Reviewer's report

Title: Pleural Effusion as the Initial Clinical Presentation in Disseminated Cryptococcosis and Fungaemia: An Unusual Manifestation and a Literature Review

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Reviewer: Joshua Rhein

Reviewer's report:

Chen et al outline an interesting case of cryptococcosis in a renal transplant patient, initially presenting as a pleural effusion but culminating in disseminated disease including meningitis. Overall, I feel that this case presentation can contribute well to the clinical literature of cryptococcal disease, but only after some major revision have been made. In particular, the time line needs to be tightened-up and there needs to be less repetition of the case presentation in the discussion. I believe the discussion is overall misdirected and would be much more interesting if the authors expanded their discussion on treatment and potential reasons for unusual presentation, as outline below.

Major Compulsory Revisions

Major revision 1: The dates indicated in the text have no meaning to the reader as date of admission is not indicated. I recommend that the authors count in days rather than using dates, with the day 1 being the date of admission. In general, the timeline is somewhat confusing, and would go back and clarify throughout. This is important as the timing of things could give some insight into possible immune reconstitution inflammatory syndrome (patient was immunosuppressed then given rhG-CSF which could have stimulated immune system resulting in hyperinflammatory syndrome).

Major revision 2: There is overall too much repetition of the case presentation in the discussion section. Do not need to go over the entire history of the case in the discussion. Recommend revising, deleting repetitious material, and instead focus on diagnosis (done well), misdiagnosis of TB (done well), treatment (discussed little), and potential reasons why this was an unusual presentation (not discussed at all).

Major revision 3: I would recommend adding some of the following to the discussion:

1. Why did you choose the treatment you did? The 3-drug combination (ampho, flucytosine, and voriconazole) for extended duration of 8 weeks is a little unusual and outside of many international guidelines. Are the guidelines different in China? Would be an interesting discussion.

2. Why the unusual presentation? Is this a function of being a transplant patient (vs HIV-associated cryptococcosis)? Was he perhaps receiving too much...
immunosuppression? Did rhG-CSF contribute to the pathology of his presentation or perhaps the rapid deterioration of the patient? My guess is that it absolutely did, and would give for an interesting discussion.

Minor Essential Revisions

Minor revision 1: Please italicize 'C. neoformans' throughout.

Minor revision 2: Suggest placing sentence starting on line 35 further down in abstract, before the sentence that starts out as 'Cryptococcus spores were found...' on line 41.

Minor revision 3: Need to define acronym RICU on line 40 as this is the first occurrence in the manuscript.

Minor revision 4: Delete 'spores' in line 41 of abstract and where it appears again in the discussion. Cryptococcus appears as budding yeast in the CSF, not spores, so the statement is inaccurate.

Minor revision 5: Delete the sentence in line 43 as this is a complete repetition of the sentence that appeared earlier in the paragraph.

Minor revision 6: Indent new paragraphs in text.

Minor revision 7: Regarding the medication sulperazone in line 94. This may be a common antibiotic in China, but it is not used in much of the world, and readers might not be familiar with it. Suggest changing brand name to 'cefoperazone + sulbactam', which will help readers identify it as a broad-spectrum antibiotic.

Minor revision 8: Remove urine from the sentence in line 233. It is unusual to make a diagnosis of cryptococcosis by antigen found in urine.

Discretionary Revisions

1) Delete words 'the initial' in line 38
2) Delete comma in line 74.
3) Delete word ‘repeatedly’ in line 87.
4) Change ‘presented’ to ‘present’ in line 99.
5) Change word ‘transferred’ to ‘obtained and sent’ in line 134.
6) Insert word 'opening' between cerebrospinal and pressure in line 141.
7) Change word ‘dehydration’ to ‘intravenous hydration’ in line 143.
8) Change word ‘target’ to ‘targeted’ in line 191.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published
Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests.