

OBSTETRICS & GYNECOLOGY



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- Comments from the reviewers and editors (email to author requesting revisions)
- Response from the author (cover letter submitted with revised manuscript)*

**The corresponding author has opted to make this information publicly available.*

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Questions about these materials may be directed to the *Obstetrics & Gynecology* editorial office:
obgyn@greenjournal.org.

Date: Mar 13, 2020
To: "Anna Beavis" [REDACTED]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-20-201

RE: Manuscript Number ONG-20-201

Recurrent Low Grade Endometrial Stromal Sarcoma Diagnosed 8 years after Laparoscopic Morcellation during Presumed Benign Hysterectomy: A Case Report

Dear Dr. Beavis:

Your manuscript has been reviewed by the Editorial Board and by special expert referees. Although it is judged not acceptable for publication in Obstetrics & Gynecology in its present form, we would be willing to give further consideration to a revised version.

If you wish to consider revising your manuscript, you will first need to study carefully the enclosed reports submitted by the referees and editors. Each point raised requires a response, by either revising your manuscript or making a clear and convincing argument as to why no revision is needed. To facilitate our review, we prefer that the cover letter include the comments made by the reviewers and the editor followed by your response. The revised manuscript should indicate the position of all changes made. We suggest that you use the "track changes" feature in your word processing software to do so (rather than strikethrough or underline formatting).

Your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Apr 03, 2020, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: Recurrent Low Grade Endometrial Stromal Sarcoma Diagnosed 8 years after Laparoscopic Morcellation during Presumed Benign Hysterectomy: A Case Report

The authors present a well written and researched case report of a case of recurrent LGESS in a patient who underwent morcellation for presumed benign leiomyomoma 8 years prior.

Please include in the manuscript the pathology of the robotically excised mass from behind the cecum (referring to figure 3). Was this also recurrent LGESS?

Page 7, lines 140-142: The authors suggest that preoperative EMB may help rule out malignancy. The author may consider including that in the case of mesenchymal tumors - emb is not sampling this tissue, so is of little benefit in this case. EMB is appropriate for endometrial based pathology, but a negative emb does not decrease the already low chance of LMS or other mesenchymal bases tumors. The authors also state that MRI improves the sensitivity and specificity of LMS detection. This statement does not have an associated reference, please include- and consider noting that the current ACOG committee opinion 770 states "Dynamic magnetic resonance imaging and lactate dehydrogenase isoenzyme testing have been suggested as diagnostic methods for leiomyosarcoma in the preoperative evaluation; however, the evidence for these methods is weak and based on limited clinical studies".

Reviewer #2: The authors made an interesting discovery on a case recurrent of undiagnosed LGESS pre-surgically after laparoscopic hysterectomy with morcellation on consideration of benign tumors. There are several shining points. The finding results of this paper did meet the impact and innovation criteria of this journal. The recurrent of neoplasm lesion of urine have been rarely been correlated to history of morcellation. With carefully re-reviewing on this case, highlighting of suspicion consideration after morcellation performance even with diagnosed benign tumor and additional assessment of tissue section so deserve more attention.

The paper is of great quality in presented work while being scientifically sound. The shape of this work is well written, well organized and understandable for nonspecialists. Several details may readers be curious are as follows,

1. It is not perfectly clear the diagnosis process before the hysterectomy procedure performing, is there any imaging

modality was applied? To what extent LGEES could be diagnosed ahead of treatment using various modality? From my understanding, this is crucial to make a verification that the misleading diagnosis is not likely to be complemented through other technique, which could have weaken the correlation between findings and conclusion in this work.

2. It is not clear of the details on how morcellation was performed? (e.g. time after diagnosis, particular site)

3. Did the pathological diagnosis re-reviewed in the same institution for a second time and compared with the first-hand result and another re-reviewed diagnosis in a tertiary medical center? What is the diagnosis experience of pathologists in authors' institution and tertiary center. The separation of working experience may be a great impact factor on the diagnosis results.

4. It is not clear on the pathology results of ovaries.

Reviewer #3: Thank you for your case report.

Your teaching points are valid. I would reword the second to remove reference to your case, make it more general.

