Peer Review File

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<mark>Reviewer A</mark>

Comment 1: According to the author's instruction (<u>https://amj.amegroups.com/pages/view/guidelines-for-authors#content-3-3-1</u>), the format of Highlight Box should be template1 rather than template 2.

- "Key recommendations" should be revised to "key findings". The key findings should include all urinary complications in this case and surgical management for treating them. For the authors' reference, "To our knowledge, this is the first case to result in the simultaneous combination of massive hemorrhage, cystotomy, bladder necrosis, vaginal cuff necrosis, and vesicovaginal fistula formation. And many surgical techniques (such as XXX) were used to preserve bladder tissue and function"
- "What was recommended and what is new?" should be revised to "What is known and what is new?". The authors should also highlight the unique point of this case in the part
- In the "What is the implication?" part, it's advised to talk about the importance of preoperative consultation and the several surgical techniques that can be employed to preserve bladder tissue and function, i.e. the content of lines 181-188.

Reply:

Thank you for taking the time to review our manuscript and provide feedback. We appreciate and agree with your suggestion to revise the Highlight Box according to template1, and we have made the necessary changes. Additionally, we have revised "Key recommendations" to "Key findings" and included all urinary complications in this case along with the surgical management for treating them. We have also highlighted the unique point of this case in the "What is known and what is new?" section. Lastly, we have included the importance of preoperative consultation and several surgical techniques that can be employed to preserve bladder tissue and function, as you suggested, in the "What is the implication?" part. We believe that these changes have significantly improved the quality of our case report and we appreciate your valuable input.

Changes in the text:

Highlight Box

Key findings

- This case demonstrates placental invasion of the urinary bladder, which was treated with cesarean section, hysterectomy, and dissection of invasive placental tissue.
- Inadvertent cystotomy was created during surgical removal of placental tissue.
- Surgical dissection of placental tissue was complicated by massive hemorrhage, necessitating therapeutic embolization.
- Postoperative course was complicated by necrosis of both the vaginal cuff and cystotomy repair, resulting in a large vesicovaginal fistula (VVF).
- The vaginal cuff and bladder were closed in a manner that avoided overlapping suture lines. A flap of omentum was interposed between vagina and bladder for optimal to decrease risk of VVF reformation.

What is known and what is new?

- Urologic complications of PAS are relatively rare but can be severe.
- This is the first case to result in the simultaneous combination of massive hemorrhage, cystotomy, bladder necrosis, vaginal cuff necrosis, and vesicovaginal fistula formation.

What is the implication, and what should change now?

- Multidisciplinary preoperative consultation is crucial to prepare for potentially life-threatening complications of PAS.
- There are several surgical techniques that can be employed to preserve bladder tissue and function:
 - Filling the bladder prior to vesicouterine dissection, the use of hemostatic clips during dissection, and the "Triple P Procedure."

Comment 2: It's good to see that the authors provided the detailed surgical treatment process in the abstract section. Considering some readers may only read the abstract part, I hope the authors also add the history of three prior cesarian sections, the previous diagnosis (MRI and ultrasound), outcomes (recovered well and was discharged home two days after surgery), and follow-up (approximately 3 months after the repair, she had no urinary complaints and reported feeling like herself again).

Reply: We agree with your comment that providing a comprehensive summary in the abstract section is important, especially for readers who may not have the opportunity to read the full text. Therefore, we have revised the abstract to include the history of three prior cesarean sections, the previous diagnosis (MRI and ultrasound), outcomes (recovered well and was discharged home two days after surgery), and follow-up (approximately 3 months after the repair, she had no urinary complaints and reported feeling like herself again). We believe that these additions will enhance the understanding and clinical relevance of the case report.

Changes in text:

Abstract case description:

A 30-year-old woman with a past medical history significant for 3 prior cesarean sections, found to have placental invasion of the bladder (detected by ultrasound and confirmed by MRI), presented at 33 weeks with premature labor ...[unchanged text truncated for brevity]... The patient recovered well, was discharged home two days after surgery; she reported feeling like herself again, without urinary complaints at 3 months after the surgery.

Comment 3: The number of keywords should be no more than 5. For "surgical management" and "surgical technique", please just reserve one.

Reply: We agree with your recommendation to limit the number of keywords to no more than five, and we apologize for the oversight in our initial submission.

