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Journal Name:	Ophthalmology Research: An international Journal
Manuscript Number:	2014_OR_12474
Title of the Manuscript:	Immune Reconstitution Inflammatory Syndrome (IRIS) Presenting As Bilateral Severe Granulomatous Sclerouveitis In A HIV-Infected Patient With Mycobacterium Tuberculosis Infection: A Case Report
Type of the Article	Case Study

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

(<http://www.sciencedomain.org/page.php?id=sdi-general-editorial-policy#Peer-Review-Guideline>)



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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
<u>Compulsory</u> REVISION comments	There is a substantial revision that should be made to this manuscript before it is ready for publishing.	
<u>Minor</u> REVISION comments	MS:2014_OR_12474 Immune Reconstitution Inflammatory Syndrome (IRIS) Presenting As Bilateral Severe Granulomatous Sclerouveitis In A HIV-Infected Patient With Mycobacterium Tuberculosis Infection: A Case Report There should be changes made to the heading itself. Namely, material which has been provided would suggest that the patient had immune recovery uveitis (IRU) rather than immune reconstitution inflammatory syndrome (IRIS) as the authors suggest. (Please refer to opportunistic vs. IRU comment below).	Dear reviewer, Thank you for the review and constructive comments. We have selected IRIS as the title for the case as we think IRIS is more suitable in describing in this case. IRU is a form of IRIS and most of the IRU were associated with CMV retinitis. The patient was first diagnosed as bilateral panuveitis with differential of VZV or TB. Mantoux test was negative and ESR was not raised at presentation and the patient was then treated with IV antiviral. Ocular sample for PCR for TB/ VZV was not done as at this point, we think clinical diagnosis is sufficient. The patient failed to respond to the antiviral treatment and at this time, he developed cervical lymph node which yield positive for TB, repeated Mantoux was positive. Presumed ocular TB was diagnosed based on the Mantoux test and positive culture from lymph node biopsy. This was further supported by the response to antituberculosis treatment.



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	In addition there is a dilemma if the patient in question had uveitis due to varicella zoster virus (VZV) infection or due to tuberculosis (TB) seeing that VZV has not been excluded. On the other hand it was stated that the patient had TB but this was not properly substantiated i.e. enlarged lymph nodes which were present on the second test and negative TB biopsy bring this to question. How do the authors explain repeated lymphadenopathy and negative biopsy? Clinical aspect of uveitis (necrotizing scleritis; mutton fat precipitates; disk edema, etc.) present one with the possibility of it being VZV imposing sclerouveitis. According to authors “herpetic infection due to negative TB workout” which suggests that the conclusion was reached based on empirical deduction and not evidence based data. Why did the authors not use (precise) PCR method for diagnosing the above mentioned, and if they did, they did not mention the fact. What was the authors excluding diagnostic criteria? As far as the abstract, and the manuscript itself, is	The TB after ART could be due to ongoing immunodeficiency. However, the initial anergy Mantoux test and positive repeated Mantoux test within 2 weeks; and a paradoxical inflammatory response after the treatment started for the opportunistic infection made the possibility of reconstitution inflammatory response to the tuberculosis antigen; therefore raise the possibility of “unmasking” IRIS in this scenario. When he developed paradoxical deterioration 6 weeks after antituberculosis treatment, we have ruled out the possibility of other infection and toxicity to antituberculosis therapy. A new lymph node was seen however the cultures was negative. This supported the possibility of paradoxical IRIS as usually the new site of inflammation will yield sterile cultures. A CD4 count was repeated at this time and showed increment from 104 to 243. PCR and CD4 were not routinely due to the limited resource setting.
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	concerned I am of the opinion that the work should be revised and written in accordance with the new data. The authors should maybe add to the reference material that they used and make their introductory section a bit fuller. As far as therapy is concerned – particular medication used as part of the treatment plan should be precisely and concisely stated. (i.e. both regarding ART; anti – TB and anti – VZV treatment). Initial manifestation here is typical of granulomatous uveitis, total uveitis, (“mutton-fat keratic precipitates”; “hyperemic optic disc with presence of choroiditis”; “no evidence of choroidal tubercle”), with possible opportunistic infection in HIV positive individual. So, it should be clear that this is not the case of iridocyclitis. It would have been interesting for the authors to perform precise testing during this phase. In case that they have, they should state it in their work. Did the patient have an improvement of his	
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	immune system following ART therapy? The authors did not precisely state what exactly “restoration of immune response” entails and what are the reasons behind it. There is no comparative data with other authors and/ the authors themselves (such as for example CD4 levels, and other indicators, before and after ART therapy and/ certain period of time). So there is a question raised. Is it possible that this is a case of TBC lymphadenitis as a secondary, opportunistic, infection in presence of HIV infection? There is no evidence which confirms that sclerouveitis is a VZV infection as opposed to TBC immune recovery uveitis. Once the authors decide if this is the case of: immune recovery uveitis in the first place or an opportunistic infection VZV / TB; IRIS / IRU; they should consider revising and rewriting their discussion as well. Figures are clear but, due to the previously mentioned facts, not supported by the data provided.	
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	In conclusion, I am of the opinion that this case report requires further evaluation before it is ready for publishing.	
<u>Optional/General</u> comments		