Lines 56-62: I would include one sentence commenting on this discrepancy (why the first estimate was falsely high)

In your case and discussion it is not clear if the original provider and or pathologist was clear that the diagnosis of "cellular leiomyoma" was interpreted as needing further evaluation. It might be useful to indicate if the pathology report made clear that this was not a regular finding, as a generalist might not know that. As always, hind sight is 20/20, how likely is this truly to be missed on morcellated specimen, and are there other cases such as this reported?

I would include up front in the case that you do not have indication of whether endometrial sampling was done prior to hysterectomy. While MRI may not be standard of care prior to hysterectomy, endometrial sampling in a 49 yo with abnormal menses or menorrhagia is. I would also add into the discussion how likely is this type of tumor to be picked up on sampling.

EDITOR'S COMMENTS:

We no longer require that authors adhere to the Green Journal format with the first submission of their papers. However, any revisions must do so. I strongly encourage you to read the instructions for authors (the general bits as well as those specific to the feature-type you are submitting). The instructions provide guidance regarding formatting, word and reference limits, authorship issues, and other things. Adherence to these requirements with your revision will avoid delays during the revision process, as well as avoid re-revisions on your part in order to comply with the formatting.

Line 25: not sure this is a true statement. What is the risk of dissemination if there is an undiagnosed malignancy? There is an overall minimal risk (according to most but not all people) since the rate of undiagnosed uterine malignancies in women undergoing morcellation is low, but in the presence of such a disease (which is the way you've written the background statement) do we know what the rate of dissemination is and that it is "minimal"?

Line 33: Was the diagnosis of LGEES dependent on matching the findings in the 2 specimens (as you have written) or could the pathology on the pelvic mass treated 8 years after her hysterectomy been enough to make the diagnosis? I just want you to be really clear in your wording. Maybe what you mean is "Therefore, a diagnosis of low grade endometrial stromal sarcoma present at the time of hysterectomy and recurrent at the current surgery was made"? Or something like that.

Teaching point 1: maybe "which MAY prevent adequate...." Also, were there features originally for smooth muscle or endometrial stromal neoplasm? If not, would an expert path review/second opinion been called for in your case?

Teaching point 2: Delete "this case also highlights". Just state the teaching point. "In women with a pelvic mass or intra-abdominal metastasis and a history of uterine morcellation, maintain a high index of suspicion for recurrent disease of a previously undiagnosed uterine malignancy" or something similar.

Line 48: I recommend a change here. . If the only issue were the potential spread of occult disease, there would be no controversy. The controversy as I understand it is that this risk has to be balanced against the relative infrequency of such occult tumors, the inability to diagnosis stromal sarcoma reliably without a tissue sample, and the benefit for many women who would be candidates for morcellation and MIGS procedures related to operative morbidity with open procedures. Perhaps your opening statement could provide this type of description of the controversy?

Line 53: As there are some who believe a risk of 2-3/1000 is not "exceedingly low", please just report the numbers without the qualifiers.

Lines 76-87: she's had 2 MRI, a CT and Ultrasound. Wow. What information (either positive or negative) was obtained by any of the imaging done after the original MRI that influenced her care? Please comment in the discussion section.

Line 88: was this just a diagnostic laparoscopy? Seems to me, it was a therapeutic procedure.

111: was this the differential diagnosis on re-review of the slides or on the original interpretation?:

Line 172: Are these tumors hormone dependent? Is that why recurrence would be decreased if oophorectomy had occurred? What about the role of endometriosis?

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:

- A. OPT-IN: Yes, please publish my point-by-point response letter.
- B. OPT-OUT: No, please do not publish my point-by-point response letter.

2. As of December 17, 2018, Obstetrics & Gynecology has implemented an "electronic Copyright Transfer Agreement" (eCTA) and will no longer be collecting author agreement forms. When you are ready to revise your manuscript, you will be prompted in Editorial Manager (EM) to click on "Revise Submission." Doing so will launch the resubmission process, and you will be walked through the various questions that comprise the eCTA. Each of your coauthors will receive an email from the system requesting that they review and electronically sign the eCTA.

Please check with your coauthors to confirm that the disclosures listed in their eCTA forms are correctly disclosed on the manuscript's title page.

3. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric and gynecology data definitions at <https://www.acog.org/About-ACOG/ACOG-Departments/Patient-Safety-and-Quality-Improvement/reVITALize>. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

4. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Case Reports should not exceed 8 typed, double-spaced pages (2,000 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and print appendixes) but exclude references.

5. Titles in Obstetrics & Gynecology are limited to 100 characters (including spaces). Do not structure the title as a declarative statement or a question. Introductory phrases such as "A study of..." or "Comprehensive investigations into..." or "A discussion of..." should be avoided in titles. Abbreviations, jargon, trade names, formulas, and obsolete terminology also should not be used in the title. Titles should include "A Randomized Controlled Trial," "A Meta-Analysis," or "A Systematic Review," as appropriate, in a subtitle. Otherwise, do not specify the type of manuscript in the title.

6. Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines:

- * All financial support of the study must be acknowledged.
- * Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
- * All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your response in the journal's electronic author form verifies that permission has been obtained from all named persons.
- * If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting).

7. The most common deficiency in revised manuscripts involves the abstract. Be sure there are no inconsistencies between the Abstract and the manuscript, and that the Abstract has a clear conclusion statement based on the results found in the paper. Make sure that the abstract does not contain information that does not appear in the body text. If you submit a revision, please check the abstract carefully.

In addition, the abstract length should follow journal guidelines. The word limits for different article types are as follows: Case Reports, 125 words. Please provide a word count.

8. Only standard abbreviations and acronyms are allowed. A selected list is available online at <http://edmgr.ovid.com/ong/accounts/abbreviations.pdf>. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

9. The journal does not use the virgule symbol (/) in sentences with words. Please rephrase your text to avoid using "and/or," or similar constructions throughout the text. You may retain this symbol if you are using it to express data or a measurement.

10. Figures

Figures 1–3: Files are corrupted. Please upload new versions of these figures.

Figure 2: Please upload a version without the A–D labels. These will be added back per journal style.

11. Authors whose manuscripts have been accepted for publication have the option to pay an article processing charge and publish open access. With this choice, articles are made freely available online immediately upon publication. An information sheet is available at <http://links.lww.com/LWW-ES/A48>. The cost for publishing an article as open access can be found at <http://edmgr.ovid.com/acd/accounts/ifauth.htm>.

Please note that if your article is accepted, you will receive an email from the editorial office asking you to choose a publication route (traditional or open access). Please keep an eye out for that future email and be sure to respond to it promptly.

12. If you choose to revise your manuscript, please submit your revision through Editorial Manager at <http://ong.editorialmanager.com>. Your manuscript should be uploaded in a word processing format such as Microsoft Word. Your revision's cover letter should include the following:

- * A confirmation that you have read the Instructions for Authors (<http://edmgr.ovid.com/ong/accounts/authors.pdf>), and
- * A point-by-point response to each of the received comments in this letter.

If you submit a revision, we will assume that it has been developed in consultation with your co-authors and that each author has given approval to the final form of the revision.

Again, your paper will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by Apr 03, 2020, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Nancy C. Chescheir, MD
Editor-in-Chief

2018 IMPACT FACTOR: 4.965
2018 IMPACT FACTOR RANKING: 7th out of 83 ob/gyn journals

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: <https://www.editorialmanager.com/ong/login.asp?a=r>). Please contact the publication office if you have any questions.

Dr. Nancy C. Chescheir
Editor-in-Chief
Obstetrics & Gynecology

March 30th, 2020

Dear Dr. Chescheir,

Please find our revised case report manuscript, entitled “Low Grade Endometrial Stromal Sarcoma Diagnosed 8 years after Hysterectomy with Morcellation” for your consideration for publication in *Obstetrics and Gynecology*. I

We confirm that we have reviewed the Instructions for Authors and have made appropriate edits to our original submission in line with these instructions. The total word count is 1998; the word count for the abstract is 124.

We have reviewed and appreciate the thoughtful comments provided by the reviewers and editor. A detailed point-by-point response can be found in the following pages.

We would like to opt in for publication of our point-by-point response letter.

