

Dear Editor and Reviewers,

Thanks for your comments concerning our manuscript entitled “Intraocular fluid metagenomic detection and diagnosis tuberculous uveitis: A case and literature review” (Manuscript ID: 79721). Those comments are all valuable and helpful for revising and improving our paper. We have studied all comments carefully and have made conscientious correction. Revised portion are marked in red in the paper. I have modified and supplemented my manuscript based on each point raised by the Editor and Reviewers, and replied the advice piece by piece. Below I have attached the new edition of my manuscript for Editor and Reviewers. Please find my itemized responses in below and my revisions in the re-submitted files.

Title: Please rewrite the title in a more specific manner.

Response: the title has changed from “Intraocular fluid metagenomic detection and diagnosis tuberculous uveitis: A case and literature review” to Diagnosis of tuberculous uveitis by macrogenome of intraocular fluid: a case report and literature review”

Key Words: Please rewrite ‘Metagenomic sequencing; Xpert test for tuberculosis’ as ‘metagenomic next-generation sequencing; Xpert’ in the Key Words list and add more relevant keywords if any.

Response: the key words has changed from “Metagenomic sequencing; Xpert test for tuberculosis” to “metagenomic next-generation sequencing; Xpert”, and “case report” was added.

Abstract: Do the authors mean ‘Metagenomic next-generation sequencing (mNGS)’ by ‘tested for intraocular infection by second-generation gene’?

Response: Thank you for reminding, the “tested for internal infection by second-generation generation” was the correct expression.

Case Presentation: Chief Complaints 1. Please revise as ‘occasional dry cough’ instead of mentioning cough twice.

Response: The expression in the manuscript is “occidental dry cough”

2. Cephalosporin is not an anti-inflammatory treatment, please revise appropriately.

Response: Thanks for reminding, “anti-inflammatory treatment” has been deleted.

3. Please use ‘days’ instead of ‘d’. Physical examination upon admission 1. Please rewrite the paragraph in a more systematic and scientific manner. Laboratory examinations 1. Please mention whether Xpert was carried out for IO fluid or any other sample. Final diagnosis 1. Please use same terminology for gene test throughout the article (e.g. mNGS). 2. It’s Brain MRI, not Head MRI. 3. Please rewrite the systemic diagnosis without numbering. 4. Please clarify and

rewrite the sentence ‘Through a variety of molecular biological detection means, the etiological diagnosis is clear’ .

Response: “days” is expressed as “d” , which meets the writing requirements of WJCC. Xpert is not only used to check sputum and placental tissue, but also used to extract anterior chamber aqueous from intraocular fluid. Because there are few samples, only mNGS was sent for examination in our research. Laboratory examinations has rewrite. “Head MRI” has changed to “Brain MRI” Systemic diagnosis as changed to Acute hematogenous disseminated pulmonary tuberculosis; Tuberculous pleurisy; Tuberculous encephalitis Left tuberculous meningitis. Ophthalmologic diagnosis: Tuberculous uveitis in both eyes; Retinal vasculitis in both eyes. Through a variety of molecular biological detection means, the etiological diagnosis is clear. The differential diagnosis of tuberculous uveitis includes Non-infectious uveitis: rheumatic disease, Behcet’ s disease, VKH, ankylosing spondylitis, etc., Other infectious uveitis: syphilitic uveitis, viral uveitis, toxoplasmic chorioretinitis, etc.; and masquerade syndrome: uveitis caused by intraocular tumor or intraocular metastasis of tumor. “Through a variety of molecular biological detection means, the etiological diagnosis is clear” as changed to “Determine the cause of diagnosis through a variety of molecular biological detection methods”.

4. Differential diagnosis should come before final diagnosis. Please note these are the differentials of Granulomatous Uveitis. Treatment 1. Please use ‘day’ instead of ‘d’ . 2. Please clarify regarding the drugs ‘pralprofen eye drops and compound topicamide eye drops’ and also regarding the phrase ‘3 times/bedtime’ .

