Reviewer's report

Title: P. marneffei Infection Involves the Primary Tracheal Structure: the First Case Report

Version: 2 Date: 3 March 2014

Reviewer: lina lee

Reviewer's report:

Manuscript: Penicillium marneffei infection involves the primary tracheal structure: the first case report

The manuscript reports a non-HIV-infected 28 y-o male who presented with pulmonary opacities and neurologic disease, was initially treated as tuberculosis, improved, then developed tracheal stenosis, was later diagnosed as having Penicillium marneffei infection by bronchoalveolar lavage fluid culture and tracheal biopsy specimen culture, and finally received antifungal therapy as well as tracheal reconstruction.

The topic is interesting and relevant to the journal. The case report is novel and adds medical knowledge to readers. There are, however, major flaws:

[A] Major compulsory revision:

1. The diagnosis of tuberculosis:

In the Introduction the authors wrote that the 28 y-o man presented with “neuromyelitis” (blurred vision, numbness of limbs), fever and pulmonary lesions, and was “misdiagnosed” as tuberculosis. Yet in the Case report the authors wrote that “tuberculosis and neuromyelitis were confirmed” (Case report line 5). Was tuberculosis diagnosed by sputum smear, sputum culture, CSF culture? Or is it a clinical diagnosis? Is there drug susceptibility test for the M. tuberculosis (MTB) isolate? The susceptibility test results are important because a resistant (or multi-drug resistant ) MTB isolate may lead to treatment failure with resultant tracheal stenosis.

The word “neuromyelitis” is also difficult to understand. Does it mean meningitis? In the case report the authors wrote that “Tuberculosis and neuromyelitis were confirmed. He was treated with isoniazid, rifampicin, pyrazinamide and ethambutol for tuberculosis and prednisolone 50 mg daily........Three months later, his vision recovered and numbness disappeared......” From these descriptions, it seems that the patient presented with meningitis and improved after anti-TB plus prednisolone therapy. Thus tuberculosis is not necessarily a misdiagnosis. At least neurologic symptoms improved after anti-TB treatment.

2. The diagnosis of Penicillium marneffei infection:

The authors wrote that 11 months after his initial presentation, the patient was referred to the authors’ hospital due to hoarseness and sore throat.
Bronchoscopy showed multiple protrusions on tracheal wall. Bronchoalveolar lavage fluid and tracheal nodule culture grew P. marneffei. The authors did not describe histology of the tracheal nodules, however, and it is not known if the histology shows specific findings of P. marneffei or MTB infection. With anti-fungal therapy including amphotericin B and itraconazole, the authors wrote that patient’s symptoms improved. Yet trachea lesions progressed to cause severe tracheal stenosis in 3 weeks. The authors did not discuss potential causes of anti-fungal therapy failure. It is possible that in this patient P. marneffei is a secondary infection that superimposed on a pre-existing laryngeal and tracheal TB. In that case the anti-fungal therapy is effective on penicillosis but could not stop the progression of laryngotracheal TB which ended up with severe tracheal stenosis. Co-infection of M. tuberculosis and P. marneffei has been reported in HIV patients (Deesomchok A, Tanprawate S. A 12-case series of Penicillium marneffei pneumonia. J Med Assoc Thai 2006; 89(4): 441). Although the present case is negative for anti-HIV, he is most likely immunocompromized (His CD4 T cell count was only 370) and could be co-infected with M. tuberculosis and P. marneffei.

3. Patient’s immunological status:

The authors wrote that HIV blood testing of the patient was negative. Yet his CD4 T cell count was only 370/uL. The authors did not perform immunological work-up to seek for possible causes of immunodeficiency, and did not discuss why this non-HIV patient contracted this rare infection. Because P. marneffei infection rarely occurs in normal hosts, such work up and discussion are mandatory.

4. The writing is redundant and way too long.

The manuscript needs extensive editing and to be greatly shortened. The authors always need to write a complete wording when an abbreviation first appears (such as bronchoalveolar lavage fluid for BALF, in Case report, P. 4, line 7). Some words are hard to understand or incorrect, like: delitescence (Introduction, line 10), neuromyelitis (in Introduction and Case report), primary trachea (Introduction, P. 2 line 2), lethal tracheostenosis (Introduction, P. 2, line 3; the patient survived, therefore the stenosis was not lethal), ecphyma (in Introduction and Case report).

5. In the legend of Figure 7b the authors wrote that “the yeast form of P. marneffei has a characteristic morphology including a transverse septum”. Yet in the photo no such septum can be seen.

6. There are two incorrect marks on figures (Figure 1 and Figure 2).

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

**Quality of written English:** Not suitable for publication unless extensively edited
**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.