This revision has been developed in consultation with the co-authors and each author confirms their approval of the final form of the revision. The lead author, Anna Beavis, affirms that this manuscript is an honest, accurate, and transparent account of the case being reported, and that no important aspects of the case have been omitted.

We re-affirm that this manuscript is not being considered for publication by any other journal, nor has it been presented at any scientific meetings. All authors listed have contributed significantly to the drafting of this report. We have no conflicts of interest to disclose.

Per Johns Hopkins Medicine Institutional Review Board (IRB) policy 102.3 regarding single case reports, no IRB review was required for this report. Written informed consent was obtained from the patient featured in the report, and has been filed to our records. Additionally, the patient was given the opportunity to review and provide feedback on the manuscript.

Thank you kindly for your consideration. We look forward to your correspondence.


Sincerely,



Anna Beavis, MD, MPH

Assistant Professor, Johns Hopkins Medicine

The Kelly Gynecologic Oncology Service, Department of Gynecology and Obstetrics



Reviewer #1: *Recurrent Low Grade Endometrial Stromal Sarcoma Diagnosed 8 years after Laparoscopic Morcellation during Presumed Benign Hysterectomy: A Case Report*

Reviewer comment #1:

The authors present a well written and researched case report of a case of recurrent LGESS in a patient who underwent morcellation for presumed benign leiomyomoma 8 years prior. Please include in the manuscript the pathology of the robotically excised mass from behind the cecum (referring to figure 3). Was this also recurrent LGESS?

Author response:

Yes, this was diagnosed as metastatic LGESS. This has been added to line 113; additionally, we updated the duration for which she has now been without evidence of disease (line 114).

Reviewer comment #2:

Page 7, lines 140-142: The authors suggest that preoperative EMB may help rule out malignancy. The author may consider including that in the case of mesenchymal tumors - emb is not sampling this tissue, so is of little benefit in this case. EMB is appropriate for endometrial based pathology, but a negative emb does not decrease the already low chance of LMS or other mesenchymal bases tumors.

Author response:

The reviewer's point on the decreased utility of endometrial sampling in identifying uterine sarcomas is well taken. The authors believe there could be some utility in endometrial biopsy, and recognize that the literature is sparse and not consistent: studies range in their sensitivity from 38% (Leibsohn et al, AJOG, 1990; PMID 2327466) to 84% (Bansal et al, Gynecol Oncol, 2008; PMID 18445505).

We did attempt to highlight the lack of good preoperative test in our original statement: "A careful preoperative work-up with endometrial sampling and imaging may help rule out malignancy; however, endometrial sampling has been shown to have a lower predictive value for uterine sarcomas compared to epithelial malignancies."

However, in response to the reviewer's comment we have changed this wording to highlight the lower sensitivity endometrial biopsy to diagnose sarcomas: Preoperative endometrial sampling and imaging can help rule out epithelial malignancy; however, endometrial sampling is not as sensitive or specific for mesenchymal malignancies" (lines 122-123).

Reviewer #2 comment:

The authors also state that MRI improves the sensitivity and specificity of LMS detection. This statement does not have an associated reference, please include- and consider noting that the current ACOG committee opinion 770 states "Dynamic magnetic resonance imaging and lactate dehydrogenase isoenzyme testing have been suggested as diagnostic methods for leiomyosarcoma in the preoperative evaluation; however, the evidence for these methods is weak and based on limited clinical studies".

Author response:

Due to the reference limitations of the case report format, we could not include multiple references for this statement. The review article by Ricci et al, 2017 is now referenced, which includes a review of several studies evaluating the utility of contrast-enhanced MRI. However, as ACOG notes, these are small studies. Therefore, we have changed the sentence to the following to be more in line with ACOG's perspective: "Additionally, while small studies suggest contrast-enhanced MRI might improve detection of leiomyosarcoma, the overall data is weak and is particularly lacking for low-grade lesions such as LGESS" (lines 123-125).

Reviewer #2

The authors made an interesting discovery on a case recurrent of undiagnosed LGESS presurgically after laparoscopic hysterectomy with morcellation on consideration of benign tumors. There are several shining points. The finding results of this paper did meet the impact and innovation criteria of this journal. The recurrent of neoplasm lesion of urine have been rarely been correlated to history of morcellation. With carefully re-reviewing on this case, highlighting of suspicion consideration after

morcellation performance even with diagnosed benign tumor and additional assessment of tissue section so deserve more attention.

The paper is of great quality in presented work while being scientifically sound. The shape of this work is well written, well organized and understandable for nonspecialists. Several details may readers be curious are as follows,

Reviewer #2 comment:

It is not perfectly clear the diagnosis process before the hysterectomy procedure performing, is there any imaging modality was applied? To what extent LGESS could be diagnosed ahead of treatment using various modality? From my understanding, this is crucial to make a verification that the misleading diagnosis is not likely to be complemented through other technique, which could have weaken the correlation between findings and conclusion in this work.

Author response:

Unfortunately, because the patient was not seen at our institution until her recurrence was diagnosed, we were unable to obtain the preoperative records including if any imaging or biopsy was performed. The initial hysterectomy was performed in 2011 at a community hospital. Records obtained from that episode of care did not contain evidence of preoperative endometrial sampling or magnetic resonance imaging (MRI). This has been clarified in lines 69-70. While an endometrial biopsy could have been helpful in diagnosing an endometrial malignancy, the sensitivity and specificity of biopsy are significantly lower for the detection of mesenchymal tumors, including low grade endometrial stromal sarcoma (see lines 123-124).

We believe that the key learning point from the case report is not that preoperative workup would have led to the diagnosis of malignancy preoperatively, but that once the specimen was morcellated, an accurate diagnosis very difficult to make due to the lack of tumor-myoetrial interface.

Reviewer #2 comment:

It is not clear of the details on how morcellation was performed? (e.g. time after diagnosis, particular site)

Author response:

The information about the original hysterectomy was obtained from the operative report from the outside institution. Per the operative report, after attempted delivery of the uterus through the vagina, the solitary large uterine fibroid was too large to be delivered through the vagina; therefore the surgeon stated that “the morcellator was placed in the right lower quadrant port and the fibroid was morcellated until it was small enough to remove through the vagina”. Though the exact term “power morcellator” is not stated, it is most likely what was used. Edits were made to lines 71-73 to clarify this.

Reviewer #2 comment:

Did the pathological diagnosis re-reviewed in the same institution for a second time and compared with the first-hand result and another re-reviewed diagnosis in a tertiary medical center? What is the diagnosis experience of pathologists in authors' institution and tertiary center. The separation of working experience may be a great impact factor on the diagnosis results.

Author response:

We agree that the level of expertise of the pathologist likely played a role in the original diagnosis.

The initial hysterectomy specimen was reviewed at a community hospital at the time of hysterectomy, where it was performed.

When the adnexal mass was discovered 8 years later, the patient sought care at Johns Hopkins Hospital, tertiary care center with expert gynecologic pathologists. After the first debulking surgery, the original histologic slides from the hospital where the hysterectomy was performed were requested so that the tissue could be compared between the newly resected masses and the original hysterectomy specimen by the expert gynecologic pathologists at Johns Hopkins Hospital.

The newly resected masses were consistent with a diagnosis of LGESS, however, due to the lack of tumor-myoetrial interface, and therefore, necessity to infer a diagnosis of LGESS on hysterectomy slides, both pathology cases were then sent to a second tertiary care center also with expert gynecologic pathologists (Memorial Sloan Kettering Hospital) to obtain consensus.

We have clarified this in lines 68, 89, 103-109.

Reviewer #2 comment:

It is not clear on the pathology results of ovaries.

Author response:

The ovaries were benign and unremarkable; this has been added to line 90.

Reviewer #3

Reviewer #3 comment:

Thank you for your case report. Your teaching points are valid. I would reword the second to remove reference to your case, make it more general.

Author response:

Thank you for the suggestion. Teaching point 2 has been edited as suggested. (see lines 47-48).

Reviewer #3 comment:

Lines 56-62: I would include one sentence commenting on this discrepancy (why the first estimate was falsely high)

Author response:

Critics of the FDA estimates highlight the poor quality of studies included their calculations; many of the studies were retrospective, and they included a case report, non-peer-reviewed reports, and excluded studies where final pathology was negative for malignancy which all contributed to the overestimated risk of occult malignancy. (Parker et al., 2016). The text has been edited to reflect this, lines 58-60.

Reviewer #3 comment:

In your case and discussion it is not clear if the original provider and or pathologist was clear that the diagnosis of "cellular leiomyoma" was interpreted as needing further evaluation. It might be useful to indicate if the pathology report made clear that this was not a regular finding, as a generalist might not know that. As always, hind sight is 20/20, how likely is this truly to be missed on morcellated specimen, and are there other cases such as this reported?

Author response:

The pathology report from 2011 indicated that the histology was a cellular leiomyoma with no evidence of cellular atypia. No explicit recommendation was made for further evaluation by the pathologist or the gynecologist. "Without atypia" added to pathology description in the case in lines 78.

A cellular leiomyoma and endometrial stromal tumors are differentiated based on tumor-myometrial interface and immunohistochemical (IHC) stains (if needed) (described in lines 136-139). A cellular leiomyoma is considered benign and no further follow-up would be recommended. However, it is critical to differentiate a cellular leiomyoma from a low grade endometrial stromal sarcoma. A general surgical pathologist may be unaccustomed to the subtle morphologic differences and additional work up (IHC stains or additional tissue sections looking for tumor-myometrial interface). This point is described in lines 141-142.

Our understanding from our review of the literature and talking with pathologists is that this is very rare and as such, we have not encountered other cases that have reported this.

Reviewer #3 comment:

I would include up front in the case that you do not have indication of whether endometrial sampling was done prior to hysterectomy. While MRI may not be standard of care prior to hysterectomy, endometrial sampling in a 49 yo with abnormal menses or menorrhagia is. I would also add into the discussion how likely is this type of tumor to be picked up on sampling.

Author response: The case presentation has been updated to reflect lack of evidence of endometrial sampling prior to the hysterectomy, lines 69-70; while this tumor can be detected on endometrial sampling, the sensitivity and specificity are lower than for that of endometrial neoplasms (see lines 122-123).

EDITOR'S COMMENTS:

We no longer require that authors adhere to the Green Journal format with the first submission of their papers. However, any revisions must do so. I strongly encourage you to read the instructions for authors (the general bits as well as those specific to the feature-type you are submitting). The instructions provide

guidance regarding formatting, word and reference limits, authorship issues, and other things. Adherence to these requirements with your revision will avoid delays during the revision process, as well as avoid rerevisions on your part in order to comply with the formatting.

Author response: Thank you, we have updated the document as specified in the instructions for authors, including revising the title to be <100 characters with spaces and the 2,000 word limit. All authors included in the submitted manuscript meet ICMJE criteria for authorship.

Editor comment:

Line 25: not sure this is a true statement. What is the risk of dissemination if there is an undiagnosed malignancy? There is an overall minimal risk (according to most but not all people) since the rate of undiagnosed uterine malignancies in women undergoing morcellation is low, but in the presence of such a disease (which is the way you've written the background statement) do we know what the rate of dissemination is and that it is "minimal"?

Author response:

We appreciate this comment, and highlighting the nuance of the statement. The background statement has been re-worded to better reflect our intended meaning, and now reads "Morcellation at the time of minimally invasive hysterectomy or myomectomy for presumed benign indications carries a risk of disseminating undiagnosed uterine malignancies" (lines 31-33).

To answer the editor's question, in morcellated occult uterine malignancies, the rate of dissemination is 64% according to a retrospective study by Seidman et al. at Brigham Women's Hospital (Seidman et al., 2012). We would agree this is not minimal.

Editor comment:

Line 33: Was the diagnosis of LGEES dependent on matching the findings in the 2 specimens (as you have written) or could the pathology on the pelvic mass treated 8 years after her hysterectomy been enough to make the diagnosis? I just want you to be really clear in your wording. Maybe what you mean is "Therefore, a diagnosis of low grade endometrial stromal sarcoma present at the time of hysterectomy and recurrent at the current surgery was made"? Or something like that.

