy was performed.”

In page 5 line 112, the word “cyst” was revised to “pseudoaneurysm”.

In page 5 line 115, “A uterine artery pseudoaneurysm is” was revised to “Uterine artery pseudoaneurysms are”.

In page 5 line 116, the wording “One of its causes is” was revised to “Potential causes include”.

In page 5 line 117, the word “or” was revised to “and”.

In page 5 lines 118-120, “Ultrasonography was useful in detecting the formation of the pseudoaneurysm in this case, both by 2-dimentional and Doppler scans” was revised to “In this case, both two-dimensional and Doppler ultrasound scans were useful in detecting the pseudoaneurysm.”

In page 5 line 121, “Using 2-dimentional ultrasonography,” was revised to “In two-dimensional ultrasonographic images,“.

In page 6 line 137, we added “Repeating these examinations several times
over a short time period might allow early diagnosis of a pseudoaneurysm, when it is still small in size.” in the end of this paragraph.

In page 6 line 140-142, “The wall was very thin with a high risk of rupture.” was revised to “The wall of the pseudoaneurysm was very thin and at high risk of rupture, it should have been treated as rapidly as possible.”

In page 6 line 143, we revised “Endovascular treatment is often the first-line therapy.” to “In such cases, endovascular treatment is often the first-line therapy.”

In page 6 line 143, “It can be achieved with embolization with coils, stents and injectable liquids” was revised to “Embolization can be achieved with coils, stents and injectable liquids”.

In page 6 lines 147-151, we added this paragraph: If time allows, and if embolization is not an option, intra-operative ligation of the pseudoaneurysm feeding vessels should be attempted prior to resorting to hysterectomy, especially in patients with low parity [12]. Ligation of the ascending branch of the uterine artery may successfully stop postabortal hemorrhage in approximately 90% of patients. We cited a new reference [12] you provided here.

In page 7 lines 152-153, “Another possible treatment method was direct thrombin injection into the mass” was revised to “Another possible treatment method was direct injection of thrombin into the pseudoaneurysm”. The reference [12] in former version was changed to [13] because we added a new reference [12].

In page 7 line 155, we added “associated with this procedure” in the end of the sentence “we lack knowledge on the scope of possible complications”.
In page 7 lines 158-161 in Conclusion, “It is highly advisable for patients to undergo a Doppler ultrasound examination as a required postoperative investigation to rule out a uterine artery pseudoaneurysm, in cases of a cesarean scar pregnancy.” was revised to “A delay in diagnosis of uterine artery pseudoaneurysms may be caused by a long period between the curettage and follow-up examination. Ultrasound and Doppler ultrasonography are recommended to be performed repeatedly at short intervals to rule out them, especially in cesarean scar pregnancies.” to highlight the cause for the delay in the diagnosis.

In page 7 lines 161-166, “For such a giant uterine artery pseudoaneurysm, embolization might be the first treatment when the diagnosis is made, but hysterectomy is possible when severe bleeding occurs.” was revised to “For a giant uterine artery pseudoaneurysm, interventional embolization might be the first treatment option when the diagnosis is made. Alternatively, if time allows, intra-operative ligation of the feeding vessels should be performed prior to any decision to resort to hysterectomy. However, hysterectomy remains a possibility when severe bleeding occurs.”


In page 10 lines 231, “2” was revised to “Two”

In page 10 lines 221-232, “It showed a pseudoaneurysm in the anterior wall of the lower part of the uterus.” was revised to “The pseudoaneurysm is visible in the anterior wall of the lower part of the uterus.”

In page 10 line 233, “was” was revised to “is”.
In page 10 line 233, “the inner surface of the wall” was revised to “the luminal surface of the wall”.

In page 10 lines 234-236, “A swirl of colors was seen in the color Doppler ultrasonography image. It showed the opening of the pseudoaneurysm and its supplying artery.” was revised to “A swirl of colors, which represents the opening of the pseudoaneurysm and its supplying artery, is visible in this color Doppler ultrasonography image.”

In page 10 line 237, “Supplying artery velocity of the pseudoaneurysm.” was revised to “Blood flow velocity within the supplying artery”.

In page 10 line 241, “the size” was revised to “its size”.

Editor’s comments:

1. The role of intra-operative ligation of the feeding vessels of the pseudoaneurysm is a true fact. It should be sought prior to resorting to hysterectomy where time allows especially among cases with low-parity (Mullins JA, O’Leary JA, Askel S. Uterine artery ligation for postabortal hemorrhage. Obstet Gynecol 1979; 54: 383-84). Therefore, the role of securing hemostasis with vessel plication should be considered before a radical decision of hysterectomy is made (Reviewer#2). Further, the author(s) themselves established this statement in the previous version of the manuscript (section of background, line 5). Accordingly, the author(s) are requested to explain why they did not do so and discuss these informations in their revised new manuscript.

Author’s response: Thank you very much for your comment, and thank you for the reference that you provided. In this case, the pseudoaneurysm was
located in the cesarean scar and there were retained chorionic villi within its wall. It was big and the bleeding was severe. Ideally, the lesion would have been completely resected and the uterus repaired after ligation of the uterine artery supplying the pseudoaneurysm. However, we didn’t have enough time to do this. To stop the bleeding quickly and save the patient’s life we resorted to hysterectomy.

