Author’s response to reviews

Title: Atypical acute retinal necrosis accompanied by Terson's syndrome: A case report

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Reviewer reports:

Ester Carreño (Reviewer 1): Although an interesting case, there are important issues that need to be clarified before considering publication.

- There is a lack of spaces between words along the manuscript.

- I would like to thank you for your comments. I apologize for any confusion caused by errors in the word program. I have reviewed the manuscript and revised the spacing between words.

- Intravitreal foscarnet is most commonly used than intravitreal ganciclovir worldwide, equally viral culture is currently abandoned as PCR technology is broadly used.

- Please rewrite introduction.

- As you mentioned, I agree that the intravitreal foscarnet is most commonly used than intravitreal ganciclovir worldwide and viral culture is currently abandoned as PCR technology is broadly used. Therefore, the second and third paragraph on page 4 of the introduction (background) has been modified as follows.

The diagnosis of ARN is usually based on clinical appearance and confirmation of causative viral DNA using serum or intraocular fluid antibody testing, viral culture, retinal biopsy, and polymerase chain reaction (PCR) [7,8]. It is now more preferable to test focal samples rather than conducting a serum antibody titer for viruses. Use of polymerase chain reaction (PCR)
system in aqueous humor and vitreous fluid samples is useful for identifying the viral origin [9,10,11].

The initial treatment for ARN is intravenous acyclovir (1500 mg/m2/day) for 5–10 days, followed by oral acyclovir (800 mg five times/day) for 4-6 weeks. Intravitreal foscarnet or ganciclovir injection may also have a role as adjunctive therapy in the management of patients with ARN. Intravitreal foscarnet in combination with systemic antiviral therapy may reduce the risk of retinal detachment in VZV associated ARN [12, 13].

I have also added the associated references on page 10.

Reference


- A positive serology does not confirm the diagnosis of ARN, the PCR positive for VZV confirms the diagnosis of VZV retinitis.

-> As you mentioned, I agree that the PCR positive for VZV confirms the diagnosis of VZV retinitis. Therefore, the 40 to 41 line on page 2 of the abstract has been modified as follows.

As a result of the polymerase chain reaction (PCR) analysis, varicella zoster virus (VZV) DNA was identified in the aqueous humor.

Also, the second paragraph on page 5 of the abstract has been modified as follows.

Anterior chamber paracentesis and PCR analysis of the aqueous humor have been performed. VZV DNA was identified in the aqueous humor. But, DNA for HSV-1, HSV-2, and cytomegalovirus was not detected.

- Not sure how Terson's syndrome was diagnosed. Did the patient had a subarachnoid haemorrhage? This is not clear as currently written. Fluorescein angiography at the moment of the vitreous haemorrhage could be helpful to prove that the vitreous haemorrhage was not secondary to retinal neovascularization due to the occlusive arteritis, which is rather more common than a Terson's syndrome.

-> I would like to sincerely thank you for your comments. Although the SAH finding was not found and the FAG was not performed at the time of vitreous hemorrhage increased in this case, there is an article in which Terson’s syndrome is reported by a suddenly increased intracranial
pressure (IICP) without the SAH. On the fluorescein angiography study, the non-perfusion area was localized at peripheral retina, and new vessel was not observed in the initial visit. In this case, the spinal tapping was performed in the department of neurology in our hospital at the time when the patient complained of headache, and intracranial pressure was 31 mmHg. Although the patient had been treated with intravenous acyclovir and oral prednisolone, the retinal lesions was worsened. At that time, the patient complained of headache and infarction was observed in the brain MRI image. The IICP was confirmed through spinal puncture. This suggests that the possibility of Terson’s syndrome due to suddenly increased intracranial pressure in this case. Therefore, the third paragraph on page 5 has been modified as follow and I have added the associated reference on page 10.

The spinal tapping was performed in the department of neurology in our hospital at the time when the patient complained of headache, and intracranial pressure was 31 mmHg. This suggests that the possibility of Terson’s syndrome due to suddenly increased intracranial pressure in this case [15].


- What was the time frame between intravitreal ganciclovir injections?

-> The second paragraph on page 6 of the case presentation has been modified as follows.

After 5 intravitreal injections (from the 5 to 15 day of the admission),

- What was the dose of the oral prednisone/prednisolone?

-> The second paragraph on page 6 of the case presentation has been modified as follows.

combined with an oral prednisolone (tapering dose, 0.5m/kg/day).

- What was the evolution of the brain findings? Were this findings a consequence of viral encephalitis?

-> It may be thought of as viral encephalitis for lesions in the right occipital area. However, in the case of viral encephalitis, symmetrical lesions of the left and right brains are seen, and the meninges tend to thicken. But, in this case, the lesion of brain was localized in the right hemisphere, and no evidence of thickness of the meninges was observed. Also, according to the reading of a specialist in the department of radiology in our hospital, the brain image was interpreted as hemorrhagic infarction. Therefore, this case is more likely to cause lesions due to hemorrhagic infarction than viral encephalitis.

Francesco Pichi (reviewer 2)

The Abstract is difficult to read because of extensive english misspells.
I would like to sincerely thank you for your comments. I apologize for any confusion caused by errors in the word program. I have reviewed the manuscript and revised misspells.

It is not very clear from reading the Abstract how the diagnosis of Terson was made; the MRI findings seems consistent with herpes encephalitis, or am I mistaken?

As you mentioned, I agree that there is not clear explanation about the diagnostic method of the Terson’s syndrome. Therefore, the 47 to 49 line on page 2 of the abstract has been modified as follows.

The spinal tapping was performed in the department of neurology in our hospital at the time when the patient complained of headache, and intracranial pressure was 31 mmHg. This suggests that the possibility of Terson’s syndrome due to suddenly increased intracranial pressure.

It may be thought of as viral encephalitis for lesions in the right occipital area. However, in the case of viral encephalitis, symmetrical lesions of the left and right brains are seen, and the meninges tend to thicken. But, in this case, the lesion of brain was localized in the right hemisphere, and no evidence of thickness of the meninges was observed. Also, according to the reading of a specialist in the department of radiology in our hospital, the brain image was interpreted as hemorrhagic infarction. Therefore, this case is more likely to cause lesions due to hemorrhagic infarction than viral encephalitis.

The conclusion of the Abstract is a bit far fetched... MRI can help identify "other causes of atypical clinical features of ARN accompanied with Terson's syndrome"? I am not sure about the meaning of this sentence.

I totally agree with your comments. Therefore, the second paragraph on page 3 of the conclusion has been modified as follows.

In the event of a poor response to traditional treatment such as intravenous acyclovir, intravitreal ganciclovir may have a role as an adjunctive therapy in patients of VZV associated ARN combined with Terson’s syndrome.

BACKGROUND

Some repetitions that render the reading difficult (retinal retinitis).

As you mentioned, I do not use the terms consistently, and I think it can cause confusion in the interpretation of the background. Therefore, I have unified the term of the diffuse necrotizing retinitis on page 2 of the abstract and the first paragraph on page 4.

Please remove the sentence "hemorrhage of the retina...is uncommon".

I totally agree with your comment. Therefore, I have removed the sentence.
CASE PRESENTATION

Once again, no spaces between the words. The Authors seem not to have checked the pdf before approving the manuscript.

-> I apologize for the any confusion that may have caused by not checking the pdf file before approving the manuscript. I have reviewed the entire manuscript and revised the spacing between words and misspells.

I have some issues with this Person diagnosis. The Author mention that a "headache was diagnostic of increased intracranial pressure". Was a lumbar puncture performed?

The diagnosis of Terson seems to be based here only on vitreous hemorrhage, can the Author confirm that a tap was high and thus the intracranial pressure was elevated? Otherwise this Terson seems a bit stretched.

-> I would like to thank you for your comments. I agree with your opinion. Although the SAH finding was not found and the FAG was not performed at the time of vitreous hemorrhage increased in this case, there is an article in which Terson’s syndrome is reported by a suddenly increased intracranial pressure (IICP) without the SAH. On the fluorescein angiography study, the non-perfusion area was localized at peripheral retina, and new vessel was not observed in the initial visit. In this case, the spinal tapping was performed in the department of neurology in our hospital at the time when the patient complained of headache, and intracranial pressure was 31 mmHg. Although the patient had been treated with intravenous acyclovir and oral prednisolone, the retinal lesions was worsened. At that time, the patient complained of headache and infarction was observed in the brain MRI image. The IICP was confirmed through spinal puncture. This suggests that the possibility of Terson’s syndrome due to suddenly increased intracranial pressure in this case. Therefore, the third paragraph on page 5 has been modified as follow and I have added the associated reference on page 10.

The spinal tapping was performed in the department of neurology in our hospital at the time when the patient complained of headache, and intracranial pressure was 31 mmHg. This suggests that the possibility of Terson’s syndrome due to suddenly increased intracranial pressure in this case [15].

The third paragraph on page 6 has been modified as follows.

The spinal tapping was performed in the department of neurology in our hospital at the time when the patient complained of headache, and intracranial pressure was 31 mmHg.

Reference

The images are striking but major editing to the manuscript language and clarification on the Terson diagnosis are necessary.

I sincerely appreciate your hard work and effort in reviewing the manuscript. Thanks to your sincere comments, the manuscript could be a valuable and meaningful paper. Once again thank you for reviewing.