Author response:

Yes, you are correct- the diagnosis of LGEES was dependent upon comparison of the findings in the 2 specimens. As endometrial stromal tumors mainly arise from endometrial stroma, a primary uterine endometrial stromal tumor should be confirmed before making a diagnosis of extra-uterine recurrence. This was a very difficult and fraught decision amongst the physicians caring for this patient and the pathologists determining her diagnosis. However, based on the clinical behavior, morphologic and immunohistochemical profile (complicated by the absence of tumor-myometrial interface) the tumor was diagnosed as a LGEES in the hysterectomy and the recurrent surgical specimens. Thank you for your suggestion, we have edited to clarify in lines 103-109.

Editor comment:

Teaching point 1: maybe "which MAY prevent adequate...." Also, were there features originally for smooth muscle or endometrial stromal neoplasm? If not, would an expert path review/second opinion been called for in your case?

Author response:

We have edited teaching point to include "may prevent."

The original pathology was diagnosed as a cellular leiomyoma, indicating a smooth muscle neoplasm which was not typical of a classic leiomyoma in appearance. Cellular leiomyomas must be differentiated from LGEES because of the similarities of their histologic appearance, and the extreme difference in their clinical characteristics (benign and malignant, respectively). We believe it would be reasonable to obtain an expert gynecologic review of any morcellated cellular leiomyoma or leiomyoma with concerning features, and should prompt submission of additional tissue for additional histologic review (see lines 140-142).

Editor comment:

Teaching point 2: Delete “this case also highlights”. Just state the teaching point. “In women with a pelvic mass or intra-abdominal metastasis and a history of uterine morcellation, maintain a high index of suspicion for recurrent disease of a previously undiagnosed uterine malignancy” or something similar.

Author response:

Teaching point 2 has been edited to incorporate editor’s suggestions (lines 47-48)

Editor comment:

Line 48: I recommend a change here. If the only issue were the potential spread of occult disease, there would be no controversy. The controversy as I understand it is that this risk has to be balanced against the relative infrequency of such occult tumors, the inability to diagnosis stromal sarcoma reliably without a tissue sample, and the benefit for many women who would be candidates for morcellation and MIGS procedures related to operative morbidity with open procedures. Perhaps your opening statement could provide this type of description of the controversy?

Author response:

We appreciate the recommendation, and have reworded the first few sentences to reflect your suggestions. “Uterine morcellation is a controversial topic: it provides many women significant benefit in terms of operative morbidity, but has the potential to spread occult uterine malignancy. In women with large uteri, morcellation as part of minimally invasive surgery has many benefits compared to open surgery: shorter hospital stays, faster recovery times, fewer complications and re-admissions, and lower postoperative mortality¹. Unfortunately, the potential for morcellation to allow peritoneal spread of undiagnosed malignancies is particularly problematic for stromal malignancies, for which there is no reliable preoperative test¹.” (lines 49-55)

Editor comment:

Line 53: As there are some who believe a risk of 2-3/1000 is not “exceedingly low”, please just report the numbers without the qualifiers.

Author response:

This has been edited to remove qualifier (line 57)

Editor comment:

Lines 76-87: she’s had 2 MRI, a CT and Ultrasound. Wow. What information (either positive or negative) was obtained by any of the imaging done after the original MRI that influenced her care? Please comment in the discussion section.

Author response:

The imaging was done over a period of appropriately 8 months. The initial MRI was for back pain, and the adnexal mass was an incidental finding in that process – this MRI was suboptimal for the characterization of the location of the mass and was not available for review when she presented for a second opinion. The follow up pelvic ultrasounds were performed as part of nonsurgical surveillance over several months. By the time she presented to our clinic, she had had no imaging in several months; the CT was ordered to rule out metastatic disease given the elevated CA 125 and known adnexal mass, as is standard prior to surgery for a suspected malignancy. Then, because the CT scan expectedly was concerning for rectal involvement and was not ovarian in origin, an MRI to better characterize the mass’s location with relation to the rectum and vaginal cuff was performed for surgical planning including consenting the patient preoperatively for rectal resection. We have edited the case to clarify, see lines 74-82. Due to word count limits, additional discussion was not included as we hope the changes demonstrate the reasoning behind each of the imaging tests.

