Reviewer's report

Title: Histoplasmosis Infection in Patients with Rheumatoid Arthritis, 1998-2009

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Reviewer: chadi hage

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The authors report on a very relevant topic in today's medical practice; histoplasmosis in the era of biologics (in this case used for the treatment of RA). This kind of data is needed to help clinicians who practice in parts of the world that are endemic to Histoplasma with potential applicability to other endemic mycosis as well.

This manuscript suffers from a major flaw: the selection of the cases was based solely on laboratory criteria with no consideration for the necessary clinical criteria of compatible clinical illness. As a result a number of the included patients did not have active disease but most likely old (healed) infection. This led to a dilution of the data and that might lead to confusion in their interpretation. For example 3 of the 4 cases where anti-TNF was restarted, did not appear to have active disease at the time of the diagnosis and therefore did not experience recurrence after anti-TNF was restarted. Since all 4 four are grouped as histoplasmosis that developed in patient taking anti-TNF, one might conclude that in 75% of the cases anti-TNF can be safely restarted after short duration of antifungals (case #1) or no antifungals (case #8). I strongly recommend that the cases be divided based on clinical review into two groups: active disease and inactive disease and the data reanalyzed especially in regards to the diagnostic tests, treatment and outcome. Such analysis might prove very valuable, as it may hint to how to distinguish active disease that requires anti-fungals and close follow-up from those with old/healed infection in whom treatment may not be indicated and anti-TMNF could even be continued.

The authors should acknowledge the fact that pulmonary involvement could have been underestimated because a sizable number of patients had only chest X-rays and no CT.

In the discussion section, the authors recommend using CXR to screen for “previous granulomatous infection, including histoplasmosis” prior to the initiation of DMARD/biologics. There is very little data to support such strategy. As quoted by the authors, Vail et al (transpl infec dise 2002) showed that pre-transplantation serology or radiographs did not predict development of histoplasmosis after the transplant. Similar data were reported in a review by Hage et al (CID 2010 Recognition, diagnosis, and treatment of histoplasmosis complicating tumor necrosis factor blocker therapy).

Level of interest: An article of importance in its field
Quality of written English: Acceptable

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