Reviewer's report

Title: Influenza A H5N1 and HIV co-infection: Case Report

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Reviewer: Julian Wei Tze Tang

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Major Compulsory:

There are some details which are rather vague in the case report. Whilst it is understood that the authors are focusing on investigating the immune responses that may be relevant to the pathogenesis of H5N1 in an HIV-infected patient with a specific type of immunodeficiency, the lack of detail elsewhere make their findings (as reported) less convincing. Also, such details need further clarification for infectious disease physicians who may not be specialists in H5N1 or HIV/AIDS, per se, as well as to make this case report a more authoritative reference for future studies.

The authors refer to secondary pneumonia in their Conclusions, as well as the starting of broad spectrum antibiotics in their case history, as well as reporting the findings of Aspergillus fumigatus in the nasopharyngeal aspirate. Since secondary bacterial pneumonia is a significant cause of mortality in human influenza infections, they should be more specific about these details (some of which can be supplied as online material - only the authors' cover letter was supplied with this manuscript for review).

What antibiotics were started?
What bacterial cultures were requested?
What were their results (presumably all negative)?
Was P jiroveci eventually found/excluded in this patient? The presenting symptoms may be due to this agent, particular since he had another AIDS-defining illness - Aspergillus fumigatus?

What about TB/MAC, etc.? Given that Aspergillus was present, these other opportunistic HIV/AIDS respiratory pathogens (or their absence) should at least be mentioned - some of these may present in similar ways and may also confound their findings and conclusions with regard to the interpretation of the cytokine responses as related to the clinical outcomes of this patient.

Also, although the rising CRP, neutrophilia and return of the patient's fever is mentioned, only the findings related to Aspergillus are mentioned. Here the (presumably) negative findings for other secondary bacterial pathogens should be mentioned. Are these clinical findings explained by the Aspergillus alone?
There may be other local unusual, bacterial or parasitic infections to which this household chicken farmer (presumably) may have been exposed - were such
pathogens excluded (e.g. atypical pneumonias)

Oseltamivir was not started until admission, 4-days post-illness onset, and testing showed that the H5N1 viral load was decreasing in the NPA and undetectable in the plasma. So it is unlikely that the oseltamivir contributed much to this patient’s clearance of H5N1 - the authors should briefly mention this - again for less specialised readers.

Please would the authors add the presenting CD4 cell count in the case history. Although this is shown in Figure 1, this would be helpful, particularly in light of the presenting low HIV load of 510 cop/mL. Also, this is a low presenting viral load for a new HIV diagnosis - is this typical of the patients presenting with newly diagnosed HIV infection in Vietnam? Most newly diagnosed cases of HIV elsewhere would have much higher viral loads. For the purposes of this report, would this be an unusual case? Can the authors speculate on the possible difference in presentation and outcomes for patients with H5N1-HIV co-infection in patients with higher (more typical?) HIV loads at diagnosis?

Finally, the authors list a series of cytokines they have measured, but simply state that these were raised in a similar manner to previous H5N1 patients. Could they expand on this by describing and comparing how such cytokines behave in HIV-infected patients? How do the authors know that these cytokine profiles are not a result of the HIV-infection, or at least have not been influenced in anyway by the HIV-co-infection? There should be some additional discussion about this.

In short, the authors present many results, but (and possible word limitations apply) they do not seem to have discussed them in much detail in this perhaps unique case of H5N1-HIV adult co-infection.

Minor Essential - see above

Discretionary - none

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

**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'