

OBSTETRICS & GYNECOLOGY



NOTICE: This document contains correspondence generated during peer review and subsequent revisions but before transmittal to production for composition and copyediting:

- 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: Sep 12, 2019
To: "Roberto Xavier Calix" [REDACTED]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-19-1480

RE: Manuscript Number ONG-19-1480

Acute herpes simplex virus hepatitis in pregnancy: an atypical case report and literature review

Dear Dr. Calix:

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 Oct 03, 2019, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: This well-written case report describes a rare case of HSV hepatitis in pregnancy. Such cases have been reported before but as the authors point out, only a few cases in the literature have been associated with HSV-1 and there were unique clinical features of this patient.

The title accurately describes the focus of the case.

The precis, abstract and teaching points succinctly summarize the key points and take home messages.

The introduction does a good job of outlining the context of the problem with appropriate use of references. It emphasizes the severity of the condition (i.e. potentially fatal).

The first paragraph of the case description is perhaps too brief and should include one sentence explicitly stating that the patient has no other medical history and an uncomplicated pregnancy. The time sequence and clinical logic and decision-making are clearly reported. Were any outside consultations obtained aside from infectious disease on POD 6 (i.e. hepatology, critical care)?

The discussion and conclusion sufficiently emphasize why this case should be reported.

References are appropriate

Reviewer #2: The authors present a case report of acute HSV hepatitis in pregnancy. The following items should be addressed:

1. Abstract, background (line 49) - please provide a reference for the statement that "pregnant women are at higher risk for HSV hepatitis."
2. Teaching point #3 - the authors should provide a reference for this recommendation; if it represents the expert opinion of the authors, that should be stated. Reference #19 is a case series of two patients, and reference #30 is a letter to the editor.
3. Line 240-242 -this publication from the USPSTF recommends against universal screening for HSV, however the

authors cite it as a source after suggesting that screening may be appropriate for high risk populations. Please clarify further that generalized screening is not appropriate; in fact, for the patient whose case is presented, screening would not have been appropriate as she had no risk factors.

EDITOR COMMENTS:

1. Thank you for your submission to Obstetrics & Gynecology. In addition to the comments from the reviewers above, you are being sent a notated PDF that contains the Editor's specific comments. Please review and consider the comments in this file prior to submitting your revised manuscript. These comments should be included in your point-by-point response cover letter.

The notated PDF is uploaded to this submission's record in Editorial Manager. If you cannot locate the file, contact Randi Zung and she will send it by email - rzung@greenjournal.org.

- The précis is a single sentence of no more than 25 words, written in the present tense and stating the conclusion(s) of the report (ie, the bottom line). The précis should be similar to the abstracts conclusion. Do not use commercial names, abbreviations, or acronyms in the précis. Précis should be the "hook" for people who scan the Table of Contents to see what to read. It shouldn't include statements like "in this study" or "we found". Just state what you found.

- 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.

- 2-4% rate of association with or risk of acute hepatitis? You don't need to add "viral" as it's obvious that HSV hepatitis would be viral.

- Higher than what? One reviewer asked that you reference this statement (in the manuscript, not the abstract).

- you mention her fever at presentation. Otherwise, it sounds like she just got febrile post partum.

- why was a cesarean done?

- what type of testing was diagnostic? What was status of the neonate? How soon post partum did she get sick? Remember your abstract needs to be able to stand alone. If you knew a reader wouldn't read your paper, what would you want him or her to know? Is there something about HSV hepatitis that should trigger it on one's differential diagnosis? Should that be highlighted in your conclusion?

- any patient? Any pregnant patient? Which is correct?

- could you tell us what the range of transaminitis is associated with HSV hepatitis rather than a rather vague "Marked" increased?

- For clarity: Are these rates of HSV 1 (67%) only for sexually transmitted infections? That's what you've said.

- characterized AS a primary infection

- exposed or infected?

- might be good to explain that this (Starting line lin 90) is because recurrent infection is more common than primary infection during pregnancy.

- you make the point in the abstract that the lab diagnosis is highly sensitive (not challenging?). Probably good to emphasize that here rather than say it's challenging...challenging really because we don't think of it.

- may have fatal consequences? How frequently is transplantation required?

- does it matter that she is married?

- how could that be if she was febrile?

- I'm confused. You say she had a fever of 100.2 at presentation but now she says "she became febrile". please clarify the course of her fever.

- fundal tenderness?
- They could be "again started" or "restarted" but no "again restarted" which would be started 3x.
- why did she have an echo a month earlier? Perhaps her course was atypical because she has some underlying medical problem? This needs to be addressed.
- You present this as a review of the topic, as well as a case report. In your discussion, please tell us how you did your review (what data base searched? What search terms?)
- This is known as a primacy claim: yours is the first, biggest, best study of its kind. In order to make such a claim, please provide the databases you have searched (PubMed, Google Scholar, EMBASE for example), the years searched, and the search terms used. IF not done, please edit it out of the paper.
- Not sure what this sentence refers to. I think its pretty common for women to deteriorate post partum after cesarean delivery. what are you referring to here?
- is this clear from the case description?
- causing or associated with proteinuria?
- is this only 1/3 all pregnant women with HSV hepatitis or only 1/3 of those who died?
- I'm confused here. You say that mortality is higher in the treated cases but are advocating for empiric therapy. Are these conflicting?
- I agree with one reviewer that this statement needs clarity. Is this your opinion or that of others as well?
- Though viral reactivation may be the source, this condition is usually....
- please add some comment about screening for HSV 1 v 2.

2. 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.

3. 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.

4. 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.

5. Starting with the January 2020 issue, Case Reports will be lengthened to include a brief literature search. We have not settled on word count or page length limit yet, so please try to keep your submission at its current length when you make your revisions.

6. 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.

7. 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).

8. Provide a *précis* on the second page, for use in the Table of Contents. The *précis* is a single sentence of no more than 25 words that states the conclusion(s) of the report (ie, the bottom line). The *précis* should be similar to the abstract's conclusion. Do not use commercial names, abbreviations, or acronyms in the *précis*. Please avoid phrases like "This paper presents" or "This case presents."

9. 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.

10. 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.

11. 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.

12. Line 173: We discourage claims of first reports since they are often difficult to prove. How do you know this is the first report? If this is based on a systematic search of the literature, that search should be described in the text (search engine, search terms, date range of search, and languages encompassed by the search). If on the other hand, it is not based on a systematic search but only on your level of awareness, it is not a claim we permit.

13. The American College of Obstetricians and Gynecologists' (ACOG) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite ACOG documents in your manuscript, be sure the reference you are citing is still current and available. If the reference you are citing has been updated (ie, replaced by a newer version), please ensure that the new version supports whatever statement you are making in your manuscript and then update your reference list accordingly (exceptions could include manuscripts that address items of historical interest). If the reference you are citing has been withdrawn with no clear replacement, please contact the editorial office for assistance (obgyn@greenjournal.org). In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript (exceptions could include manuscripts that address items of historical interest). All ACOG documents (eg, Committee Opinions and Practice Bulletins) may be found via the Clinical Guidance & Publications page at <https://www.acog.org/Clinical-Guidance-and-Publications/Search-Clinical-Guidance>.

14. Figure 1: Please upload the original file type to Editorial Manager (eps, tiff, jpeg, etc.). Items pasted into Word often lose resolution.

15. 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.

16. 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 Oct 03, 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

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.



Nancy C. Chescheir, MD
Editor-in-chief
Obstetrics & Gynecology

October 2, 2019

Dear Dr. Chescheir,

Thank you for reviewing our updated manuscript, entitled “Acute herpes simplex virus hepatitis in pregnancy” We very much appreciate the thoughtful comments and suggestions from the reviewers, and have carefully revised the manuscript accordingly.

As instructed, we have responded to each received comment in a point-by-point format in a form that follows this letter. The responses have been marked using blue font text, and we directly implemented changes to the manuscript. The revised manuscript contains 2315 words in the main text, and 124 words in the abstract.

There is no funding or conflict of interests to disclose. This manuscript has not been previously published and is not under consideration for publication elsewhere. However, the case will be presented at ISUOG’s 29th World Congress on Ultrasound in Obstetrics and Gynecology in Germany on October 12-16, 2019. All authors listed have reviewed and approved the manuscript for submission to this journal. All authors report no duality of interest.

I have read the Green Journal Instructions for Authors and believe our manuscript complies with these guidelines.

We have obtained a signed consent form from the patient in the case report and this form will be filed with our records.

Thank you for reconsidering our manuscript for publication. We hope that our responses and revisions are satisfactory to you and the reviewers. Should you need any addition information, please let us know.

We appreciate your time and look forward to your response.

Sincerely,



Roberto Calix, M.D.

Instructor, Department of Obstetrics, Gynecology and Reproductive Sciences

Yale School of Medicine

The lead author* affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Signed by:  (CALIX)

*The manuscript's guarantor.

POINT-BY-POINT RESPONSE TO EACH COMMENT FROM REVIEWERS AND EDITOR
(AUTHOR RESPONSES IN BLUE):

Reviewer #1: This well-written case report describes a rare case of HSV hepatitis in pregnancy. Such cases have been reported before but as the authors point out, only a few cases in the literature have been associated with HSV-1 and there were unique clinical features of this patient.

The title accurately describes the focus of the case.

The precis, abstract and teaching points succinctly summarize the key points and take home messages.

The introduction does a good job of outlining the context of the problem with appropriate use of references. It emphasizes the severity of the condition (i.e. potentially fatal).

The first paragraph of the case description is perhaps too brief and should include one sentence explicitly stating that the patient has no other medical history and an uncomplicated pregnancy.

Thank you very much for your thoughtful review of this article and appreciate the suggestion. We have added the article (Lines 124 – 126) to reflect the fact that this patient had a prior history of a sleeve gastrectomy in 2016 and had an otherwise uncomplicated pregnancy prior to presentation.

The time sequence and clinical logic and decision-making are clearly reported. Were any outside consultations obtained aside from infectious disease on POD 6 (i.e. hepatology, critical care)?

We have updated the manuscript's case to reflect the consultations obtained during the diagnostic work up: maternal-fetal medicine, hepatology, surgery, cardiology. We also had to call a rapid response on the patient on POD 5 given her hypotension, though ICU was not deemed necessary during her stay. MFM was consulted on POD 5 for ongoing postpartum abdominal pain and lab abnormalities. Surgery was consulted on POD 4 to rule out cholecystitis for which a HIDA scan was performed. A hepatology consult was obtained on POD 6 the basis of her transaminitis and fever. A cardiology consult was obtained for her abnormal echocardiogram showing mild cardiomyopathy. A comparison echocardiogram had been done in 2017 for an episode of syncope the patient had experienced in the postoperative setting.

Reviewer #2: The authors present a case report of acute HSV hepatitis in pregnancy. The following items should be addressed:

1. Abstract, background (line 49) - please provide a reference for the statement that "pregnant women are at higher risk for HSV hepatitis."

Thank you for your thoughtful review of our manuscript.

A reference was placed in the manuscript supporting this point – Reference #4, Kourtis AP, Read JS, Jamieson DJ. Pregnancy and infection. N Engl J Med 2014 Jun 5;370(23):2211-8.

2. Teaching point #3 - the authors should provide a reference for this recommendation; if it represents the expert opinion of the authors, that should be stated. Reference #19 is a case series of two patients, and reference #30 is a letter to the editor.

Thank you for this clarification. Yes, the teaching point is based on expert opinion from prior publications (References #21, #28, #35 and #36) as well as from the authors based on our literature review and experience with this case. We have added our statement to the following: “3) Based on expert opinion, acute febrile hepatitis in pregnancy warrants a low threshold to initiate empirical treatment for HSV with IV acyclovir while awaiting confirmatory testing with serum PCR.” (Line 70 – 72)

3. Line 240-242 -this publication from the USPSTF recommends against universal screening for HSV, however the authors cite it as a source after suggesting that screening may be appropriate for high risk populations. Please clarify further that generalized screening is not appropriate; in fact, for the patient whose case is presented, screening would not have been appropriate as she had no risk factors.

Thank you for pointing out this discrepancy. The manuscript was updated to be consistent with USPTF screening guidelines. (Lines 264 – 266)

EDITOR COMMENTS:

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Thank you very much for your comments on this manuscript.

The Précis has been updated to meet these criteria. (Lines 25 – 27)

- 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.

Thank you for highlighting this. We have made every attempt to ensure the manuscript fits within the Green Journal formatting requirements.

- 2-4% rate or association with or risk of acute hepatitis? You don't need to add "viral" as its obvious that HSV hepatitis would be viral.

Thank you. We have made the changes in the manuscript. (Line 48)

- Higher than what? One reviewer asked that you reference this statement (in the manuscript, not the abstract).

The manuscript has been added to clarify this point. (Line 49). The reference was added to the manuscript to reflect this point – Reference #4, Kourtis AP, Read JS, Jamieson DJ. Pregnancy and infection. N Engl J Med 2014 Jun 5;370(23):2211-8.

- you mention her fever at presentation. Otherwise, it sounds like she just got febrile post partum.

Thank you for the clarification.

On admission, she had a temperature of 98.8F. Her reported temperature at home was 100.2. Soon after admission, she became febrile and had subsequent PROM.

The manuscript has been added to clarify the timing of her fever. Abstract (Line 52 – 54), body (Lines 123, 129 and 133).

