November 10th, 2022

Dear Editor,

We really appreciate the efficient review of our manuscript entitled "*Systemic combined with intravitreal methotrexate for relentless placoid chorioretinitis: A case report and literature review*" (Manuscript ID: 80565). Thank you so much for kindly supplying us this precious opportunity to revise our paper. We have studied the reviewers' insightful and constructive comments carefully and have made point-by-point responses and corrections through which we hope the revised manuscript can fulfill the standards of '**World Journal of Clinical Cases'** for publication. In the resubmitted manuscript, we have highlighted all the amends in red font. The main corrections in the paper and the responses to the reviewer's comments are as below. Thank you so much for handling with our manuscript.

All the best.

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Reviewer #1:

Specific Comments to Authors: I would like to congratulate the authors on a very interesting and well written manuscript. I would like to suggest the authors to polish the language of the manuscript and also to comment on the reported incidence, gender predisposition and common age of presentation in the first para of introduction section.

Response 1: Thank you for your valuable comment and suggestions. We have polished the language of the manuscript. The epidemiology of relentless placoid chorioretinitis has not yet been clearly elucidated due to the rarity of this disease. In a retrospective study of a case series by Jyotirmay et al [1], the average age of morbidity was 34 years old and males more than females. We have revised and added description about the epidemiology in the part of Introduction as follows.

Introduction: "Relentless placoid chorioretinitis (RPC), also referred to as ampiginous choroiditis[1], is a relatively new and rare entity that was proposed by Jones BE *et al.*[2] in 2000. The average age of morbidity was 34 years old and a male preponderance was found in a case series by Jyotirmay et al [3]."

References:

[1] **Jyotirmay B,** Jafferji SS, Sudharshan S and Kalpana B. Clinical Profile, Treatment, and Visual Outcome of Ampiginous Choroiditis. *Ocular Immunology and Inflammation* 2010; **18**: 46-51 [DOI: 10.3109/09273940903402637]

Reviewer #2:

Specific Comments to Authors: Case presentation section: it can be written in two or three paragraphs under a single heading. Because the content of each title consists of only one sentence and looks very disjointed.

Response 1: Thank you for your insightful suggestion. We have to apologize for disjointed paragraphs in the part of Case presentation. As you kindly reminded, we have removed excessive subheadings and made the CASE PRESENTATION part a whole as follows.

Case presentation: "A 16-year-old male was hospitalized complaining of progressive painless blurred vision and temporal scotoma in his right eye for one week. The patient denied any previous ophthalmic diseases, febrile or flu-like episodes. On initial examination, his visual acuity was 20/20 and intraocular pressure was normal in both eyes. Anterior segment examination was unremarkable. Fundoscopic examination of the right eye revealed 1+ vitreous cell, along with well-circumscribed fresh creamy-white serpiginous-like lesions around the optic disc and multiple pigmented scars in nasal and inferior mid-peripheral retina (Figure 1A). The lesions around the optic disc showed hyperfluorescent in autofluorescence (AF) and in the late phase of fundus fluorescein angiography (Figure 1B and 1C). Optical coherence tomography (OCT) revealed normal fovea but disorganization of outer retina in nasal macular area (Fig. 1d). The fundus of the left eye was unremarkable (Figure 1E). Uveitis workup including complete blood count, blood biochemistry, urinalysis, erythrocyte sedimentation rate, c-reaction protein， chest CT and brain magnetic resonance imaging were all normal. Serology for syphilis, toxoplasma, human immunodeficiency virus and T-SPOT were all negative. Peribulbar injection of triamcinolone acetonide (TA) 20mg

was prescribed by the first consultant.

Two weeks later, however, his right eye's vision declined to 20/50. Fundus examination revealed lesion extension which was hyperfluorescent in AF and hypofluorescent in indocyanine green angiography (Figure 2A-C). OCT showed fovea involvement, as well as atrophy of outer retinal layers and subretinal fibrosis (Figure 2D). The left eye remained unremarkable (Figure 2E). The patient was then referred to us by the first doctor. The widespread, multifocal and serpiginous-like pattern, together with the multimodal imaging features and poor response to treatment led us to the diagnosis of RPC and oral MTX (20mg/week) and prednisolone (0.6mg/kg/day) were administered. Considering the rapid progression and central involvement, intravitreal MTX 0.4mg was also given in order to preserve vision.

Two weeks later, the fresh lesions in the right eye started to become transparent and pigmented (Figure 3A). No progression in the right eye was seen in OCT (Figure 3B), but a new creamy-white lesion appeared at six-o'clock in the equator of the left eye (Figure 3C). Considering the relatively short period of oral MTX after initiation, no further adjustment of treatment was adopted.

Another two weeks later, the lesions in the right eye were almost transparent and hypofluorescent in AF (Figure 3D,E). OCT showed no further progression with ellipsoid zone at the central fovea partially recovered (Figure 3F), and his visual acuity also improved to 30/50. In the left eye, the newly occurred lesion also started to turn transparent, but kept hyperfluorescent in AF (Figure 3G,H). The prednisolone was then tapered off gradually, leaving oral MTX as maintenance therapy.

The patient was then followed for 21 months, and his vision improved to 20/20 and remained stable. At last visit, MTX had been discontinued, and no appearance of new lesions or enlargement of the scars were further noted in both eyes (Figure 3I-M)."