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.*

Personal or nonessential information may be redacted at the editor's discretion.

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

Date: Aug 08, 2019
To: "Angela B Lu" [redacted]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-19-1249

RE: Manuscript Number ONG-19-1249

Pregnancy Prolongation Following Eculizumab Use in Early-Onset Preeclampsia: A Case Report

Dear Dr. Lu:

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 Aug 29, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: This is a case report that describes a pregnancy affected by atypical hemolytic uremic syndrome at 22 weeks and development of preeclampsia at 24 weeks. Eculizumab was given to treat the aHUS from weeks 22-26 and an improvement in the platelet count was noted, although ongoing blood transfusions were required. She developed worsening of preeclampsia and was delivered at 27 weeks gestation.

The case report is well-written and provides an excellent description of the timeline of care and methods of diagnosis. I have a few minor suggestions:

Line 71: I was unfamiliar with the term "blood film". Consider using the term "peripheral smear".

Lines 76, 86, 90, 112, and 130: Consider using or including the units of mg/dL for haptoglobin, creatinine, and urea.

Line 80: I am unfamiliar with the term "biophysically active". Consider using another terminology.

Lines 128-131: It was not clear to me when her hemoglobin stabilized at 9.0 g/dL or when she progressed to end-stage renal failure and commenced peritoneal dialysis. Did this all occur at the 1 year mark? Is there any further follow-up on her current status?

Was any treatment delayed due to pregnancy? If so, did prolongation of the pregnancy potentially affect long term maternal health?

Reviewer #2: Review of ONG-19-1249

The case report entitled, "Pregnancy prolongation following Eculizamab use in early-onset preeclampsia: A case report" by Lu et al describes a single case of a patient that first diagnosed with atypical hemolytic uremic syndrome at 22 weeks followed by early onset preeclampsia at 24 weeks. I have the following questions and comments.

The patient was diagnosed with atypical hemolytic uremic syndrome just 2 weeks before being diagnosed with early-onset preeclampsia, presumably because she was not hypertensive at 22 weeks, but became so at 24 weeks. It seem possible that the patient actually had preeclampsia with severe features or atypical HELLP syndrome at 22 weeks. A notable

percentage of patient with HELLP syndrome will be normotensive on initial presentation, but go on to develop hypertension later. This possibility should be discussed in the Comment section.

The authors report that the patient's platelet count improved after administration of eculizamab, but did not report if the patient's renal function improved or worsened during that same time period. As thrombocytopenia and decrease renal function are features of both HUS and preeclampsia with severe features/HELLP syndrome it is necessary to understand the trend of her renal function to fully understand if eculizamab actually help prolonged her pregnancy.

The changes in s-Flt and PlGF after administration of eculizamab are important to the author's claim that the medication help prolong her pregnancy. However, they are not mentioned until the comment section. I understand that these values are not used to guide clinical care, but including these values in the Case section would be helpful to put the patient's clinical course in the proper perspective.

Although the Eculizamab does seem to have improved several of her lab values, there is insufficient evidence to conclude causation. The authors' claims about Eculizamab prolonging the patient's pregnancy are too strongly worded based on the evidence provided in this case report.

Reviewer #3: The authors present a case report of a pregnancy affected by microangiopathic hemolytic anemia and early onset preeclampsia that was successfully prolonged using Eculizumab.

The following items should be addressed:
1. The authors chose to begin aspirin for preeclampsia prevention in this patient who was already >20 weeks, and had thrombocytopenia. Please discuss this further.

2. Please discuss further the diagnosis of superimposed preeclampsia; how did the authors determine that the elevation in blood pressure noted at 24 weeks gestation was not a consequence of her MAHA and renal involvement?

3. Did the patient undergo testing for antiphospholipid antibody syndrome?

4. Why were the authors collecting SFLT and PGIF levels at 21 weeks before her blood pressure rose, were there concerns about preeclampsia then as well?

EDITOR 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

Figure 1: Current file may be resubmitted as-is.

Figure 2: Please upload a high resolution version of this figure. We recommend using the original figure file (eps, tiff, jpeg, etc.) rather than Word.

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 Aug 29, 2019, 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

August 12, 2019

RE: Resubmission of manuscript *Pregnancy Prolongation Following Eculizumab Use in Early-Onset Preeclampsia: A Case Report*, ONG-19-1249

Prof Nancy C. Chescheir,
Editor-in-Chief
Obstetrics & Gynecology
409 12th Street, SW
Washington, DC 20024-2188

Dear Prof Chescheir,

Thank you for the opportunity to revise our manuscript, *Pregnancy Prolongation Following Eculizumab Use in Early-Onset Preeclampsia: A Case Report*. We appreciate the careful review and constructive suggestions, and believe our manuscript is improved with the suggested edits. We thank the reviewers for their time.

Following this letter are the editor and reviewer comments with our responses in italics, including how and where the text was modified. Changes in the manuscript are marked using track changes. The revision has been developed in consultation with all co-authors, and each author has given approval to the final form of this revision.

Thank you for your consideration.

Sincerely yours,

Angela B. Lu, MBBS

REVIEWER COMMENTS

Reviewer #1

This is a case report that describes a pregnancy affected by atypical hemolytic uremic syndrome at 22 weeks and development of preeclampsia at 24 weeks. Eculizumab was given to treat the aHUS from weeks 22-26 and an improvement in the platelet count was noted, although ongoing blood transfusions were required. She developed worsening of preeclampsia and was delivered at 27 weeks gestation.

The case report is well-written and provides an excellent description of the timeline of care and methods of diagnosis. I have a few minor suggestions:

- Line 71: I was unfamiliar with the term "blood film". Consider using the term "peripheral smear".
  "Blood film" has been amended to "peripheral smear".

- Lines 76, 86, 90, 112, and 130: Consider using or including the units of mg/dL for haptoglobin, creatinine, and urea.
  These units have been modified as requested.

- Line 80: I am unfamiliar with the term "biophysically active". Consider using another terminology.
  This has been modified from "a biophysically active fetus" to "an active fetus".

- Lines 128-131: It was not clear to me when her hemoglobin stabilized at 9.0 g/dL or when she progressed to end-stage renal failure and commenced peritoneal dialysis. Did this all occur at the 1 year mark? Is there any further follow-up on her current status? Was any treatment delayed due to pregnancy? If so, did prolongation of the pregnancy potentially affect long term maternal health?
  Thank you for these observations. We have clarified the patient's postpartum timeline at lines 140-151, and updated this as she has commenced workup for renal transplantation since the initial manuscript submission.
  No treatment was delayed due to pregnancy. We have clarified at lines 85-86 that termination of pregnancy was also offered as an option. At each stage of diagnosis thereafter, the patient was managed with the best available treatment i.e. symptom control initially, eculizumab for aHUS and antihypertensives for preeclampsia.
  It is not possible to determine whether prolongation of pregnancy affected the patient's long-term health. However, given she clinically and biochemically appeared to improve and stabilize on eculizumab, we suggest that her ongoing pregnancy may not have impacted on her long-term outcome.

Reviewer #2

The case report entitled, "Pregnancy prolongation following Eculizamab use in early-onset preeclampsia: A case report" by Lu et al describes a single case of a patient that first diagnosed

with atypical hemolytic uremic syndrome at 22 weeks followed by early onset preeclampsia at 24 weeks. I have the following questions and comments.

The patient was diagnosed with atypical hemolytic uremic syndrome just 2 weeks before being diagnosed with early-onset preeclampsia, presumably because she was not hypertensive at 22 weeks, but became so at 24 weeks. It seem possible that the patient actually had preeclampsia with severe features or atypical HELLP syndrome at 22 weeks. A notable percentage of patient with HELLP syndrome will be normotensive on initial presentation, but go on to develop hypertension later. This possibility should be discussed in the Comment section.
We agree with the reviewer's suggestions. The differential diagnosis between aHUS and HELLP syndrome may be very challenging as the two conditions may be part of a spectrum. At lines 157-158, we have added a definition for atypical preeclampsia. We have also included a further discussion of the differential diagnoses at various stages of this case, including an atypical preeclampsia initially presenting without hypertension, at lines 166-173.

The authors report that the patient's platelet count improved after administration of eculizamab, but did not report if the patient's renal function improved or worsened during that same time period. As thrombocytopenia and decrease renal function are features of both HUS and preeclampsia with severe features/HELLP syndrome it is necessary to understand the trend of her renal function to fully understand if eculizamab actually help prolonged her pregnancy.
Thank you for your observations. We have added the following sentence at lines 109-110 to clarify the trend of her renal function following the commencement of eculizumab therapy: "Her renal function improved, and stabilized (creatinine 0.8 mg/dL, urea 60 mg/dL,)."

The changes in s-Flt and PlGF after administration of eculizamab are important to the author's claim that the medication help prolong her pregnancy. However, they are not mentioned until the comment section. I understand that these values are not used to guide clinical care, but including these values in the Case section would be helpful to put the patient's clinical course in the proper perspective.
We acknowledge that the s-Flt and PlGF trends are useful in understanding the patient's clinical course. We have now included the values for this analysis in the Case section, from lines 136-139. Placement of the findings here reflects the availability of the results postpartum, where they did not impact on the clinical decision making antenatally.

Although the eculizamab does seem to have improved several of her lab values, there is insufficient evidence to conclude causation. The authors' claims about eculizamab prolonging the patient's pregnancy are too strongly worded based on the evidence provided in this case report.

