Case Report

A case of pseudomembranous tracheitis caused by *Mycoplasma pneumoniae* in an immunocompetent patient

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Abstract: Pseudomembranous tracheitis (PMT) is a rare condition characterized by pseudomembrane formation in the tracheobronchial tree that may be associated with infectious and noninfectious processes. However, PMT attributed to *Mycoplasma pneumoniae* (*M. pneumoniae*), a common atypical respiratory infectious pathogen, has not been reported till date. Here, we report about a 29-year-old woman with complaints of severe persistent cough and radiographic deterioration despite antibiotics administration for pneumonia at an outside facility. She was finally diagnosed as having PMT with bilateral diffuse bronchiolitis caused by *M. pneumoniae* infection. The diagnosis was made based on a bronchoscopic finding of a pseudomembrane that partially covered the membranous portion of the upper and middle trachea, a positive polymerase chain reaction (PCR) test with bronchial aspirate, and a positive serological test for *M. pneumoniae* without detection of any other causative pathogen through an extensive workup. Her symptoms and radiographic findings improved in response to moxifloxacin and corticosteroid treatment. This case is a rare presentation of *M. pneumoniae* infection complicating PMT in a young adult without any known risk factors.

Keywords: Tracheitis; bronchiolitis; *Mycoplasma pneumoniae* (*M. pneumoniae*)

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Introduction

Mycoplasma pneumoniae (*M. pneumoniae*) is a cause of atypical pneumonia worldwide and occurs with a wide spectrum of symptoms (1). Radiologic findings of *M. pneumoniae* pneumonia are also diverse and nonspecific, although characteristic computed tomography (CT) features have been described (2,3).

Pseudomembranous tracheitis (PMT) is a rare condition characterized by pseudomembrane formation that involves the tracheobronchial tree. PMT caused by fungal infections, such as those caused by aspergillus fumigatus, has mostly been reported in immunocompromised hosts, such as those who underwent chemotherapy or transplantation (4,5). However, PMT can also be caused by bacterial species or in immunocompetent patients although a very rare basis (6-14). To our knowledge, PMT caused by *M. pneumoniae* has not yet been reported in immunocompetent adults. Here, we present a case of *M. pneumoniae* infection that caused PMT and bilateral diffuse bronchiolitis in a previously healthy adult.

Case presentation

A 29-year-old woman with no history of underlying illness was presented as a transfer from an outside local medical center because of persistent coughing and chest radiographic deterioration (despite treatment with antibiotics) for suspected community acquired pneumonia. The patient was initially admitted because of dry cough, sore throat, and fever that lasted for 5 days. Her initial chest radiograph showed a slight peribronchial infiltration of the right lung (*Figure 1*), and she received intravenous ceftriaxone and clarithromycin treatment. After 7 days

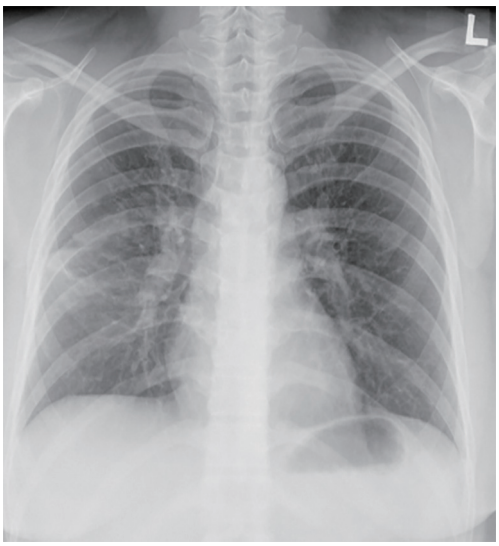

Figure 1 The initial chest radiograph reveals peribronchial infiltrates in the right lung.

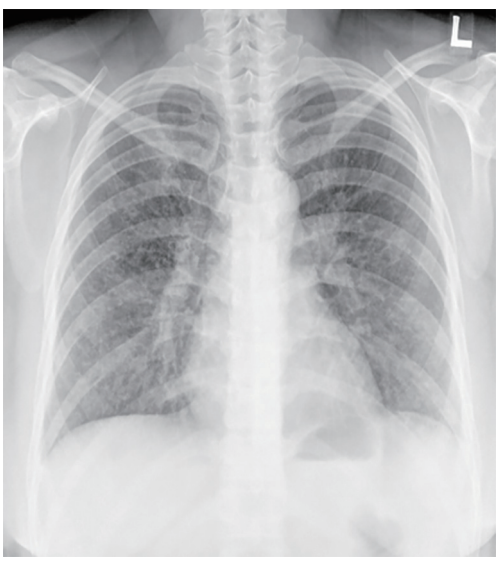

Figure 2 Follow-up chest radiograph showing an increased peribronchial infiltration in both the lungs compared to the initial radiograph.

of treatment, cough and dyspnea deteriorated along with the worsening of the radiological finding; thus, she was transferred to our institution for further evaluation and management.

On admission, her vital signs were as follows: blood pressure, 156/87 mmHg; pulse rate, 72 beats/minute; respiratory rate, 25 breaths/minute; and body temperature, 37.5 ℃. Oxygen saturation from pulse oximetry was 95% with 3 L/min of oxygen via nasal cannula. On auscultation, coarse breathing sounds were noted in both the lung fields. Laboratory test results were as follows: white blood cell count, 14,840 cells/mm^3 (neutrophils, 84.7%); hemoglobin level, 12.4 g/dL; platelet count, 393,000 cells/mm^3; lactic acid level, 2.6 mmol/L; and C-reactive protein level, 3.02 mg/dL. Procalcitonin level was 0.06 ng/mL (0–0.1 ng/mL). Other laboratory findings, including electrolyte and creatinine levels and liver function tests, were normal. No virus was identified from throat swab specimens using multiplex polymerase chain reaction (PCR) assay, which detects 16 respiratory viruses (Allplex Respiratory Panel; Seegene Biotechnology Inc., Korea). A urine antigen analysis for *Streptococcus pneumoniae* and *Legionella pneumophila* tested negative for both the organisms. A chest radiograph showed an increased peribronchial infiltration in both whole lung fields compared to the initial one (*Figure 2*). Chest CT showed diffusely scattered centrilobular micronodules and tree-in-bud opacity involving both the lungs (*Figure 3*). Also, asymmetrical wall thickening with contrast enhancement was observed in membranous portion of the upper part of trachea. Given the poor response to previous antimicrobial therapy, antibiotics were switched to intravenous piperacillin/tazobactam and moxifloxacin. In addition, bronchoscopy was performed to determine the presence of atypical pathogen or noninfectious processes. The vocal cords were not swollen and inflamed. Mucosal ulceration and white exudative plaques, partially covering the membranous portion of the upper and middle trachea, were noted, whereas the distal trachea and all the bronchi were unremarkable except for the mucosal hyperemia (*Figure 4*). Bronchial aspirate from the lesion were examined using GeneXpert MTB/RIF assay (Cepheid, Sunnyvale, USA) and AmpliSens Mycoplasma pneumoniae/Chlamydia pneumoniae-FRT PCR kit (InterLabService Ltd., Russia), and the results were positive for *M. pneumoniae*. However, microbial staining and culture examination for common bacteria, fungi, and *Mycobacterium tuberculosis* were all negative in those specimens. A biopsy of the pseudomembrane revealed inflammatory exudate with necrotic debris and squamous metaplasia (*Figure 5*). Necrotic tracheitis was diagnosed. Subsequently, tests for IgM and IgG antibodies against *M. pneumoniae* were positive [IgM >27 index (<10 index); IgG 86.3 AU/mL (<10 AU/mL)]. Testing for cold agglutinin also revealed

