

Dear editor and reviewers

Thank you very much for your letter and advice. We are resubmitting the Manuscript NO: 77385 entitled "Common carotid artery thrombosis and cerebral infarction following ovarian hyperstimulation syndrome: a case report" to World Journal of Clinical Cases. Our responses to the comments by the reviewers are outlined below. Please also see the revised manuscript for details. For easily reading, we use the TRACK function of MICROSOFT WORD. Please simply select "Accept changes" to get rid of the TRACK markers if you do not like the tracks.

We hope that the revision is acceptable, and I look forward to hearing from you soon.

With best wishes,

Yours sincerely,

Dr. Zhaorong Guo, Department of Obstetrics and Gynecology, Weihai Central Hospital Affiliated to Qingdao University, No. 3 West of Mishan East Road, Wendeng District, Weihai 264400, China. Tel.: 86-13220822642. Email: gzhr0631@163.com

Reviewer #1:

Scientific Quality: Grade D (Fair)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Minor revision

Specific Comments to Authors: This is an interesting manuscript that describes a rare case of ovarian hyperstimulation syndrome (OHSS) complicated with common carotid artery thrombosis and cerebral infarction after egg retrieval and before embryo transfer. The authors may consider the following criticisms and questions in revising their manuscript.

- Some major English issues need to be addressed, for instance: Page 2, line 26- "Admitted at" –The preposition use is incorrect

Response: Sorry for the mistakes. We have gotten editorial help to further improve the English writing of the revised manuscript. For example, the above mentioned sentence has been revised into "A 32-year-old female with family history of thrombosis and undergoing in vitro fertilization due to unexplained infertility, was admitted due to abdominal distension for 3 days and coma for 2 hours. She received egg retrieval 7 days ago and embryo transfer was not performed yet." Please check!

- here Page 2, line 20- "That palpable masses"- The conjunction use is incorrect here

Response: Sorry for the mistakes. We have deleted the conjunction "that". Please check!

-Please, arrange laboratory data in table format for easy reading. -

Response: As suggested, we have listed the laboratory data in the revised Table 1. Please check!

Table 1. Laboratory data.

Items	Results
Blood count	white blood cell count $29.82 \times 10^9/L$, hematocrit 0.454, platelet count $269 \times 10^9/L$, hemoglobin 151 g/L
Coagulation factor	fibrinogen content 5.19 g/L, antithrombin III 85.3%
Blood lipid level	total cholesterol 5.71 mmol/L, triglycerides 2.81 mmol/L, free fatty acids 1.34 mmol/L, low-density lipid cholesterol 3.76 mmol/L, homocysteine 9.4 $\mu\text{mol/L}$, high-density lipid cholesterol 1.05 $\mu\text{mol/L}$
Hormone level	estrogen 15781 pmol/L

- Please, define OHSS, and how it is diagnosed and classified in the manuscript text.

Response: Ovarian hyperstimulation syndrome (OHSS), a rare and unique complication associated with in vitro assisted reproduction, is an excessive response to exogenous gonadotropins, which is characterized by multiple follicles in bilateral ovaries, enlarged ovaries, abnormal capillary permeability, and abnormal extravasation of body fluids and proteins. It is diagnosed based on symptoms (such as abdominal distension), physical examination (such as enlarged ovaries), imaging examination (such as ascites), and laboratory examination (such as coagulation abnormalities and hormone levels). According to Golan's classification, it is divided into mild (grade 1 and 2), moderate (grade 3) and severe OHSS (grade 4 and 5). As suggested, we have added the requested information of OHSS in section of Introduction. Please check!