Editor comment:

Line 88: was this just a diagnostic laparoscopy? Seems to me, it was a therapeutic procedure.

Author response:

After laparoscopy confirmed the presence of a mass which was adherent to the rectum, we proceeded with exploratory laparotomy to complete the low anterior resection as described – this has been clarified in lines 82.

The term diagnostic has been removed as some dissection was attempted prior to the conversion to open procedure.

Editor comment:

Line 111: was this the differential diagnosis on re-review of the slides or on the original interpretation?:

Author response:

This differential was based on the specimen from re-review of the hysterectomy slides (edited in lines 104-106). This differential diagnosis was not present on the original pathology report.

Editor comment:

Line 172: Are these tumors hormone dependent? Is that why recurrence would be decreased if oophorectomy had occurred? What about the role of endometriosis?

Author response:

Yes, these tumors are estrogen sensitive, which is why the chance of recurrence is higher with the ovaries left in situ. We have added clarification to this in lines 144-45 and 151-152. The role of the endometriosis in this case is not clear.

EDITORIAL OFFICE COMMENTS:

1. The Editors of Obstetrics & Gynecology are seeking to increase transparency around its peer-review process, in line with efforts to do so in international biomedical peer review publishing. If your article is accepted, we will be posting this revision letter as supplemental digital content to the published article online. Additionally, unless you choose to opt out, we will also be including your point-by-point response to the revision letter. If you opt out of including your response, only the revision letter will be posted. Please reply to this letter with one of two responses:

A. OPT-IN: Yes, please publish my point-by-point response letter.

Author response: we have opted in, as indicated in the cover letter.

B. OPT-OUT: No, please do not publish my point-by-point response letter.

2. As of December 17, 2018, Obstetrics & Gynecology has implemented an "electronic Copyright Transfer Agreement" (eCTA) and will no longer be collecting author agreement forms. When you are ready to revise your manuscript, you will be prompted in Editorial Manager (EM) to click on "Revise Submission." Doing so will launch the resubmission process, and you will be walked through the various questions that comprise the eCTA. Each of your coauthors will receive an email from the system requesting that they review and electronically sign the eCTA. Please check with your coauthors to confirm that the disclosures listed in their eCTA forms are correctly disclosed on the manuscript's title page.

3. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric and gynecology data definitions at <https://www.acog.org/About-ACOG/ACOG-Departments/Patient-Safety-and-Quality-Improvement/reVITALize>. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

4. Because of space limitations, it is important that your revised manuscript adhere to the following length restrictions by manuscript type: Case Reports should not exceed 8 typed, double-spaced pages (2,000 words). Stated page limits include all numbered pages in a manuscript (i.e., title page, précis, abstract, text, references, tables, boxes, figure legends, and print appendixes) but exclude references.

Author response: the resubmitted manuscript is 1998 words including all numbered pages minus the references.

5. Titles in Obstetrics & Gynecology are limited to 100 characters (including spaces). Do not structure the title as a declarative statement or a question. Introductory phrases such as "A study of..." or "Comprehensive investigations into..." or "A discussion of..." should be avoided in titles. Abbreviations, jargon, trade names, formulas, and obsolete terminology also should not be used in the title. Titles should include "A Randomized Controlled Trial," "A Meta-Analysis," or "A Systematic Review," as appropriate, in a subtitle. Otherwise, do not specify the type of manuscript in the title.

Author response: the title has been altered to meet these regulations.

6. *Specific rules govern the use of acknowledgments in the journal. Please note the following guidelines:*

** All financial support of the study must be acknowledged.*

** Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.*

** All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your response in the journal's electronic author form verifies that permission has been obtained from all named persons.*

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In addition, the abstract length should follow journal guidelines. The word limits for different article types are as follows: Case Reports, 125 words. Please provide a word count.

Author response: The word count for our abstract is: 124

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10. *Figures*

Figures 1–3: Files are corrupted. Please upload new versions of these figures.

Author response: these have been uploaded

Figure 2: Please upload a version without the A–D labels. These will be added back per journal style.

Author response: this has been uploaded.

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** A point-by-point response to each of the received comments in this letter.*

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