Changes in text: After careful consideration, we have decided to include the keyword "surgical technique" and remove "surgical management" to comply with the guidelines.

Comment 4: In the introduction part, the authors should highlight the unique point by comparing it with other case reports about PAS, such as PMID 34804697, 27579379, etc.

In response to your comment, we have added a statement to the introduction highlighting the unique aspects of our case report and how it differs from previous case reports. Specifically, we have compared our case report with other case reports about PAS, including one that you mentioned, and highlighted that while individual complications have been reported before, to our knowledge, this is the first case report documenting the simultaneous combination of such complications. We believe that this addition strengthens the introduction by emphasizing the novelty and significance of our case report.

Changes in text: The following two sentences were added to the introduction.

"Urologic complications of PAS, including inadvertent cystotomy during hysterectomy, massive hemorrhage requiring therapeutic embolization and subsequent bladder necrosis, vaginal cuff necrosis, and vesicovaginal fistula formation, have all been described as individually rare in case reports (4-7), but are particularly notable in combination. To our knowledge, this is the first case report documenting the simultaneous combination of such complications."

Comment 5: Comment For the authors' kind reference, we prefer the detailed time information of the case report (Date, Month, Year) in the manuscript.

Reply:

Thank you for your comment regarding the inclusion of detailed time information in our case report manuscript. We understand the importance of precise reporting of clinical information and appreciate your feedback. However, we would like to bring to your attention our department's policy for publishing case reports, which restricts us from including specific dates of care in order to protect patient privacy.

Changes in the text: Although we were unable to make direct changes to address your request, we did create a timeline figure to visually display the time course of the case report. We believe that this figure will provide a clear representation of the timeline without compromising patient confidentiality. We hope that this will adequately address your concerns and improve the clarity of the manuscript.

Comment 6: "the subsequent hysterectomy was complicated by severe hemorrhage requiring activation of a massive transfusion protocol". The description of severe hemorrhage is vague, preferably with specific data about bleeding volume.

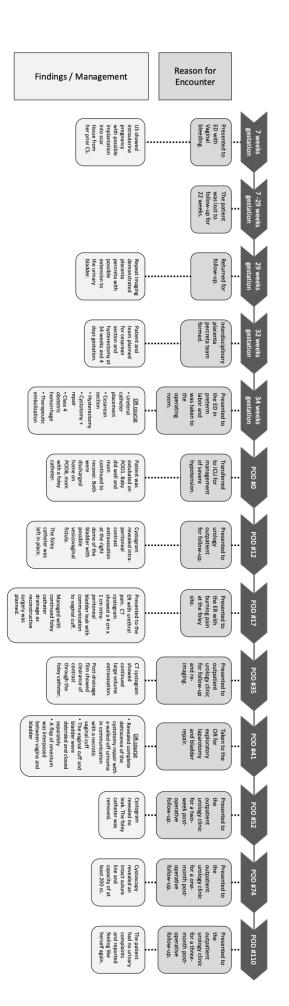
Reply: Thank you for your comment regarding the description of severe hemorrhage in our case report. We appreciate your feedback and have updated the manuscript to include specific data about bleeding volume, including obstetric hemorrhage class, estimated blood loss and the number of blood products transfused. We hope that these additions provide a more detailed and accurate account of the patient's clinical course, and we thank you for your valuable input in improving our manuscript.

Changes in the text:

The description of blood loss now reads as follows: "After a cesarian section was performed and the baby was delivered, the subsequent hysterectomy was complicated by class 4 obstetric hemorrhage, with an estimated blood loss of 40 liters, requiring activation of a massive transfusion protocol. The patient received 76 units of packed red blood cells, 36 units of fresh frozen plasma, 18 units of cryoprecipitate and 14 units of platelets."

Comment 7: I suggest the authors add a timeline. The timeline should present relevant events in the patient's history in chronological order (gestational and post-operative) in a figure or table, enabling the core elements of the case report to stand alone.

Thank you for your suggestion. We appreciate your feedback, and we agree that a timeline figure would be useful in presenting the patient's history in a clear and concise manner. Therefore, we have added a timeline figure to the manuscript, which presents relevant events in the patient's gestational and postoperative history in chronological order. We believe this figure will enhance the readability of the case report and enable the core elements of the case report to be more salient to the reader.



Comment 8: Does any pharmacologic be given post-operative? If done, please report them, including the dosage and duration.