We agree with the reviewer's comments and have tried to use language throughout the manuscript that reflects the lack of evidence available to imply causality. We state that eculizumab 'may' contribute to pregnancy prolongation (lines 25, 36, 42-43, 55-57, 180). Phrases like "suggesting potential benefit of eculizumab in preeclampsia" (line 205) highlight that there may be a causal link, but that conclusions need to be drawn carefully. The conclusion of the Comment also acknowledges that "further research into the role of eculizumab in preeclampsia is needed to investigate its efficacy and long-term safety." (lines 207-208).

Reviewer #3

The authors present a case report of a pregnancy affected by microangiopathic hemolytic anemia and early onset preeclampsia that was successfully prolonged using Eculizumab.

The following items should be addressed:

1. The authors chose to begin aspirin for preeclampsia prevention in this patient who was already >20 weeks, and had thrombocytopenia. Please discuss this further.
   At presentation, the patient was considered high-risk for preeclampsia due to her type 1 diabetes, particularly due to her known renal manifestations in the form of proteinuria. Her nulliparous status also conferred a moderate risk factor for the development of preeclampsia. Although the maximum benefit of aspirin intake in the prevention of pre-eclampsia relates to initiation of prophylaxis before 20 weeks, the ACOG Committee Opinion No. 743 on 'Low-dose aspirin use in pregnancy (Obstet Gynecol 2018;132:e44–52.) recommends low-dose aspirin prophylaxis for women at high risk of preeclampsia between 12 weeks and 28 weeks. The mechanism by which low-dose aspirin prevents pre-eclampsia is not completely elucidated yet, but may involve reduction in inflammation and endothelial dysfunction. Aspirin prophylaxis also seems very safe with several randomized trials showing no increase in adverse events or bleeding episodes. We have amended the manuscript at lines 89-91 to "Aspirin 150mg daily for preeclampsia prevention was commenced due to her increased risks as a nulliparous diabetic with preexisting renal disease, in the absence of bleeding issues from thrombocytopenia." to clarify this decision.

2. Please discuss further the diagnosis of superimposed preeclampsia; how did the authors determine that the elevation in blood pressure noted at 24 weeks gestation was not a consequence of her MAHA and renal involvement?
   We acknowledge the challenges in diagnosing the underlying cause of this patient's disease process, particularly as aHUS and early onset preeclampsia share many features as highlighted in this report. We have included a further discussion of the differential diagnoses at various stages of the case, including at 24 weeks' gestation, at lines 166-173. Management with oral antihypertensives was required regardless of the diagnosis, and with expectant management further features of preeclampsia (worsening proteinuria, escalating hypertension) developed.

3. Did the patient undergo testing for antiphospholipid antibody syndrome?

The patient was tested for antiphospholipid antibody syndrome early in her admission, with normal anticardiolipin IgG and beta-2 glycoprotein antibody levels, and negative lupus anticoagulant. These normal screen results have been added in at line 80.

4. Why were the authors collecting SFLT and PGIF levels at 21 weeks before her blood pressure rose, were there concerns about preeclampsia then as well?
   Analysis of this patient's sFlt-1 and PlGF levels occurred retrospectively, as referred to on line 136, on stored serum samples. Although the earliest sample was from 21 weeks, analysis only began a few days before delivery and therefore did not influence management prior to delivery. We hope that these retrospective analysis of angiogenic and anti-angiogenic factors add to the understanding of the disease and contribute to the knowledge of how the complement pathway may be implicated in the origins of microangiopathic hemolytic anemia spectrum in pregnancy (including aHUS and HELLP syndrome). Their use, while retrospective, also indicates the potential benefit these markers, which are increasing in clinical use, may also provide in assisting with diagnosis and observation of the impact of therapeutic interventions.

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

   We agree to opt-in to publication of this 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.
   We confirm that there are no disclosures from our coauthors as 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.
We have no concerns with use of the reVITALize definitions in our manuscript.

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.
Excluding references, the word count is 1,970 words.

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.
"A Case Report" has been accordingly removed from the title of the manuscript

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).

    We meet the aforementioned rules.
    Content in this manuscript, as previously disclosed in the cover letter of the initial submission, has been presented as an e-poster at the Royal Australian and New Zealand College of Obstetricians and Gynaecologists' Annual Scientific Meeting on 14-16

October 2018 in Adelaide, Australia. We are unclear where to note this in the manuscript.

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.
   The word count for the abstract is 111 words.

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.
   All virgules have been removed except for use in data or measurements.

10. Figures
    - Figure 1: Current file may be resubmitted as-is.
    - Figure 2: Please upload a high resolution version of this figure. We recommend using the original figure file (eps, tiff, jpeg, etc.) rather than Word.

    A eps version of figure 2 has been uploaded in addition to the original figure 1 image.

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.
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- 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.