We have added this information to the “Case Presentation” as follows:

“During the operation, a $60 \times 70 \times 50$ mm pseudoaneurysm was located within the cesarean scar (Fig. 4). Ideally, the lesion would have been completely resected and the uterus repaired after ligation of the uterine artery feeding the pseudoaneurysm. However, the hemorrhage was immediately life-threatening. Therefore, to stop the bleeding quickly and save the patient’s life a hysterectomy was performed.”

Since we agree with your comment we have also added the following sentences to the “Discussion”:

“If time allows, and if embolization is not an option, intra-operative ligation of the pseudoaneurysm feeding vessels should be attempted prior to resorting to hysterectomy, especially in patients with low parity [12]. Ligation of the ascending branch of the uterine artery may successfully stop postabortal hemorrhage in approximately 90% of patients.”

We have also cited the reference that you suggested.

In addition, we have similarly revised the “Conclusion” as follows: “For a giant uterine artery pseudoaneurysm, interventional embolization might be the first treatment option when the diagnosis is made. Alternatively, if time allows, intra-operative ligation of the feeding vessels should be performed prior to any
decision to resort to hysterectomy. However, hysterectomy remains a possibility when severe bleeding occurs."

-Section of "Abstract":
It did not reflect the core and the context of this report. The abstract should be re-written in a way highlighting the cause for the delay in the diagnosis and the main message for the reader to manage such cases.

Author’s response: Thank you very much for your constructive comment. We have revised the “Abstract” as follows:

**Background**
Uterine artery pseudoaneurysms are dangerous and can lead to severe hemorrhage. We report an uncommon cause of a giant pseudoaneurysm in a missed miscarriage in a woman with a cesarean scar pregnancy.

**Case presentation**
The patient was a 25-year-old woman with a missed miscarriage in a cesarean scar pregnancy. Curettage was performed under ultrasound monitoring. A uterine artery pseudoaneurysm measuring $71 \times 44 \times 39$ mm was detected the next day by Doppler ultrasonography. While waiting for admittance to an advanced institution to undergo embolization treatment, the pseudoaneurysm ruptured spontaneously. The subsequent severe hemorrhage necessitated hysterectomy.

**Conclusion**
A delay in diagnosis of uterine artery pseudoaneurysms may result from a long period between the curettage and follow-up examination. Ultrasound and
Doppler ultrasonography should be performed repeatedly at short intervals to rule out them, especially in cesarean scar pregnancies. For a giant uterine artery pseudoaneurysm, interventional embolization might be the first treatment choice. If time allows, intra-operative ligation of the feeding vessels should be attempted before any decision to perform a hysterectomy is made. However, hysterectomy remains a possibility when severe bleeding occurs.

-Section of "Case presentation", lines 71-73:

Please change wording of the past obstetric history in a more favourable linguistic form (poor language).

**Author’s response:** Thank you for your constructive comment. The patient’s past obstetric history is now written as follows: “Four years ago she had a missed miscarriage at 9 weeks of gestation, which was managed by surgical curettage. Two years prior to presentation she had delivered a baby by elective cesarean.”

-Section of "Discussion", lines 127-37:

This paragraph should be moved to the main text of presentation of your case.

**Author’s response:** Thank you very much. We have moved this paragraph to the Case Presentation section, lines 96-106:

The patient was examined by interventional radiologists; however, they lacked experience in treating such a giant lesion and thought that repeated treatment might be required. A persistently high serum β-hCG concentration suggested that there were retained chorionic villi present within the pseudoaneurysm. Thus, recanalization of the pseudoaneurysm by rapid recruitment of collateral
vessels might occur even after arterial embolization. Repeated uterine curettage immediately after embolization, or methotrexate therapy, might decrease the likelihood of recanalization. Therefore, the patient sought admittance to an advanced institution for embolization treatment. However, while waiting to be admitted, massive bleeding occurred suddenly at day 10 and emergency surgery was performed.

-Section of "Discussion", line 136:

Please change wording "when waiting" into "while waiting".

Author’s response: Thank you very much for your suggestion. We have changed the wording from “when waiting” to “while waiting”.

-Section of "Conclusion":

Please change wording in a more favourable languistic form (poor language).

Author’s response: Thank you very much. We have revised the “Conclusion” as follows:

A delay in diagnosis of uterine artery pseudoaneurysms may be caused by a long period between the curettage and follow-up examination. Ultrasound and Doppler ultrasonography are recommended to be performed repeatedly at short intervals to rule out them, especially in cesarean scar pregnancies. For a giant uterine artery pseudoaneurysm, interventional embolization might be the first treatment option when the diagnosis is made. Alternatively, if time allows, intra-operative ligation of the feeding vessels should be performed prior to any decision to resort to hysterectomy. However, hysterectomy remains a possibility when severe bleeding occurs.
Sections of “Case presentation” & “Discussion” should be subdivided into smaller sequential paragraphs.

Author’s response: Thank you for your comment. As per your suggestion, we have subdivided the “Case presentation” and “Discussion” sections into smaller, sequential paragraphs.

To reviewer:
Reviewer: Shigeki Matsubara
Reviewer’s report:
The discussion section consists of ONE paragraph. Please trim this ugly style for the sake of your Journal reputability.

Author’s response: Thank you very much for your comment. We have subdivided the “Discussion” section into smaller, sequential paragraphs.

Reviewer:nidhi sharma
Reviewer's report:
The changes are apt.

Author’s response: Thank you very much for your comment.

Reviewer:Lorraine Corfield
Reviewer’s report:
My points have been answered and the report amended appropriately.

Author’s response: Thank you very much for your comment.