Response: Thank you for your reminder. After verification, Differential diagnosis of "tuberculous uveitis includedNon-infectious uveitis: rheumatic disease, Behcet's disease, VKH, ankylosing spondylitis, etc., Other infectious uveitis: syphitic uveitis, virtual uveitis, toxoplasmic chorioretinitis, etc.; and masked syndrome: uveitis caused by intraorganic tuner or intraorganic r metastasis of tumor" delete, displayed can be without any need, It has been deleted in the text. “days” is expressed as “d” , which meets the writing requirements of WJCC. pralprofen eye drops has changed to pranopfen eye drops, compound topicamide eye drops has changed to compound tropicamide eye drops, 3 times/bedtime’ has changed to three times before bed.

Outcome and Follow-up 1. Please note it’ s known as ‘anterior chamber reaction and vitreous haze’ , not ‘opacity’ . 2. There are separate grading systems available for AC Cells and Flare and Vitreous Haze. Thus, rewrite the paragraph accordingly.

Response: Thank you for your reminder. anterior chamber reaction and vitreous opacity has changed to anterior chamber reaction and vitreous haze. Output and Follow-up have been rewritten: After systematic treatment, the general condition gradually improved, and the corrected vision of the left eye gradually increased from 0.08 to 1.0. According to uveitis standard working group (Standardization of Uveitis Nomenclature, SUN) standard assessment, the grade of anterior chamber cells and vitreous opacity was evaluated. The patient's anterior chamber aqueous was from three grades: the anterior chamber had 21 to 50 cells/field of vision, and the iris and lens were difficult to recognize gradually to grade 1: the aqueous humor had no anterior chamber flash

or weak anterior chamber flash, and no inflammatory cells. Vitreous opacity gradually changed from 4+ to 0.5+. The fundus photography is shown in Figure 1A-F, and the changes of ocular B-ultrasound are shown in Figure 2 A-D. The changes of anterior segment photography are shown in Figure 3 A-B.

Discussion: 1. It's not clear from the study whether Xpert was used for only sputum and placental tissue or was used for IO fluid also, along with mNGS.

Response: Xpert is not only used to check sputum and placental tissue, but also used to extract anterior chamber aqueous from intraocular fluid. Because there are few samples, only mNGS was sent for examination.

2. Rather than mentioning IO fluid, please clearly mention whether it's Vitreous Humor or Aqueous Humor throughout the article.

Response: In this case, the patient's Aqueous Humor was sampled for macrogene sequencing.

3. Please clarify what it means by 'single case report with a small number of samples'. Figures: 1. Please clarify what the numbers (e.g. 8-1) signify. 2. In Figure 3, please describe all the findings clearly in a standardized manner. 3. Please clarify what is suttonoid KP.

Response: Thank you for your reminder. 'single case report with a small number of samples' mean that "This manuscript was only one case report", The number (e.g. 8-1) represents the date, indicating the change of the image with time, and the expression has been modified. Figure 3 has changed the findings; suttonoid KP has changed to keratic precipitate KP, the presence of keratic precipitate indicates that the patient has chronic or granulomatous inflammation.

Other Comments: 1. The authors have mentioned about the use of multimodal ophthalmic imaging in this case. However, use of multimodal imaging is not found for this case in the article. If used, please provide the relevant information. 2. Ophthalmological examination part is grossly deficient in the article. 3. The authors need to use more scientific terminologies as appropriate throughout the article. 4. Grammatical and sentence construction errors need to be rectified appropriately throughout the article.

Response: Thank you for your suggestion. 1. Multimodal optical imaging is part of the discussion, The last paragraph of the discussion was revised: This article could remind tuberculous physicians that when systemic problems such as blood type separated tuberculous lesions and tuberculous meningitis were found, should pay attention to the diagnosis of possible tuberculous eye problems, so as to avoid missing diagnosis and delayed treatment, resulting in blindness, and comprehensively consider the infection of other parts of the body in the diagnosis and treatment of tuberculous eye disease, and use molecular biological detection methods to improve detection rate, and give patients early diagnosis and standardized treatment. 2. The contents of ophthalmic examination have been supplemented in the general examination, and detailed notes have been made in the picture explanation. 3. The scientific terminologies in the full text have been checked

and corrected; 4. We have checked the full text and revised the grammar.

Please don't hesitate to contact me with any further question. Thank you again and look forward to your reply.