Response letter for #41140

Dear Fang-fang Ji,

Thank you very much for your letter and advice.

We have revised the manuscript, which we would like to submit for your consideration for publication. We have addressed the comments raised by the reviewers, and the changes are highlighted in red in the revised manuscript. Point-by-point responses to the reviewers' comments are provided below this letter.

We hope that the revised version of the manuscript is now acceptable for publication in your journal.

We look forward to hearing from you soon.

Yours sincerely,

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Answers to the reviewers

To reviewer 1:

To Summary Comments:

1. You have used “placenta Previa” and “placenta necrosis” alternately throughout the abstract, Core tip and text. Please choose one of them and amend throughout.

Response: Thanks for your suggestion. We have checked the whole manuscript carefully and made the amendments.

2. A very short introduction, not enough background information on the role of AFP during pregnancy, its normal levels, etc.

Response: Thanks for your kindly remind. We have added several background information to enrich the introduction part (Page 4, lines 7-11).

3. What was the patient’s’ parity/gravidity? Any previous history of miscarriage, abortion, CS, etc? Please indicate.

Response: Thanks for your suggestion. We have added detailed information about her medical history (Page 4, lines 14-15).

4. Does ‘intraoperative exploration’ here mean physical examination of the tissue or pathological examination? If it means physical examination, please explain here how the tissue exactly looked like during the intraoperative exploration that was an indication of necrosis tissue. Also, the Figure 2 shows the pathological examination of the tissue not physical examination. Please clarify.

Response: We agree with your opinion. We have added the description of the tissue during the intraoperative exploration and clarified Figure 2 (Page 5, lines 5-9).

5. It will be of interest to the readers if you provide brief information about the

neonatal outcome. The degree of the placenta necrosis? The baby's wellbeing? Apgar at 5th min? Admission to NICU/SCN? Etc.

Response: Thanks for your advice. We have added the detailed information about the neonatal outcome (Page 5, lines 11-15).

6. Please indicate the exact duration and time period that took the AFP levels to return to normal and how long it remained normal (exact duration: for example '1 year', '8 months' or …).

Response: Thanks for your kindly remind. We have added the required data (Page 5, lines 10-11 and 14).

7. This section should provide an in-depth discussion about the findings, how the high levels of AFP could have contributed to the placental necrosis and its potential mechanism of action.

Response: We agree with your opinion. Due to lack of continuous maternal serum AFP detection from 14 weeks to 31 weeks of gestation, we cannot determine how high the serum AFP will be to contribute to the placental necrosis. We have done the mechanism of action supplement in the discussion section (Page 6, lines 7-10).

8. What about the role of any other factors n the occurrence of placenta necrosis? Has any previous research reported on any potential association between any other variables and the placenta necrosis?

Response: Thanks for your kindly remind. Reports on potential association between any other variables and the placenta necrosis are limited. One report suggests that maternal viral infection, such as HBV and HIV infection, may increase necrotic rate of placental trophoblastic cells. This article has been cited in edited manuscript (Page 5, lines 28-29).

9. Since the normal ranges may different between different institutions in different

countries, it will be useful if you add another column and put the normal ranges approved in your institution.

Response: Thanks for your suggestion. We have added the reference ranges of each test item (Table 1).

To reviewer 2:

1. AFP elevation is related to placental necrosis, actually, the placental is from the embryo, it should have the same origin as the fetus.

Response: We agree with your opinion. It has been fully discussed in the discussion section (Page 6, lines 7-10).

2. Elevated AFP in placental previa may not be related to fetal abnormality such as open neural tube disease, but we need to exclude such kind of disease.

Response: Thanks for your suggestion. As for the baby, its weight was 1 550g. Apgar was 9 at 1^{st} minute and was 10 at 10^{th} minute. It was confirmed normal without diseases like open neural tube defects. It was soon admitted to NICU for further treatment.

3. Elevated AFP may be resulted from other conditions, such as liver disease, tumor, or fetal problem. In this case report, these points have not been discussed.

Response： We agree with your opinion. The patient was in her first pregnancy with no medical history of miscarriage, abortion, liver diseases or tumor. Her fetus was normally developed. The baby had asthma since 10 month and suffered from herpangina at one year's old. He also had mild anaemia with 99 g/L.