

Manuscript NO: 77608

Title: Intravitreal injection of conbercept for bullous retinal detachment: a case report

Point-by-Point Response

Reviewer #1:

Thank you for your favorable comments on our article. According to your comments, we provided point-by-point responses to the reviewers' comments as below.

Line 43: Delete this text. It is convenient that this therapeutic agent be briefly described in this section.

Response: Thank you for your valuable comment. We have deleted this sentence accordingly.

Line 75: How was that dose determined?

Response: We determined the injection dose to be 0.5 mg (equivalent to an injection volume of 0.5 mL) based on the recommended dose of conbercept.

Line 77: How much time passed between the first and the second injection?

Response: We used the "1+PRN" regimen. The administration was conducted, as required, after one injection, and the time interval between the two injections was not less than one month. We have modified the manuscript's content as follows:

"The patient received a second injection of the same dose 1 month after the first injection."Lines 117-118.

Line 78: Was the dose of the first injection the same as the second injection?

Response: The second dose was the same as the first dose. We have modified the manuscript's content as follows:

"The patient received a second injection of the same dose 1 month after the first injection."Lines 117-118.

Line 90: This text must be included in the pathophysiology section.

Response: Thank you for your valuable comment. We have modified the manuscript's content as follows:

"Tsukahara and Uyama^[5] further detailed the pathogenesis of this disease as follows: increased choroidal vascular permeability alters RPE, thereby damaging RPE outer blood-retina barrier. Subsequently, fibrinogen and protein leak out, and subretinal exudation occurs." Lines 137–141.

Line 125: Although it is interesting and important to note that this is the first case treated with conbercept, it is convenient to highlight the main possible advantages over other VEGF inhibitors.

Response: Thank you for your valuable comment. We have modified the manuscript's content as follows:

"Anti-VEGF drugs are used for treating such diseases because of their anti-permeability characteristics, which reduce the high permeability of choroidal blood vessels^[14-15]. To date, there has been only one case report of treatment of bCSCR with intravitreal injection of anti-VEGF without clinical improvement^[16]. The patient was treated unsuccessfully with intravitreal bevacizumab (1.25 mg) and ranibizumab (0.5 mg) followed by successful treatment with reduced fluence photodynamic therapy^[16]. Ranibizumab and bevacizumab are derived from a murine monoclonal antibody^[15]. "Lines 170–177.

“We selected the anti-VEGF agent, conbercept, which is a recombinant fusion protein with different chemical structure and pharmacological properties from other anti-VEGF drugs. Conbercept is fused by VEGF receptors 1 and 2 to the Fc portion of human immunoglobulin G1 that blocks VEGF-B, placental growth factor, and all VEGF-A isoforms^[15]. We proposed the potential efficacy of conbercept in bullous retinal detachment, considering its anti-permeability properties in decreasing choroidal vascular hyperpermeability. The current patient demonstrated a significant improvement in retinal anatomical reduction following intravitreal injections of conbercept.” Lines 178–186.

Line 137: VEGF inhibitors instead of "compatriot"? In the discussion section it is important to justify the use of conbercept instead of other therapeutic agents and delve into the possible mechanism of action of this group of drugs in DRPE.

Response: Thank you for your valuable comment. We have corrected the related errors and added relevant discussions on the possible mechanism as follows:

“This case suggests that intravitreal injection of a VEGF inhibitor may be a considered therapeutic option for patients with bullous retinal detachment of DRPE. ”Lines 196–198.

“Choroidal vascular dysfunction is an important feature of DRPE pathophysiology^[7]. DRPE is characterized by the dilation of vessels in the outer layer of the choroid, atrophy of the inner layer of the choroid, and thick choroidal features with high choroidal permeability^[7, 8]. “Lines 163–166”

“Intravitreal injection of anti-vascular endothelial growth factor (VEGF) is also considered^[13]. Anti-VEGF drugs are used for treating such diseases because of their anti-permeability characteristics, which reduce the high permeability of choroidal blood vessels^[14-15].” Lines 169–172.

Reviewer #2:

We sincerely appreciate your professional review of our article. According to your nice suggestions, we have made extensive corrections to our previous draft. The detailed corrections are listed below.

1. In the introduction (L35-37): "Bullous retinal detachment, an extremely rare manifestation of diffuse retinal pigment epitheliopathy (DRPE) or chronic central serous chorioretinopathy (CSCR), is difficult to treat and can eventually result in loss of vision due to irreversible retinal damage (1-2). " I think the sentence is too long. "Bullous retinal detachment is an extremely rare manifestation of diffuse retinal pigment epitheliopathy (DRPE) or chronic central serous chorioretinopathy (CSCR). It is difficult to treat. It can eventually result in loss of vision due to irreversible retinal damage (1-2)." would be clearer.

Response: Thank you for your valuable comment. We have revised the sentence as follows: "Bullous retinal detachment is an extremely rare manifestation of diffuse retinal pigment epitheliopathy (DRPE) or chronic central serous chorioretinopathy (CSCR). It is difficult to treat and can eventually result in loss of vision due to irreversible retinal damage^[1-2]." Lines 60–63.

2. The discussion section should start with a brief summary of the case. The strengths and the weaknesses of the work should be pointed out.

Response: Thank you for your valuable comment. We have modified the manuscript's content as follows:

"We describe a case of intravitreal injection of conbercept that cured bullous retinal detachment. After two intravitreal injections, the patient exhibited retinal reattachment." Lines 132–134.

"This case suggests that intravitreal injection of a VEGF inhibitors may be a considered therapeutic option for patients with bullous retinal detachment of DRPE. This treatment is safe and simple, avoiding the need for complex surgical techniques with high risk of complications. However, our conclusion is based on a single case report with no long-term outcomes. Therefore, a larger case series and longer follow-up periods are needed to further explore such treatment." Lines 196–201.

3. (L129-131) "At the time of presentation, our patient mentioned that she was worried about her daughter's diabetes, and was therefore in a state of long-term anxiety, which might have been one of the causes of her illness." This sentence is too long and unnecessary to write in a scientific article. I suggest " The stress factor was present in our case".

Response: Thank you for your valuable comment. We have revised the sentence as follows:

"The stress factor was observed in this case." Lines 188–189.

4. In the conclusion, the authors should summarize their case report before the scientific generalities.

Response: Thank you for your valuable suggestions; accordingly, we have revised the manuscript as follows:

"In conclusion, we describe a case of intravitreal injection of conbercept that cured the bullous retinal detachment of DRPE." Lines 195–196.

5. The reference N°16 is too old. It would be better to use an updated reference.

Response: Thank you for your valuable suggestions; accordingly, we have updated the references as follows:

“16. Wykoff CC, Lujan BJ, Rosenfeld PJ. Photodynamic therapy of bullous central serous chorioretinopathy with subretinal exudate and a tear of the retinal pigment epithelium. Retin Cases Brief Rep. 2009;3(2):218–23.” Lines 190-192