We are pleased to inform you that we have made the necessary revisions to address your concern. In particular, we have added the medications at discharge for both operations in the case report, including the dosage and duration. This information provides a detailed account of the patient's postoperative pharmacologic management, which we hope will be useful to readers interested in this aspect of our report.

Changes in text:

"She was transferred to the intensive care unit where she stabilized. She was extubated on post-operative day (POD) #1 and was ultimately discharged home on POD #8 with a foley catheter, acetaminophen 650 mg every 6 hours (q6h) for 10 days, diclofenac gel 1% q8h for 21 days, nitrofurantoin 200mg q12h for 6 days, oxycodone 5mg q4h prn for 6 days, tamsulosin 0.4mg q24h for 3 days, and oxybutynin 15mg q24h for 3 days."

...[unchanged text truncated for brevity]...

"The patient recovered well and was discharged home two days after surgery with acetaminophen 975mg q6h prn for 30 days, ketorolac 10mg q6h for 20 days, oxybutynin 15mg q24h for 30 days."

Comment 9: If it's available, please also provide the important follow-up diagnostic results (e.g. the cystoscopy images).

We appreciate your interest in this aspect of the case and understand the importance of providing comprehensive follow-up information to readers. Unfortunately, in this particular case, cystoscopy images were not available for inclusion in the manuscript. However, we have provided as much follow-up information as was available, including the patient's subjective report of her symptoms and the recorded finding of her follow-up testing, as was documented in her record. We believe that this information, together with the detailed description of the surgical technique and postoperative management, provides a comprehensive and informative case report that will be useful to other clinicians and researchers.

Comment 10: A paper published in AJOG (PMID36201777) showed that prophylactic ureteral stent placement was associated with a reduced risk of genitourinary injury during implantable placental hysterectomy, and the importance of prophylactic ureteral stent was also highlighted in this case report (<u>https://doi.org/10.1016/j.eucr.2013.11.010</u>). So, I prefer to see any points about prophylactic ureteral stent placement from authors in the discussion, including whether tell the patient about prophylactic ureteral stent placement when the ultrasound demonstrated placenta percreta with possible extension to the bladder.

Reply: Thank you for your valuable comments on our case report. We appreciate your insights regarding the prophylactic ureteral stent placement during implantable placental hysterectomy, and the possible need for mentioning this in our discussion section. We agree that prophylactic ureteral stent placement is an important consideration to prevent genitourinary injury during hysterectomy, as highlighted in the articles you mentioned. In fact, our interdisciplinary team was aware of this and discussed this with the patient prior to the hysterectomy. The patient agreed to have urology place the stents prior to the procedure.

However, in our case report, we chose not to discuss the utility of prophylactic stent placement for several reasons. Firstly, our aim of this case report was to focus on surgical techniques specific to bladder preservation, rather than for the entire urogenital tract. Secondly, no injury to the ureter occurred in our case, therefore, mention of techniques for prevention of ureteral injury were deemed less relevant to the discussion. Thirdly, we concluded that we were unable to comment on ureteral injury during hysterectomy in a manner that would significantly contribute to what is already known about this complication, given that it is the most comment urologic complication of hysterectomy and there is already a considerable amount of literature on the topic.

Comment 11: It is highly recommended that authors use one separate paragraph to LIST BOTH strengths and limitations of this case in a logical way.

Reply: We appreciate your suggestion to use one separate paragraph to list both strengths and limitations of the case in a logical way. We have incorporated your suggestion into our manuscript and added a paragraph that clearly outlines both the strengths and limitations of our case report. Specifically, we have highlighted the rare nature of the urological complications of PAS experienced by the patient, as well as the importance of interdisciplinary team management and preparation for potential surgical complications. We acknowledge the limitations of our report, including the lack of information around the patient's loss to follow-up and the absence of long-term outcomes on her quality of life. We hope that these changes have adequately addressed your concerns and improved the overall quality of our manuscript.

Changes in the text: The following paragraph was added to the discussion.

This case report details urological complications of PAS that are rare when experienced in isolation, but their co-occurrence makes them particularly remarkable. As such, the case illuminates several important considerations for patients with PAS, including the relevant medical history diagnostic testing, the importance of an interdisciplinary team approach, and the need for preparation for potentially devastating surgical complications. This report is limited by the lack of information around the patient's loss to follow-up as well as lack of long-term outcomes on her the quality of life.