-Have the authors considered the use of an Intra-arterial tissue-type plasminogen activator? Although it has had mixed outcomes; 2 cases have demonstrated successful recanalization Please, explain your treatment choice. (Elford K, Leader A, Wee R, Stys PK. Stroke in ovarian hyperstimulation syndrome in early pregnancy treated with intra-arterial rt-PA. *Neurology*. 2002; 59:1270–1272. GA, Wijdicks EF, Eggers SD, Phan T, Damario MA, Mullany CJ. Ovarian hyperstimulation syndrome with ischemic stroke due to an intracardiac thrombus. *Neurology*. 2001; 57:1342–1344)

Response: In this report, we did not use an intra-arterial tissue-type plasminogen activator for the following reason. On admission, the imaging examination already suggested thrombosis, indicating that the onset time was more than two hours before the patient was in a coma. At this time, the thrombolysis window time had been missed. Thus, thrombolysis was not suitable. However, the reviewer raised a very good point. We will consider the suggested therapy in the future.

-“She and her relatives should receive further measurement of antithrombin III

activity, protein S activity, and protein C activity to evaluate the risk of thrombosis. In addition, this patient had severe OHSS, and a high hematocrit level indicating a hypercoagulable state, which may be the cause of carotid artery thrombosis and non-atherosclerotic plaque [...] “. Surprisingly, thrombophilic disorders do not seem to be risk factors for severe OHSS. Please rephrase this part of the discussion to include this new information. (Lamazou F, Legouez A, Letouzey V, Grynberg M, Deffieux X, Trichot C, et al.. Ovarian hyperstimulation syndrome: pathophysiology, risk factors, prevention, diagnosis, and treatment. J Gynecol Obstet Biol Reprod (Paris). 2011; 40:593–611. Fábregues F, Tàssies D, Reverter JC, Carmona F, Ordinas A, Balasch J. Prevalence of thrombophilia in women with severe ovarian hyperstimulation syndrome and cost-effectiveness of screening)

Response: We have revised the Discussion section of the revised manuscript according to this suggestion. Please check!

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: The authors present a clinical note reporting a 32-year-old woman presenting with common carotid artery thrombosis with malignant middle cerebral artery infarction following ovarian hyperstimulation syndrome. This report is potentially interesting, but the manuscript can be improved according to the following suggestions:

1. Rewrite the title using ‘malignant middle cerebral artery infarction’

Response: As suggested, we have revised the title into “Common carotid artery thrombosis and malignant middle cerebral artery infarction following ovarian hyperstimulation syndrome: a case report”.

2. In the Abstract please remove duplications (ex: “..and the left internal carotid artery”)

Response: Sorry for the confusions. As suggested, we have removed the duplications in the Abstract. Please check!

3. In the Case Presentation section, please adequately describe the content of the statement: "bilateral pathological signs (+)"

Response: Sorry for the confusions. We mean Babinski sign (+). We have modified this accordingly. Please check!

4. What was the NIHSS score during hospital admission and at discharge?

Response: NIHSS (National Institutes of Health Stroke Scale) score at admission was

29 and that at discharge was 8. As suggested, we have added this to the revised manuscript. Please check!

5. Please remove in the first line of the Discussion the sentence: "Carotid artery thrombosis can cause local arterial stenosis"

Response: As suggested, we have removed the mentioned sentence from the Discussion section. Please check!

6. It would be interesting to include in the text a comment on the fact that acute ischemic stroke may also be caused by hematological diseases. This is a noteworthy aspect that should be emphasized (Expert Review of Hematology 2016; (9), 891-901). Add and comment on the reference

Response: As suggested, we have added and commented the fact that acute ischemic stroke may also be caused by hematological diseases. The reference (Expert Review of Hematology 2016; (9), 891-901) has also been cited. Please check the revised Discussion section for details.

7. It should be noted in the Discussion, that malignant middle cerebral artery infarction is a devastating type of ischemic stroke. In a recent clinical series, decreased level of consciousness, nausea or vomiting, and heavy smoking were the main associated clinical factors (REV INVEST CLIN. 2015;67:64-70). It is recommended that this reference be included and commented on.

Response: As suggested, we have added the above mentioned information. The reference (REV INVEST CLIN. 2015;67:64-70) has also been included and commented on. Please check the revised Discussion section for details.

8. Check reference #1

Response: As suggested, we have modified this reference accordingly.