- why was a cesarean done?

A cesarean was performed for fetal malpresentation (breech). We have updated the manuscript to reflect this indication. (Line 53)

- what type of testing was diagnostic? What was status of the neonate? How soon post partum did she get sick? Remember your abstract needs to be able to stand alone. If you knew a reader wouldn't read your paper, what would you want him or her to know? Is there something about HSV hepatitis that should trigger it on one's differential diagnosis? Should that be highlighted in your conclusion?

Thank you for this point. We performed polymerase chain reaction (PCR) analysis for diagnosis. This abstract has been updated to reflect this. (Lines 56 and 61)

We have updated the abstract to reflect the succinct clinical course of the patient and added the conclusion to reflect the most pertinent findings and recommendations.

- any patient? Any pregnant patient? Which is correct?

Thank you. We have clarified the conclusion as follows: This should read "Pregnant or recently pregnant women...". The manuscript has been updated. (Lines 66 – 67)

- could you tell us what the range of transaminitis is associated with HSV hepatitis rather than a rather vague "Marked" increased?

Thank you for this recommendation. Per published data (included in our references):

#12, Norvell JP, Blei AT, Jovanovic BD, Levitsky J. Herpes simplex virus hepatitis: an analysis of the published literature and institutional cases. Liver Transpl 2007 Oct;13(10):1428-34.

#25, Masadeh M, Shen H, Lee Y, Gunderson A, Brown K, Bellizzi A, et al. A fatal case of herpes simplex virus hepatitis in a pregnant patient. Intractable & rare diseases research 2017 May;6(2):124-7.

#36, McCormack AL, Rabie N, Whittemore B, Murphy T, Sitler C, Magann E. HSV Hepatitis in Pregnancy: A Review of the Literature. Obstet Gynecol Surv 2019 Feb;74(2):93-8.

...values can peak at 4000 units/L for ALT and 8000 units/L for AST, but values are typically > 2000 units/L. The manuscript has been updated. (Line 69)

- For clarity: Are these rates of HSV 1 (67%) only for sexually transmitted infections? That's what you've said.

Thank you for this clarification. These are the worldwide infection rates, not necessarily sexually transmitted infection rates. The manuscript was updated to clarify this point. (Lines 89 – 90)

- characterized AS a primary infection

Thank you, the manuscript was corrected. (Line 90)

- exposed or infected?

Thank you, it should read infected. The manuscript was corrected. (Line 91)

- might be good to explain that this (Starting line 90) is because recurrent infection is more common than primary infection during pregnancy.

Thank you, the manuscript was added to include this important point. (Line 92 – 95)

- you make the point in the abstract that the lab diagnosis is highly sensitive (not challenging?). Probably good to emphasize that here rather than say it's challenging...challenging really because we don't think of it.

Thank you, the manuscript was updated for clarity. (Line 107 – 108)

- may have fatal consequences? How frequently is transplantation required?

Thank you, the manuscript was corrected to read “may have fatal...” (Line 112)

Percentages vary in different reports and may be subject to various forms of bias, so it is difficult to determine the actual risk of needing a liver transplantation in the setting of HSV hepatitis. The mortality rate being so high may also confound the reported values. The manuscript was added to clarify that liver transplant may be required in cases of fulminant liver failure (Lines 113 – 114)

- does it matter that she is married?

We have updated the manuscript to reflect the patient's social history “long-term heterosexual relationship”. (Lines 126 – 127).

- how could that be if she was febrile?

Thank you. The manuscript was updated to clarify this point. The patient presented with premonitory signs and symptoms of an infection, and a reported temperature of 100.2 at home. However, her initial temperature was only 98.8F and did not meet criteria for fever. After admission, the patient became febrile to 101.5 overnight. (Lines 123, 129 and 133)

- I'm confused. You say she had a fever of 100.2 at presentation but now she say "she became febrile". Please clarify the course of her fever.

Please see above for clarification and update in the manuscript.

- fundal tenderness?

Thank you, the manuscript was edited with this change. (Line 142)

- They could be "again started" or "restarted" but no "again restarted" which would be started 3x.

Thank you, the manuscript was updated to reflect this change. "were restarted". (Line 149)

- why did she have an echo a month earlier? Perhaps her course was atypical because she has some underlying medical problem? This needs to be addressed.

Thank you, we have updated the manuscript to reflect the timing and context of the prior echocardiogram. (Lines 162 – 164)

- You present this as a review of the topic, as well as a case report. In your discussion, please tell us how you did your review (what data base searched? What search terms?)

