

Dear Editors and Reviewers,

On behalf of all authors, I would like to thank you for giving us an opportunity to revise our manuscript entitled “**Pre-eclampsia with new-onset systemic lupus erythematosus during pregnancy: A case report and literature review**” (Manuscript NO: 49867). We appreciate editors and reviewers very much for the careful and thoughtful comments and suggestions. The manuscript has been extensively revised with substantial new information included to address these comments and suggestions. We would like to submit a revision for your kind consideration, and hope that the correction will meet with approval. The revised manuscript has been edited according to the suggestions of the editor. All major changes towards the reviewer are marked in yellow in the revised manuscript and discussed in the following sections.

Response to comments by the reviewer

Comment 1: The main issue with this case is actually the clinical management. It seems that there was a big delay on proper diagnosis and treatment of the severe preeclampsia which in the end became eclampsia and fetus demise was the outcome. Patient should have been delivered from the 2nd day according to the results presented.

Response: We thank the reviewer for this thoughtful question and regret for the fetal demise. This patient was diagnosed with severe preeclampsia on the first day of admission to our hospital at 27th week of gestation. Magnesium sulfate, labetalol and glucocorticoid were prescribed for spasmolysis, anti-hypertention and promotion of fetal lung maturation. Considering the small gestational age and low survival rate of the preterm infant, we wished to prolong the pregnancy without decision of delivery. However, although proteinuria reached 4+ one day before admission, we ignore the possibility that preeclampsia could be complicated with SLE. After the patients manifested with convulsion, emergent delivery was not carried out since the patients' families did not have high expectations for the premature infant. But we have been monitoring the maternal and fetal condition besides medications and have consulted with the vascular surgeon for preparations of the inferior vena cava filter before cesarean section in order to prevent the potential pulmonary embolism that could be resulted from the lower limb venous thrombosis which may fall off from the vein into the pulmonary artery via the pulmonary circulation. However, the disease developed so rapid that induced eclampsia and fetal demise in the end, which caution us

the potential occurrence of new-onset SLE in patients with preeclampsia and that effective managements should be taken in time for the optimal maternal and fetal outcomes.

Comment 2: On the third day when eclampsia occurred why was MGSO₄ not administered and why the patient didn't have an immediate delivery?

Response: We apologize for unclear presentation about the administration of magnesium sulfate and have added details in the revision manuscript (page 7 and 8, marked yellow). Magnesium sulfate was administered with the loading dose of 5.0g, followed by the 20.0g pumped every day since admission. When the convulsion occurs, magnesium sulfate of 1.5g/hour was pumped continuously and we did not consider the superaddition of magnesium sulfate in case of magnesium poisoning. In addition, thrombosis in both lower limbs reminded us of the convulsion may also be caused by the potential cerebral embolism and hemorrhage besides preeclampsia. The patient was in the severe condition at that time and the lupus encephalopathy could not be ruled out since the thrombosis in both lower limbs. The concrete informations about the administration of magnesium sulfate have also been supplemented in the manuscript.

Comment 3: It is not clear when and why all these time consuming blood tests on antibodies took place actually.

Response: We apologize for unclear presentation about the blood tests on antibodies, which is now provided in the revision manuscript (page 7 and 8, marked in yellow). On the third day morning, the 24-hour proteinuria of the second day after admission reached 10311.0mg, which reminded us that whether there was the underlying autoimmune disease and then we prescribed immunological examination. On the third day night (54th hour of admission), the patient presented with blurred vision and involuntary convulsion. However, the patient and her families did not have high expectations for the premature infant and decided not to delivery emergently. So we have taken conservative treatments and been monitoring the maternal and fetal condition. On the fourth day morning, the blood biochemical testing and routine blood examination were carried out for further evaluation of the disease status.

Comment 4: Authors should also add some information regarding follow up of the patient before admission and in addition some details about ultrasound findings on the fetus, percentile of growth, Doppler studies, and amniotic fluid.

Response: We have added relevant information in the revision manuscript (page 5-7, marked in yellow) as the following:

Antenatal checkup was conducted regularly which showed normal outcomes except for the both limbs edema, hypertension and proteinuria before admission.

Color Doppler ultrasound examination at admission showed a second trimester pregnancy equivalent to 26th weeks of gestation as well as normal fetal movement and a fetal heart rate of 160 bpm. The fetal head was located at the uterine fundus. The placenta of Grade I was in the anterior uterine wall. The fetal weight was estimated as 790g and conditions of the fetus growth were as following: biparietal diameter: 6.6cm; femur length: 4.6cm; humeral length: 4.5cm; head circumference: 24.8cm; abdominal circumference: 20.1cm. S/D of the umbilical artery and the fetal middle cerebral artery was 3.10 and 3.30, respectively. And the amniotic fluid index was 12.9cm.

Comment 5: What do the authors mean as close monitoring of the patient and fetus?

Response: We apologize for the unclear expression, which has been added as following (page 11-12, marked yellow).

Once the patients with SLE was pregnant, regular prenatal examinations and monitoring as the following were necessary for us to learn the disease process: ①whether there is the maternal clinical manifestations that indicate the SLE flare, such as fever, facial erythema, arthralgia, photosensitivity; ②regular blood routine, urine routine, hepatic and renal functions and immunological examinations including ANA, anti dsDNA, ACL lupus, complement C3 and C4 and lupus anticoagulant assays;③regular ultrasound for detection the growth and heart developments of intrauterine fetus.

Comment 6: Add please some more details which can be useful for future reference, as despite the efforts there was a bad perinatal outcome.

Response: We thank the reviewer for this constructive suggestion and have added details about the history of present illness, Doppler ultrasound examination, administration of magnesium sulfate and exact time of symptoms or examinations in the revision manuscript (page 5 to 9, marked in yellow). As we discussed in the manuscript, preeclampsia complicated with new-onset SLE is rare and difficult to diagnose. The disease developed so

rapid in our case that the fetus was dead in the end. We hope that this case could attract obstetricians' attention towards this condition so that they could take effective measures for optimal outcome. The clinical symptoms of the patient in our case furtherest helped us to detecte the disease development and underlying SLE besides preeclampsia. So we have reorganized the process of diagnosis and treatment and added corresponding details especially the exact time of symptoms and examinations which could be helpful for future similar conditions.

Comment 7: English language is simple and easy to understand but some polishing is actually needed.

Response: The manuscript has been edited through a professional editing service.