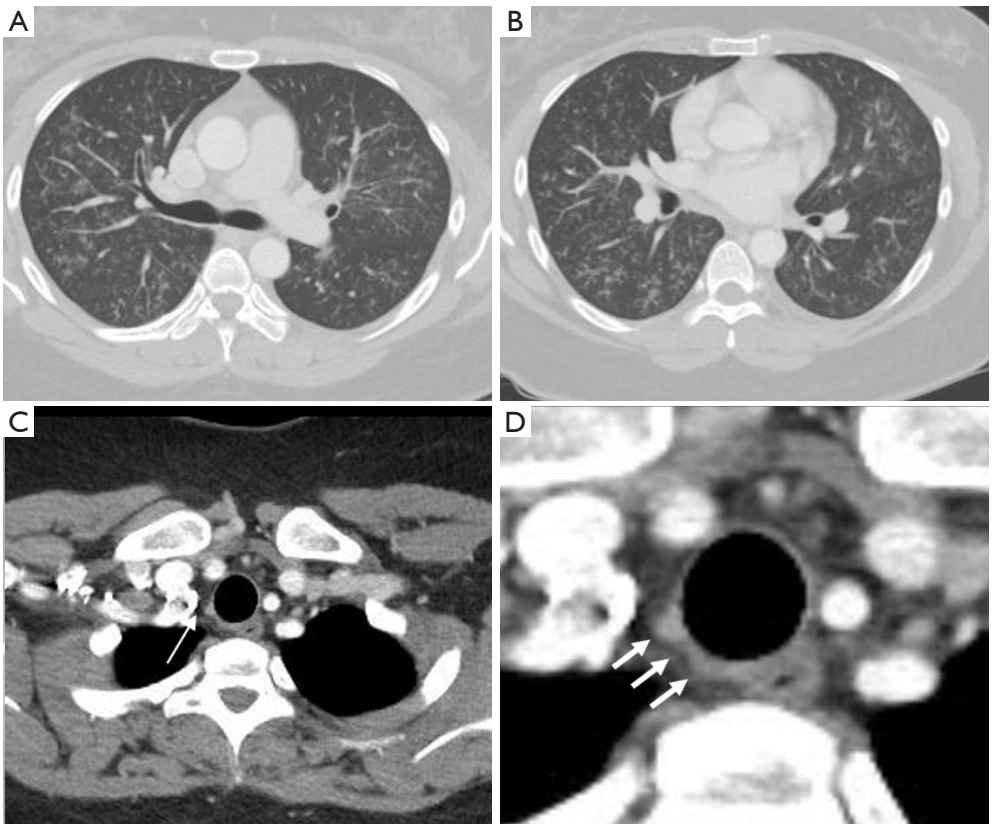

Figure 3 Chest computed tomography (CT) findings on the day of admission. (A,B) Chest CT reveals diffusely scattered centrilobular micronodules and tree-in-bud opacity in both the lungs. (C,D) Asymmetrical wall thickening with contrast enhancement is observed in membranous portion of the upper part of trachea.