Thank you, we have updated the manuscript to reflect our search criteria. (Lines 190 – 195)

- This is known as a primacy claim: yours is the first, biggest, best study of its kind. In order to make such a claim, please provide the databases you have searched (PubMed, Google Scholar, EMBASE for example), the years searched, and the search terms used. IF not done, please edit it out of the paper.

Thank you, the manuscript was updated with the search criteria. (Lines 190 – 195)

Additionally, the manuscript was added to read "This is one of the few cases..." (Line 196)

- Not sure what this sentence refers to. I think its pretty common for women to deteriorate post partum after cesarean delivery. what are you referring to here?

Thank you for the prompt for clarification. We have updated the manuscript to reflect the writer's intentions. (Lines 207 – 209)

- is this clear from the case description?

Thank you for the prompt for clarification. We have updated the manuscript to reflect that she would stabilize (not improve). (Line 226)

- causing or associated with proteinuria?

Thank you. It should read "Associated with". The manuscript was updated (Line 236)

- is this only 1/3 all pregnant women with HSV hepatitis or only 1/3 of those who died?

Thank you for pointing this out. This statement has been removed from manuscript and the following line added. (Lines 248 – 251)

- I'm confused here. You say that mortality is higher in the treated cases but are advocating for empiric therapy. Are these conflicting?

Thank you for pointing this out. The statements prior to this line were added and should clarify the statement made. (Lines 243 – 245)

- I agree with one reviewer that this statement needs clarity. Is this your opinion or that of others as well?

Thank you for the suggestion. We have updated the manuscript to reflect this is expert opinion based on other publication. It is also our recommendation from our own review of the literature and our experience with this case. (Lines 256 – 257)

- Though viral reactivation may be the source, this condition is usually....

The manuscript was edited with this change. (Line 259)

- please add some comment about screening for HSV 1 v 2.

The manuscript was added per above to reflect recommendations from the USPTF paper and this comment was removed. (Lines 264 – 268)

2. 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.

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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 will ensure all authors fill out eCTA and that disclosures listed are correct.

4. 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.

The use of reVITALize definitions is not problematic and the manuscript has been reviewed to ensure compliance in this matter.

5. Starting with the January 2020 issue, Case Reports will be lengthened to include a brief literature search. We have not settled on word count or page length limit yet, so please try to keep your submission at its current length when you make your revisions.

Attempts have been made to keep the submission at its original length.

6. 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.

The manuscript has been added. A subtitle was inserted to comply with requirements as listed. (Line 3)

7. 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).

Acknowledgment:

This case report will be presented at ISUOG's 29th World Congress on Ultrasound in Obstetrics and Gynecology in Berlin, Germany on October 12-16, 2019

8. Provide a précis on the second page, for use in the Table of Contents. The précis is a single sentence of no more than 25 words that states the conclusion(s) of the report (ie, the bottom line). The précis should be similar to the abstract's conclusion. Do not use commercial names, abbreviations, or acronyms in the précis. Please avoid phrases like "This paper presents" or "This case presents."

The précis was updated to meet required criteria. (Lines 25 – 27)

9. 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 abstract has been reviewed and is consistent with the manuscript.

Word Count: 124

10. 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.

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12. Line 173: We discourage claims of first reports since they are often difficult to prove. How do you know this is the first report? If this is based on a systematic search of the literature, that search should be described in the text (search engine, search terms, date range of search, and languages encompassed by the search). If on the other hand, it is not based on a systematic search but only on your level of awareness, it is not a claim we permit.

The manuscript has been updated with the requested terms and parameters. (Lines 190 – 195) Additionally, the manuscript has been added to read “This is one of the few cases...” (Line 196).

13. The American College of Obstetricians and Gynecologists' (ACOG) documents are frequently updated. These documents may be withdrawn and replaced with newer, revised versions. If you cite ACOG documents in your manuscript, be sure the reference you are citing is still current and available. If the reference you are citing has been updated (ie, replaced by a newer version), please ensure that the new version supports whatever statement you are making in your manuscript and then update your reference list accordingly (exceptions could include manuscripts that address items of historical interest). If the reference you are citing has been withdrawn with no clear replacement, please contact the editorial office for assistance (obgyn@greenjournal.org). In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript (exceptions could include manuscripts that address items of historical interest). All ACOG documents (eg, Committee Opinions and Practice Bulletins) may be found via the Clinical Guidance & Publications page at <https://www.acog.org/Clinical-Guidance-and-Publications/Search-Clinical-Guidance>.

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Sincerely,

Nancy C. Chescheir, MD
Editor-in-Chief

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