Comment 12: Line 173: Please provide the detailed statement about the "several surgical techniques".

Reply: Thank you for your valuable feedback on our manuscript. We have made the necessary revisions to address your comment regarding the lack of detailed statement on the "several surgical techniques". The revised line now provides specific details on the various surgical techniques that can be used to preserve bladder tissue and function. We hope that this addition clarifies this important point and provides more comprehensive information for readers. Once again, we appreciate your thoughtful review and constructive comments on our work.

Changes in text:

There are several surgical techniques that can be employed to preserve bladder tissue and function, including filling the bladder prior to vesicouterine dissection, the use of hemostatic clips during dissection, and the "Triple P Procedure."

Comment 13: According to the author's instruction (<u>https://cdn.amegroups.cn/static/public/2.5-</u> <u>Structure%20of%20Case%20Reports-template-V2022.11.4.docx?v=1676863772747</u>), the introduction and discussion should be restructured.

(1) Introduction is structured in three parts: a) Background, b) Rationale and knowledge gap, c) Objective.
(2) Similarly, discussion is structured in five parts: a) Key Findings, b) Strengths and limitations, c)
Comparison with similar researches, d) Explanations of findings, e) Implications and actions needed.

Reply: Thank you for your thorough review and constructive feedback on our manuscript. We appreciate your suggestion regarding the restructuring of the introduction and discussion sections to align with the author's instructions. We have carefully revised the manuscript accordingly, and our introduction now follows the three-part structure outlined in the instructions, including background, rationale and knowledge gap, and objective. Similarly, the discussion section has been restructured to include the five-component structure outlined in your comment (see specific identification of each component as detailed below). We believe that these changes have significantly improved the clarity and coherence of our case report, and we are grateful for your valuable input.

Changes in text: The introduction, after being altered to address concerns made in reviewer comment 4, now aligns with the structure outline in the author's instructions. Similarly, after addressing reviewer comment 11, and relocating one sentence (now the final sentence of the discussion) regarding actions needed, our discussion now aligns with the structure outlined in reviewer comment 13. Specific identification of each component is detailed below.

Introduction: Background: P1, S1 and 2. Rationale and knowledge gap: P1S3 Objective: P1S4 and 5

Discussion: a) Key Findings: P1 b) Strengths and limitations: P2 c) Comparison with similar researches: p3, p4, p5, p6, p7, d) Explanations of findings p6 sentences 3 and 4. P7S3,4 e) Implications and actions needed. P8

Comment 14: CARE checklist, The relevant page/line and section/paragraph number in the manuscript should be stated for each item in the checklist. So please kindly fill the item 11a.

Reply: We would like to express our gratitude to the reviewer for their meticulous review and constructive feedback on our manuscript. Thank you for bringing to our attention the need to state the relevant page/line and section/paragraph number in the manuscript for each item in the CARE checklist, and for specifically requesting that we fill in item 11a. We have made the necessary changes, and item 11a has been filled in accordingly in the revised manuscript.

Changes in text: identification of the component from the CARE checklist for 11a can be found on page 4, line 176-182.

<mark>Reviewer B</mark>

Comment 1: Abstract: Please describe that she is healthy and well at postoperative 3 months.

Reply: We agree that it is important to include the patient's postoperative status and outcome in the summary of the case report. Therefore, we have added a sentence at the end of the abstract to describe that the patient recovered well, was discharged home two days after surgery, and reported feeling like herself again, without urinary complaints at 3 months after the surgery. This addition provides a clear and concise conclusion to the abstract and highlights the successful management of this rare condition.

Changes in text:

The case description portion of the abstract was amended such that the final sentence now reads "The patient recovered well, was discharged home two days after surgery; she reported feeling like herself again, without urinary complaints at 3 months after the surgery."

Comment 2: PAS (creta [not accreta], increta, percreta). 2018 FIGO recommendation for the new terminology is partly to extinguish the "double meaning" of placenta accreta. Thus, now, there is no terminology of "placenta accreta". We use placenta accreta spectrum (general meaning) OR "placenta creta" (the less severe form).

Reply: We have carefully considered the reviewer's comment and made the necessary changes to the manuscript to reflect the current 2018 FIGO recommendation regarding the terminology for PAS. Specifically, we have changed the term "accreta" to "creta" in the introduction of the manuscript. We understand the importance of using correct and up-to-date terminology in academic writing, and we believe that this change will enhance the clarity and accuracy of our report. We appreciate the reviewer's recommendation and feedback, which has significantly improved the quality of our case report.

