Reviewer's report

Title: High Prevalence of Bronchiectasis is linked to HTLV-1-associated inflammatory disease

Version: 1 Date: 21 February 2015

Reviewer: Lloyd Einsiedel

Reviewer's report:

As noted by the authors, the spectrum of clinical disease that is associated with HTLV-1 infection remains to be defined. Until recently, the association between HTLV-1 infection and pulmonary disease has largely been neglected. Recent studies from central Australia have shown a clear association between infection with HTLV-1 and bronchiectasis (BEx). However, in this region the HTLV-1c subtype infects Indigenous Australians and whether infection of other populations with the cosmopolitan strain, HTLV-1a, is associated with similar lung injury warrants investigation. The attempt by Honarbakhsh and Taylor to study this association in a UK cohort is therefore welcome. However, their study is not placed in the context of the current literature and its retrospective nature results in a number of significant methodological problems that limit the validity of the conclusions drawn.

Major Revisions:

i) The authors include only a single retrospective study from central Australia (CID 2012); however, two other relevant studies have been published by this group. These include a case-control study (OFID 2014) in which higher HTLV-1 PVL were associated with BEx and a clear association was found between the extent of pulmonary injury on HRCT chest and HTLV-1 PVL. Indeed, HTLV-1 PVL was the only identifiable risk factor for BEx, the adjusted OR for BEx was 1.8. In another retrospective study that included nearly 1500 subjects of whom one-third were HTLV-1 infected (PLOS NTD 2014), HTLV-1 infection was again associated with BEx in an adjusted model. Interestingly, HTLV-1 infection was also associated with increased admission numbers for all respiratory conditions studied with the exception of COPD.

ii) The small number of patients who received CT chest imaging raises the question of selection bias and severely limits the conclusions that can be drawn from this study. Thus, (Results: line 157) only 15% (64/413) of the cohort received any imaging and in only 3% of cases was this by HRCT chest. Older CT scans in particular have a low sensitivity for detecting BEx and these were presumably performed in patients with suspected malignancy. Presumably, those patients with recurrent chest infection/chronic cough were more likely to have an HRCT chest and providing data for HRCT and conventional CT results separately would be helpful to the reader.

iii) The study is potentially further biased by the heterogeneity of a cohort in which 70% of subjects were of Afro/Carribean origin. The authors claim that this
group was less likely to be affected by BEx; however, this could also result from differences in health seeking behaviour. Were the 'other races' more likely to have HRCT?

Given that the median age of SPs and ACs was 59 and 44, respectively, claims that there were no other identifiable causes of BEx seem overstated (results, line 169). Globally, the major cause of BEx remains early childhood infection and accurately obtaining such a remote history is extremely difficult, particularly among those born overseas. Were other tests performed to exclude other causes (immunoglobulin deficiency, autoimmune disease, alpha 1 antitrypsin deficiency etc)?

iv) smoking history should be included (?traction bronchiectasis)

These limitations should be clearly stated in the discussion and the claim that there were no other identifiable causes of BEx should be removed (line 244).

Minor revisions
i) proviral load is generally used for HTLV-1 rather than viral load (line 67) because the latter implies the presence of detectable virions in plasma.

ii) Methods, line 130, the diagnostic criteria used for BEx should be described.

iii) Results, line 172, data should be provided to support the claim that the duration of symptoms was 1-3 years after HTLV-1 diagnosis.

iv) Table 1 heading implies that all subjects had HRCT (rather than any chest imaging). This should be corrected.

iv) It would be helpful to describe the extent and type of bronchiectasis in Table 2.

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

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests