

## **Response to Reviewers' comments**

Dear Editor,

We thank you for your careful consideration of our manuscript. We appreciate your response and overall positive initial feedback and made modifications to improve the manuscript. After carefully reviewing the comments made by the Reviewers, we have modified the manuscript to improve the presentation of our results and their discussion, therefore providing a complete context for the research that may be of interest to your readers.

We hope that you will find the revised paper suitable for publication, and we look forward to contributing to your journal. Please do not hesitate to contact us with other questions or concerns regarding the manuscript.

Best regards,

## Reviewer 1

*Comment 1: The authors should indicate how long they have treated the patient in case report section.*

**Response:** We thank the Reviewer for the comment. Patient was admitted to our hospital on May 7, 2018 and discharged on June 4, 2018, thus treatment took approximately 4 weeks. All time points have been added to the corresponding sections of the manuscript.

*Comment 2: The authors should explain whether other manifestations of SLE (e.g. nephritis) improved or not together with visual impairments.*

**Response:** We thank the Reviewer for the comment. Other clinical manifestations were improved along with visual acuity. Edema subsided and nausea improved. The SLE disease activity was well controlled, and related symptoms disappeared completely. We have added more detailed description of the outcomes to the corresponding section of the manuscript (Page 6, lines 138-141).

*Comment 3: I would like to see a proposal on the mechanism of choroidal involvement in discussion section.*

**Response:** We thank the Reviewer for the comment. The discussion section of the manuscript has been updated with the following:

The precise mechanisms of lupus choroidopathy remain debatable, but it is thought to involve the some of the following factors. Firstly, histopathological studies demonstrated the immune complex deposition in the choroid and the presence of autoantibodies against retinal pigment epithelium (RPE)<sup>[1]</sup>. The inflammatory cells along with the deposition of immunoglobulins and complement in the choroidal vessels might lead to choroidal hyperpermeability, breaking down the blood retinal barrier<sup>[2]</sup>. Matsuo and colleagues<sup>[3]</sup> hypothesized that anti-RPE antibodies were involved in the cause of RPE dysfunction which ultimately led to the development of serous retinal detachment. Stefater and colleagues<sup>[4]</sup> used the Light's criteria to assess the suprachoroidal fluid and proposed that choroidal effusions were exudative in SLE. Low serum protein can lead to a decrease in plasma oncotic pressure, thus, fluid is forced into compartments adjacent to the retina. Polito<sup>[5]</sup> reported that plasmapheresis could improve the choroidopathy, which indicated the importance of immune complex deposition in the pathophysiology and management strategy of the disease.

Secondly, uncontrolled hypertension may cause choroidal vascular occlusions, leading to ischemia and destruction of the external blood-retinal barrier at the RPE<sup>[6]</sup>. Thirdly, thrombosis can also lead to choroidopathy by causing microangiopathy<sup>[2]</sup>. Recurrent thromboembolisms are the hallmark of the anti-phospholipid antibody syndrome (APS) and the patients with SLE and raised levels of ACL antibodies have a higher risk of developing occlusive ocular vascular disease<sup>[7]</sup>. Hirabayashi noted that the levels of D-dimer or TAT complex (the parameters for hypercoagulation or fibrinolysis activation) were elevated during the episodes of vasculitis<sup>[8]</sup>. It is more likely that the combination of these factors contributes to choroidal capillary hypoperfusion, leading to RPE damage and fluid penetration into the subretinal space.

#### References:

- 1 Shoughy SS, Tabbara KF. Ocular findings in systemic lupus erythematosus. *Saudi J Ophthalmol.* 2016;30(2):117-121. doi:10.1016/j.sjopt.2016.02.001
2. Dammacco R. (2018). Systemic lupus erythematosus and ocular involvement: an overview. *Clinical and experimental medicine*, 18(2), 135–149. <https://doi.org/10.1007/s10238-017-0479-9>
3. Matsuo, T., et al., Multifocal pigment epithelial damages with serous retinal detachment in systemic lupus erythematosus. *Ophthalmologica*, 1987. 195(2): p. 97-102.
4. Stefater, J.A., D. Elliott and L.A. Kim, Drainage and analysis of suprachoroidal fluid in a patient with acute systemic lupus erythematosus. *American Journal of Ophthalmology Case Reports*, 2017. 5: p. 29-32.
5. Polito, M. S., Machetta, F., Fea, A. M., & Eandi, C. M. (2021). Hypertensive choroidopathy in atypical hemolytic-uremic syndrome. *European journal of ophthalmology*, 31(2), NP63–NP66. <https://doi.org/10.1177/1120672119896286>
6. Rezkallah, A., Kodjikian, L., Abukhashabah, A., Denis, P., & Mathis, T. (2019). Hypertensive choroidopathy: Multimodal imaging and the contribution of wide-field swept-source oct-angiography. *American journal of ophthalmology case reports*, 13, 131–135. <https://doi.org/10.1016/j.ajoc.2019.01.001>
7. Silva, R. A., & Moshfeghi, D. M. (2014). Antiphospholipid antibody-associated choroidopathy. *Eye (London, England)*, 28(6), 773–774. <https://doi.org/10.1038/eye.2014.39>
8. Hirabayashi, Y., et al., Mononeuritis multiplex, protein-losing gastroenteropathy, and choroidopathy seen together in a case of systemic lupus erythematosus. *Mod Rheumatol*, 2003. 13(3): p. 265-9.