Changes in text: In the introduction section, in sentence 2 the term "accreta" was changed to "creta."

Comment 3: "Morbidly adherent placenta" is not used any longer. USA doctors still use this. Your case was diagnosed as "placenta percreta". Please simply state so.

Reply: We have taken the reviewer's comments seriously and made the necessary changes to the manuscript to reflect the correct and current terminology regarding the diagnosis of placenta percreta. Specifically, we have removed the term "morbidly adherent placenta" from the text, and instead, we have described the diagnosis as "full thickness placental invasion of the anterior lower uterine segment" as confirmed by the MRI. We recognize the importance of using precise and up-to-date terminology in medical writing, and we appreciate the reviewer's recommendation and guidance, which has significantly enhanced the quality and accuracy of our report.

Changes in text: Case presentation, paragraph 1, sentence 2 now reads "MRI confirmed placenta previa with full thickness placental invasion of the anterior lower uterine segment."

Comment 4: Please confirm whether "cystotomy" is right. To me, cystotomy sounds the surgical procedure, similar to hysterotomy, gastrotomy, etc. I believe bladder injury or bladder rupture or bladder large perforation or something like that. You only wish to say bladder injury with the largest diameter of 10 cm about, right?

Reply: While "cystotomy" technically describes a surgical incision, we understand the potential confusion it may cause and have taken steps to clarify the meaning. Specifically, we have added the word "inadvertent" before "cystotomy" to more clearly describe the accidental surgical incision into the urinary bladder. Thank you for your attention to detail and for helping us improve the quality of our manuscript.

Changes in text: the term "inadvertent" was inserted before "cystotomy" in th following places: abstract background, abstract case presentation, introduction section, case presentation paragraph 3, and highlight box key findings.

Comment 5: Please describe the relationship between the trigone and the bladder injury (or villous invasion). Needless to say, if trigone has been damaged, we must choose different urinary surgery (not simple closure).

Reply: Thank you for bringing to our attention the need to describe the relationship between the trigone and bladder injury, and the potential need for different urinary surgery in cases where the trigone has been damaged. In response, we have updated the description of the inadvertent cystotomy to specify that the injury was located at the bladder dome and that the trigone and ureters were not affected. We believe that this revised description helps to clarify the extent of the injury and the associated clinical implications, and we thank the reviewer for their helpful comment in improving the quality of our case report.

Changes in text: The sentence describing the inadvertent cystotomy now reads "Once the uterus was removed, a 10 cm inadvertent cystotomy was noted at the bladder dome, without injury to trigone or ureters."

Comment 6: Please state that the ureter was free from the damage.

Please see reply and changes in text in response to comment 5.

Comment 7: Do you agree with intentional cystotomy? Do you consider that intentional cystotomy (opening the bladder technique) might have prevented the present disaster?

Reply: We appreciate your thoughtful consideration of the possibility of intentional cystotomy as a preventive measure in this case. Although we did not make any changes to the manuscript in response to your comment, we did carefully consider the potential benefits of intentional cystotomy. While it is possible that an intentional cystotomy could have allowed for a more advantageous incision location, we felt it would be speculative to include this in our discussion given the uncertain nature of this possibility.

Comment 8: I believe that MTX is not used now after French study (MTX for placenta left in situ strategy) for term PAS. Some doctors may still use MTX but this might cause misunderstanding. There are number of reasons why we do not use MTX in this "late" gestation. There are abundant literatures regarding this.

Reply: Thank you for your valuable feedback. We appreciate your concern regarding the use of MTX for the treatment of PAS during gestation. We agree that the use of MTX during pregnancy is not recommended due to its teratogenic effects, and we have made changes to the manuscript to reflect this. Specifically, we have clarified our mention of MTX for the treatment of PAS as only suggested for postpartum therapy in cases where placental tissue is left in-situ. We believe that this clarification improves the quality of the case report by providing more accurate and up-to-date information on the use of MTX in the management of PAS.

Changes in text: the mention of MTX in the manuscript now reads "Some studies suggest utilizing adjuvant methotrexate post-partum when the placental tissue is left in-situ to increase the rate of placental absorption by decreasing trophoblast activity and placental vascularity (13)."