

Article Information: <http://dx.doi.org/10.21037/tp-20-278>.

Reviewer A

General comment:

This is an interesting case described one 2-year-old girl co-infected with human bocavirus and *Mycoplasma pneumoniae*. The diagnostic process and surveys were complete and convincing. Some minor points need to be revised.

Specific comments:

Comment 1. Bacterial names (*Mycoplasma pneumoniae*, *S. aureus*...etc.) should be italicized.

Reply 1: Bacterial names had been italicized (Corrections have been made in the revised version).

Changes in the text: Pseudomembranous laryngotracheobronchitis due to co-infection with human bocavirus 1 and *Mycoplasma pneumoniae*: a case report.

Comment 2. P.2, l. 36 Consider use budesonide inhalation instead of PULMICORT RESPULES®. Suggest avoid brand name in the manuscript (ex: Mucosolvan).

Reply 2: We have modified our text as advised (see Page 4, line 8; Page 4, line 2; Page 4, line 9).

Changes in the text: Ceftriaxone, methylprednisolone, and budesonide inhalation were administered at a local hospital from 17 May 2019 to 22 May 2019. The patient was treated with azithromycin, methylprednisolone, budesonide inhalation, and oxygen inhalation. Azithromycin, methylprednisolone, budesonide inhalation, and ambroxol were continued for three days.

Comment 3. P.2, l. 38 The description of past and family history to indicate immunocompetent status is important. Consider mention these points in the beginning of case presentation.

Reply 3: We have added these data (see Page 3, line 2-3).

Changes in the text: The patient is previously healthy with an uneventful medical

history and family histories.

Comment 4. Any contact or cluster history?

Reply 4: We have added some data (see Page 3, line 3-4).

Changes in the text: There was no contact and cluster history.

Comment 5. I think presence of stridor or diminished breath sound is an important physical finding to localize the lesion. Consider briefly describe it.

Reply 5: Yes. I agree with you. Stridor, or diminished breath sound is an important physical findings to localize the lesion of larynx and trachea. Based on cough, hoarseness and dyspnea, depression of the suprasternal and supraclavicular fossa, the lesion of larynx and trachea were mainly considered in the emergency department. Therefore, flexible bronchoscopy was used to observe larynx and trachea in the patient with a stable airway. We have added comments (see Page 6, line 16 to 17).

Changes in the text: Stridor, or diminished breath sound is an important physical findings to localize the lesion of larynx and trachea.

Comment 6. P.3, l. 10-18 The diagnosis and management in ER and ward are much alike. Consider shorten the paragraph.

Reply 6: We have modified our text as advised (see Page 4, line 9-10).

Changes in the text: The sentence “At the Children’s Respiratory department, diagnoses of acute laryngitis, degree II laryngeal obstruction, and bronchopneumonia were considered.” was deleted. “Oxygen inhalation and electrocardiographic monitoring were performed and azithromycin, methylprednisolone, inhalation of Pulmicort Respules, oxygen inhalation and Mucosolvan were continued for three days” was replaced by “Azithromycin, methylprednisolone, budesonide inhalation, and ambroxol were continued for three days”.

Comment 7. P.3, l. 29 Since there were pseudomembrane formations of the trachea and ulceration of the right main bronchus, tracheobronchitis might be a better diagnosis.

Reply 7: The the main presenting symptoms of the children was horsseness and dyspnea. We considered that the larynx involved, and the larynx edema was also

confirmed by bronchoscopy. In addition, pseudomembrane formations of the trachea and ulcer of the right main bronchus were found under the bronchoscope. Therefore, we think that pseudomembranous laryngotracheobronchitis might be a better diagnosis. Thank you for your advice (see Page 5, line 17 to 19).

Changes in the text: From a monistic perspective regarding hoarseness, laryngeal edema, pseudomembrane formations of the trachea, and ulceration of the right main bronchus, the diagnosis was modified to pseudomembranous bronchitis.

Comment 8. P.3, l. 37 The rationale for 3 courses of azithromycin treatment should be briefly discussed. If poor response to azithromycin, my consideration is poor antibiotic penetration (abscess formation/much debris or exudate) or macrolide resistance. Repeat bronchoscopy or use other class antibiotic such as doxycycline/fluroquinolone might be my choice. I am curious about the reason why repeated azithromycin use. As an immune modulator or anti-inflammation agent?

Reply 8: Doxycycline is forbidden in children under 8 years old. Fluoroquinolone is not the first choice for the treatment of *Mycoplasma pneumoniae* infection in children under 18 years old. The lung tissue concentration of azithromycin was much higher than that of plasma. Azithromycin is the first choice for the treatment of mycoplasma pneumonia in children. Pseudomembranous laryngotracheobronchitis is rarely reported in children. However, there is no experience of azithromycin in the treatment of pseudomembranous laryngotracheobronchitis. Day 11 after admission, chronic inflammation of the mucous membrane, hyperplasia of granulation tissue under the squamous epithelium with hyperemia, hemorrhage, and infiltration of inflammatory cells, with cellulose exudate on the surface. We also considered the effect of pseudomembrane (much exudate) on azithromycin tissue concentration. In consideration of pseudomembranous laryngotracheobronchitis is an uncommon yet potentially life-threatening infectious, three courses of azithromycin treatment were administered (see Page 9, line 1 to 4).

Changes in the text: However, there is no experience of azithromycin in the treatment of pseudomembranous laryngotracheobronchitis. Considering the effect of pseudomembrane (much exudate) on azithromycin tissue concentration, three courses of azithromycin treatment were administered.

Comment 9. P.5, l. 8 As your statement in P.6 l.7, human bocavirus will cause severe damage to airway. It is an obvious risk factor for bacterial superinfection. Why don't you consider the fever, cough or hoarseness might be the initial presentation of viral croup? After airway damage, *Mycoplasma pneumoniae* then caused further pseudomembranous change of trachea. Just my opinion, but I think it deserves further discussion the relationship between viral and bacterial coinfections.

Reply 9: Yes. The child admitted due to cough, hoarseness and dyspnea lasting for ten days. Ceftriaxone, methylprednisolone, and budesonide inhalation were administrated at a local hospital for seven days. Her cough, hoarseness, and dyspnea did not significantly improve. It does not accord with the classic manifestation of viral croup. Throughout the course of the disease, no improvement of manifestation and becoming worse again were observed. I agree that the patient may be initially infected with human bocavirus, then coinfecting with *Mycoplasma pneumoniae* after airway damage. In the present case, *M. pneumoniae* and human bocavirus 1 were detected by next-generation sequencing. Pseudomembranous laryngotracheobronchitis is considered due to viral and bacterial coinfections (see Page 8, line 6 to 7).

Changes in the text: The patient may have been initially infected with human bocavirus and subsequently coinfecting with *M. pneumoniae* after airway damage.

Comment 10. P.5, l. 22-25 The bronchoscopy findings have been mentioned before. Maybe you don't need to repeat it.

Reply 10: We have deleted the bronchoscopy findings had been mentioned before (see Page 7, line 7-8).

Changes in the text: In our case, bronchoscopy was used to observe the formation, detachment, and ulceration of pseudomembrane in the trachea and bronchus.

Reviewer B

Comment: It is well written but case report is seldom accepted now except having great educational significance.

Reply: Thank you for your appreciation.