**Reviewer 2**

*Comment : Great case! Great images!*

**Response:** We thank the Reviewer for the positive response.

### **Reviewer 3**

*Comment 1: The abbreviations of OCT and ICGA have been used in the abstract but their definitions were not provided. Either write them with full names (Ocular Coherence Tomography, Indocyanine Green Angiography) or do not mention them.*

**Response:** We thank the Reviewer for the comment. All abbreviations in the Abstract have been explained.

*Comment 2: The conclusion section of the abstract is weak and is not specific to the case report presented.*

**Response:** We thank the Reviewer for the comment. The corresponding section of the Abstract has been amended.

*Comment 3: The core tip briefly describes the case but lacks a core message.*

**Response:** We thank the Reviewer for the comment. Authors believe that the core message should reflect that lupus choroidopathy is discussed in the context of recurrence of underlying vasculitis; serous chorioretinopathy (CSC) needs to be excluded and condition treated with immunosuppressive agents; spironolactone is safe and helpful in both lupus choroidopathy and CSC. The manuscript has been amended to clarify this.

*Comment 4: In the physical exam section authors should describe what is meant with "poor condition." Oxygen saturation and heart rate at presentation should also be provided.*

**Response:** We thank the Reviewer for the comment. "Poor condition" referred to poor general condition of the patient, including fatigue and malnutrition, heart rate 91 beats/min and breath 17 breaths/min. Unfortunately blood oxygen was not measured at the time. The corresponding section of the manuscript has been amended.

*Comment 5: The sentence "She gained 4.5kg over the past 2 weeks." should be removed from the physical exam section and put into the history of present illness section*

**Response:** We thank the Reviewer for the comment. The manuscript has been amended according to your suggestion.

*Comment 6: In the treatment section there is no mention of spironolactone use however, it was mentioned in the conclusion section of the article. Authors should provide why this treatment was not preferred in this case if as mentioned in the conclusion has been found effective by other studies. IVIG treatment for SLE is recommended for patients with increased risk for thromboembolic events or renal failüre who are resistant to conventional treatment. The main reasons regarding IVIG treatment initiation should be mentioned as this is the main point in decision making.*

**Response:** We thank the Reviewer for the comment. For the treatment of edema spironolactone was routinely administered as a diuretic, from the start of treatment, 2-3 tablets per day. The manuscript was amended to clarify that diuretics use implied specifically the use of spironolactone. IVIG was used as a part of anti-inflammatory treatment for bilateral pneumonia. It was not discussed in the manuscript, as authors made a decision to focus on the ocular findings.

*Comment 7: Figure 3, classification of case reports in terms of patient age does not provide much to the discussion. Either write a more explanatory paragraph about it in the discussion section or delete it.*

**Response:** We thank the Reviewer for the comment. Corresponding section of the manuscript has been amended. Authors intended to demonstrate that a very small proportion of patients displayed no ophthalmological symptoms although their radiologic findings were consistent with choroid involvement, and the peak period for each symptom is between 20 and 45 years of age. Those findings might contribute to the differential diagnosis of the lupus choroidopathy.

*Comment 8: Finally, from a scientific point of view, this is not a literature review. This is just a well-written discussion covering the case reports published up to date. I recommend removing the Literature review from the main title.*

**Response:** We thank the Reviewer for the comment. The manuscript has been amended according to your suggestion,

### **Science editor**

***Comment 1:** This manuscript presented a female patient with a diagnosis of Systemic lupus erythematosus who developed lupus choroidopathy. Please explain how long they have treated the patient in case report section, explain whether other manifestations of SLE are improved together with visual impairments. Please add the mechanism of choroidal involvement in discussion. Please add the full name of the abbreviations of OCT and ICGA. Please describe what is meant with "poor condition." and explain Oxygen saturation and heart rate at presentation. Spironolactone was mentioned in the discussion, but it is not used in the treatment of this manuscript, please explain.*

*Language Quality: Grade B (Minor language polishing)*

*Scientific Quality: Grade C (Good)*

**Response:** We thank the Reviewer for the comments. The manuscript has been amended according to your suggestions.

### **Company editor-in-chief**

***Comment 1:** I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office 's comments and the Criteria for Manuscript Revision by Authors. Before its final acceptance, the author(s) must provide the Signed Informed Consent Form(s) or Document(s) of treatment. Please provide the original figure documents. Please prepare and arrange the figures using*

*PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.*

**Response:** We thank the Reviewer for the comment. Manuscript has been edited according to the comments and suggestions of the reviewers. New version of the manuscript and all figures are provided.