Author's response to reviews

Title: Swine Influenza and Legionnaire's disease a Frequently Underestimated Coinfection. A case series

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Author's response to reviews: see over
Dear Editor,

Thank you for consideration of our manuscript for publication in your journal. We have reviewed the above manuscript according to reviewer’s comments. The manuscript was indeed extensively re-edited and hopefully all errors were ruled out. The paper was also rephrased in many sections as indicated below according to reviewer’s criticisms:

1. In the abstract for the sentence "Moreover, because the swine flu H1N1 pandemic occurred in Autumn in Italy, Legionnaires’ disease was to highly suspect since the peak incidence usually occurs in early fall." do the authors mean that Legionnaires’ disease was overly suspected? (in which case the word “to” should be "too").

*Reply*: The authors mean that suspicion for Legionnaires disease must be high according to seasonal epidemiology, but this point usually is still not a standard of care in many intensive care units in our region. This point was rephrased (abstract page 2). “Moreover, because the swine flu H1N1 pandemic occurred in Autumn in Italy, Legionnaires disease was to be highly suspected since the peak incidence usually occurs in early fall.”

2. In the conclusion section of the abstract, *(page 2)* I wouldn’t call two case reports a "case series". That entire sentence could be shortened as follows: "Our two case reports suggest that patients with H1N1 be screened for Legionella, which is not current common practice"

*Reply*: The sentence was modified according to reviewer suggestions “Our two case reports suggest that patients with H1N1 should be screened for Legionella, which is not current common practice.”

3. Please have the authors define all abbreviations in the text before their common
use (for example, "ER", "PCR", "BMI" ect.)

Reply: All abbreviations in the text have been defined before use.

ER = Emergency Room ; PCR = Polymerase chain reaction ; BMI Body Mass Index; ICU = Intensive Care Unit ; GCS = Glasgow Coma Score ; RT PCR = reverse transcriptase–polymerase chain reaction; SGPT= serum glutamate pyravate transaminase; SGOT= serum oxalacetate transaminase ; CPK = creatinine phosphokinase


Reply: The reference was corrected as indicated and due to text revision it is now number [7] (page 10)

5. In the discussion section, for the following sentence "In our cases all signs and symptoms (respiratory failure, refractory hypoxemia, leukopenia, lymphopenia, thrombocytopenia, and elevated levels of creatine kinase and hepatic aminotransferases) were consistent with critical illness due to 2009 H1N1 virus infection,[8][9][10][11]." at the end the reference should have just one bracket: "In our cases all signs and symptoms (respiratory failure, refractory hypoxemia, leukopenia, lymphopenia, thrombocytopenia, and elevated levels of creatine kinase and hepatic aminotransferases) were consistent with critical illness due to 2009 H1N1 virus Infection [8,9,10,11]." This same rule should apply throughout the manuscript where multiple references are cited.

Reply : Multiple references were cited in all the text as suggested. Background [1,2] (page3) Discussion [1,4,5] (page 6) [6,7] (page 7) [1,2] [12,13] (page 8)

6. In the background portion of the introduction section, for the following sentence: "Coinfection has been found in ?30% of all influenza cases in persons with seasonal influenza, and the pathogens most often involved are Streptococcus pneumoniae, Staphylococcus aureus, and Haemophilus influenza [1, 2]." please delete the symbol before "30%".

Reply : The symbol was deleted and text now is : "Coinfection has been found in 30% of all influenza cases in persons with seasonal influenza, and the pathogens most often involved are Streptococcus pneumoniae, Staphylococcus aureus, and Haemophilus influenza [1,2]."

7. The first sentence describing Case 1 needs to be reworded so it's a complete sentence and flows better. The same for Case 2.
Reply: Case 1 and 2 have been reworded.

8. In the text, sentences like "She resulted hypoxiemic..." are awkward. For this particular example, perhaps better would be "She was hypoxic..."

Reply: All awkward sentences have been re-edited and highlighted in the text.

9. At the end of the discussion section for the sentence "The lack of recent travel in H5N1 endemic areas or exposure to sick or dead poultry argue against H5N1 influenza [8]." do the authors really mean H5N1 (bird flu)? Or did they mean H1N1 (swine flu)? I suspect they really did mean the bird flu given the reference that they cite. It may lessen confusion if they use the term "H5N1 (bird flu)".

Reply: Bird flu was added in brackets so it cannot be confusing to the reader “The lack of recent travel in H5N1 (bird flu) endemic areas or exposure to sick or dead poultry argue against H5N1 influenza (bird flu) [14]." (page 8)

10. Although the authors acknowledge in their rebuttal that the bucal swab is not the ideal secretion to be tested for influenza virus, this is not emphasized in the actual text. Both of the reviewers raise this point. Please have the authors acknowledge and discuss this.

Reply: The argument is discussed in text (page 6-7) “Initial attempts to diagnose H1N1 infection using immunochromatography relied on test kits developed for seasonal influenza A and B viruses, many of which proved significantly less sensitive to H1N1. Hence tests with monoclonal antibodies that react with H1N1 but not seasonal influenza A (H1N1 and H3N2) or B viruses were developed. Recognizing viral hemagglutinin and nucleoprotein, specifically allows the detection of H1N1 virus on nasal wash fluid or nasopharyngeal fluid from patients with influenza-like illnesses. Early and rapid diagnosis of H1N1 related respiratory insufficiency needs rapid screening during a pandemic but clinicians cannot rely only on buccal swab test and need to rule out false positive and negative cases by RT PCR on oral/nasal fluids or bronchoalveolar lavage.”

11. Please create a separate discussion and conclusions section.

Reply: Separate sections have been created.

12. I am unable to read Table 1. Half of the characters are missing.

Reply: Table editing is sorted out. It was due to a problem of compatibility between MAC -OS and Windows.

13. Please have the authors provide a separate consent section specifically stating that consent was obtained from both patients for publication.

Reply: Obtained.

14. Please have the authors provide an author’s contribution section.

Reply: Done. Authors have also been re-nominated in accordance to contribution. Contribution has been specified.
15. I suggest changing the title to "Underestimated co-infection with H1N1 influenza and Legionnaire's disease: two case reports."

Reply: Done