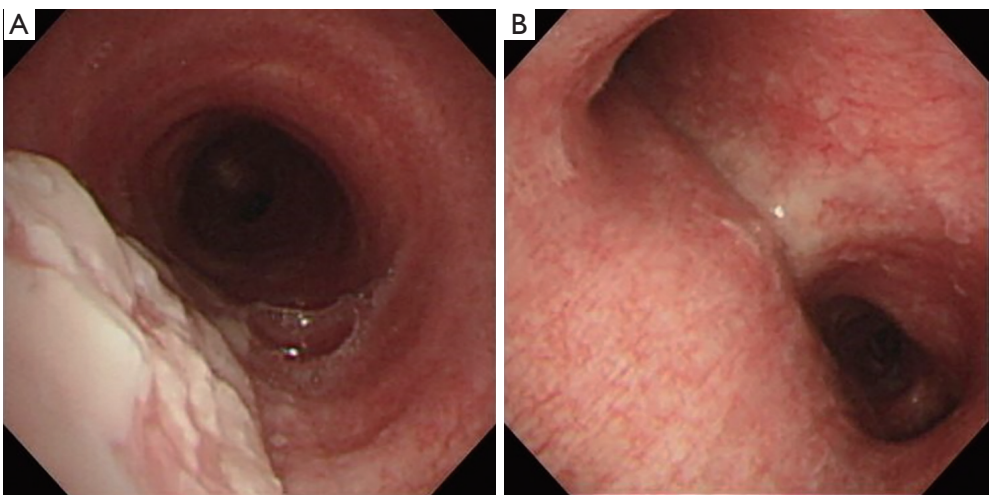

Figure 4 Bronchoscopic findings. (A) Bronchoscopy shows mucosal ulceration and white plaques along the membranous portion of the upper and middle trachea; (B) while distal trachea is unremarkable except mucosal hyperemia.

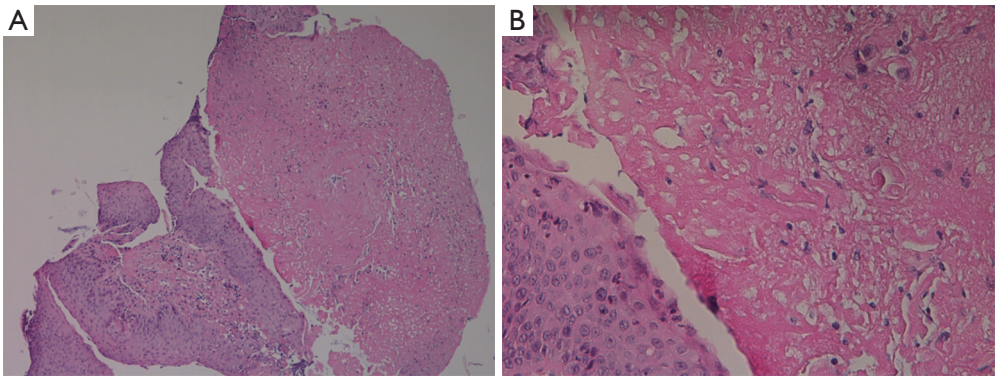

Figure 5 Pathology reveals inflammatory exudate with (A) necrotic debris and (B) squamous metaplasia (Hematoxylin and eosin stain, ×100 and ×400).

Table 1 Results of serologic and microbiologic test

Test	Result	Reference range
Serologic test		
C-reactive protein	3.02	<0.5 mg/dL
Lactate dehydrogenase	353	<250 U/L
Chlamydia pneumoniae IgM	0.4	<0.9 index
Mycoplasma pneumoniae IgM	>27	<10 index
Mycoplasma pneumoniae IgG	86.3	<10 AU/mL
Cold agglutinin	1:32	≤1:4
HIV antibody	Negative	Negative
Microbiological test		
Multiplex respiratory viruses PCR assay, throat swab	Negative	Negative
Streptococcus pneumoniae antigen, urine	Negative	Negative
Legionella pneumophila antigen, urine	Negative	Negative
Mycoplasma pneumoniae PCR, BA	Positive	Negative
Chlamydia pneumoniae PCR, BA	Negative	Negative
GeneXpert MTB/RIF assay, BA	Negative	Negative
AFB stain, BA	Negative	Negative
MTB culture, BA	Negative	Negative

HIV, human immunodeficiency virus; PCR, polymerase chain reaction; BA, bronchial aspirate; MTB, Mycobacterium tuberculosis; RIF, rifampicin; AFB, acid fast stain.

positive findings [1:32 (≤1:4)]. Serological tests regarding autoimmune diseases and other atypical pathogens, including human immunodeficiency virus (HIV), were negative. Some relevant laboratory findings are summarized in *Table 1*.

