Reviewer's report

Title: Miliary tuberculosis with co-existing pulmonary cryptococcosis in non-HIV patient without underlying diseases: a case report

Version: 0 Date: 05 Oct 2017

Reviewer: Onyema Ogbuagu

Reviewer's report:

Abstract- correct typos- example"patinet", avoid use of term "oriental", can say Asian
Background: cite this as an example of concurrent Cryptococcal disease and disseminated/military tuberculosis in an immunocompetent host- http://casereports.bmj.com/content/2016/bcr-2015-213380.abstract. yours is not the first case. Isnt being elderly an immunocompromized state?

Case presentation-

Mention pertinent negatives- curious about presence or absence of fevers, weight loss, night sweats. IS it possible that she only had 1 week of symptoms?

Would state that she had "no KNOWN history of exposure to tuberculosis"- you cannot be overconfident about lack of exposure to tuberculosis as patients may not recall or know this definitively

How can the physical exam, including the abdominal exam, be unremarkable in a patient who complained of abdominal pain?

Would avoid the term "shadows" when describing imaging findings, can use the term "infiltrates or opacities", is it accurate that both chest Xray and Chest CT showed similar findings?. CTs usually show "more". If yes, and findings were clear on CXR, why was a CT chest performed.

Why was an IL-2 soluble receptor level checked- you do not mention that she had pancytopenia which would prompt concern for macrophage activation syndrome? What was the hemoglobin level and platelet count?

I am surprised with her leukopenia that CD4 and CD8 counts were normal?
What were her liver function tests? you state that a biopsy showed granulomas suggesting liver involvement?

Why was a gastric aspirate performed to diagnose tuberculosis in an adult who was able to expectorate?

Why were so many biopsies performed including skin? what prompted it? Were there skin lesions- you say exam was totally unremarkable???

TB usually presents with caseous necrosis, all your biopsy specimens showed non caseating granulomas- could these be due to Cryptococcus rather than TB

You mention a positive PCR test for TB, was this GeneXpert test, was there any genotypic resistance reported?

Why was a three and not four drug regimen initiated in this patient (seems pyrazinamide was omitted)

Page 7, line 15- should be "...had increased..." not "was increased"

Evidence for cryptococcal disease is still weak- PAS stain is not specific to Cryptococcus (other fungi take up the stain) and a positive CrAG test while signifying exposure to Cryptococcus is not definitive evidence of disease. If organisms were present in tissue, why didn't it grow in culture (Cryptococcus is not a difficult organism to grow if present)? Moreover BAL studies were negative.

Page 10, line 7 - what do you mean by "blood diseases and kidney diseases?"

Page 11, I would be cautious with attributing a focus of infection arbitrarily to a single nodule, if solitary nodules are rare as you say for pulmonary cryptococcosis, why are you stating confidently that it represent the disease focus

It is speculative to state that a cryptococcal antigen test (which wasn't checked) would have been negative on admission.

Why advocate for Quantiferon test for diagnosing active TB? works best to define latent disease
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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