While continuing the antibiotic therapy, 20 mg methylprednisolone was administered daily for relieving severe cough that did not respond to previous cough medicines. On the sixth day of hospitalization, the patient was discharged on oral moxifloxacin, with remarkable improvement in cough and radiologic findings on chest X-ray (*Figure 6*). She was found to have completely recovered without residual symptoms in the outpatient

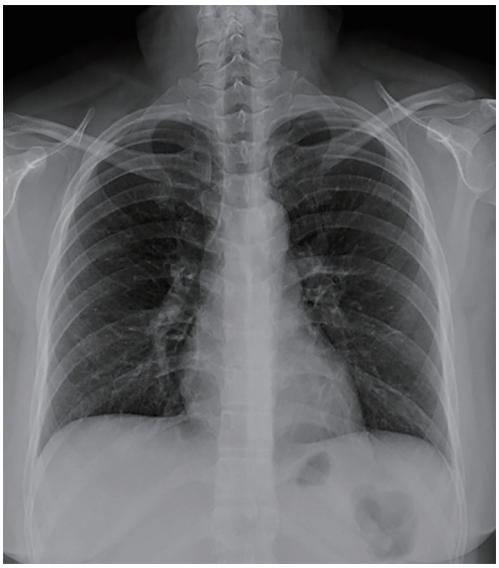

Figure 6 A chest radiograph on the sixth day shows resolution of the previously observed bilateral patchy consolidations in both lungs.

clinic after discharge although improvement of tracheal lesion was not identified by follow-up bronchoscopy because she declined it.

Discussion

M. pneumoniae infection causes diseases of varied severity, ranging from minor respiratory illness to severe atypical pneumonia (1). Our patient who presented with severe cough, worsening of dyspnea, and deterioration of radiologic findings was found to have *M. pneumoniae* infection, unusually causing PMT associated with bilateral diffuse bronchiolitis. Here, we presented a rare case of an immunocompetent adult with PMT and bilateral diffuse bronchiolitis caused due to *M. pneumoniae*.

PMT is characterized by presence of extensive inflammation and invasion of the tracheobronchial trees with formation of a pseudomembrane composed of fibrin, leukocytes, and possibly organism overlying a damaged airway mucous membrane (4). It has been proposed that diminished function of neutrophils and macrophages is implicated in the development of PMT (15). Cases with PMT have been reported in association with fungal infections caused by Aspergillus, Candida, and Rhizopus. Other rare pathogens include Pseudomonas, Corynebacterium, Bacillus, Staphylococcus, Moraxella, and Chlamydia species (4). Noninfectious causes are inflammatory bowel disease, endotracheal intubation, and post-transplantation (4). Most of them are usually developed in immunocompromised hosts and have a high morbidity and mortality. Therefore, patients suspected of having PMT need a thorough diagnostic evaluation and prompt and proper treatment for the causative organism.

Our patient did not have any of the above antecedent factors, and there was no evidence of any infection with a specific pathogen known to cause PMT. *M. pneumoniae* infection as the cause of her condition was supported by (I) radiological finding of centrilobular nodules compatible to *M. pneumoniae* bronchiolitis (2,3), (II) a positive PCR result for *M. pneumoniae* from the lesion, and (III) elevated serum antibody titer for *M. pneumoniae*. Thus, although the pathogenesis was unclear, tracheal pseudomembranous lesion was most likely caused by the *M. pneumoniae* infection. Extremely severe coughing, as seen in this case, can probably be attributed to PMT, given that the sensory nerves responsible for cough are predominantly in the upper airway, including the trachea, especially the membranous portion (16). In fact, bronchoscopy is not generally performed for patients with *M. pneumoniae* respiratory infection. Thus, the frequency of such PMT might not be so rare. Therefore, PMT can be considered in a patient with complaints of intractable cough without any response to the usual treatment for *M. pneumoniae* infection and having tracheal wall thickening in chest CT. Bronchoscopy should be performed in such circumstances.

Although data regarding the CT findings of *M. pneumoniae* infection are limited, reported findings include centrilobular nodular and tree-in-bud opacities in a patchy distribution, lobular or segmental ground-glass opacities or consolidation, and thickening of the bronchovascular bundle (2,3). In terms of the distribution of nodules on a CT scan, a patchy distribution favors infectious bronchiolitis, while diffuse distribution is usually observed in noninfectious causes, including hypersensitivity pneumonitis (17). In this aspect, diffuse distribution of centrilobular nodules throughout both the lungs in our case hindered the consideration of *M. pneumoniae* infection in the first impression. However, bronchoscopically identified tracheal lesions provided a relevant answer for these atypical, diffuse distributions of centrilobular nodules observed in our case. Tracheal mucosal lesions with necrotic materials caused by *M. pneumoniae* may lead to endobronchial spreading throughout the bilateral bronchial tree, resulting in a form

Table 2 Cases of pseudomembranous tracheitis in immunocompetent hosts

Author	Age/Sex	Cause/Organism	Underlying conditions	Treatment	Outcomes
Park *et al.* (6)	42/Female	Staphylococcus aureus	Influenza A	Ciprofloxacin and amoxicillin/clavulanate	Improved
Oh *et al.* (7)	44/Male	Aspergillus species	Hypertension	Amphotericin	Deceased
Yuan *et al.* (8)	68/Male	Aspergillus species	Chronic obstructive pulmonary disease, coronary heart disease	Voriconazole, therapeutic bronchoscopy	Improved
Franco *et al.* (9)	70/Male	Aspergillus species	Diabetes mellitus, Chronic obstructive pulmonary disease	Antifungal agent (not specified)	Improved
Boots *et al.* (10)	35/Female	Aspergillus species	Influenza A	Amphotericin, γ-interferon, GM-CSF	Improved
Shah *et al.* (11)	32/Female	Aspergillus species	Postpartum	Voriconazole	Improved
Pornsuriyasak *et al.* (12)	55/Female	Aspergillus species	Post-tuberculous tracheal stenosis	Amphotericin	Improved
Henderson *et al.* (13)	48/Male	Streptococcus pyogenes	Previously healthy	Therapeutic bronchoscopy	Improved
Guerrero *et al.* (14)	39/Female	Corynebacterium species	Dressler syndrome after coronary artery bypass surgery, diabetes mellitus	Imipenem, vancomycin, therapeutic bronchoscopy	Improved

of diffuse bronchiolitis during the clinical course.

Our patient did not show prompt improvement in response to clarithromycin administration received for 1 week before referral to our hospital. Macrolide-resistant *M. pneumoniae* is an emerging problem (1). Although the impact of macrolide resistance on the outcomes of respiratory infection is unclear, the clinical course of patients with macrolide-resistant *M. pneumoniae* infection tends to be prolonged. However, the severity of the clinical illness may correlate with an individual's immune response to *M. pneumoniae* regardless of antimicrobial resistance (18). In this context, a prolonged clinical course observed in our patient may not be associated with macrolide failure; it may rather be associated with a complicated PMT or exacerbated immune response although in-vitro macrolide susceptibility data were not obtained in this case.

Adjunctive corticosteroid therapy was administered to the patient for 5 days, following which her persistent and severe coughing with no response to prior antibiotics and cough medicines rapidly improved. Although the benefits of adjunctive steroids are controversial in patients with *M. pneumoniae* pneumonia (19), administering steroids in addition to effective antibiotics may be a good option for rapidly relieving persistent and severe coughing caused by PMT. In addition, clinical outcomes of immunocompetent patients with PMT caused by *M. pneumoniae* seem favorable compared to grave outcomes in cases with immunocompromised conditions or fungal infection. Several reported cases of PMT developing in immunocompetent patients have been outlined in *Table 2* (6-14). Most cases had favorable outcomes like our case.

In conclusion, we presented the first case of PMT associated with bilateral diffuse bronchiolitis caused by *M. pneumoniae* infection that showed a complete symptomatic and radiographic recovery after administration of moxifloxacin and adjunctive corticosteroids. *M. pneumoniae* should be considered as a causative pathogen in immunocompetent adult patients with bilateral diffuse bronchiolitis and PMT.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Informed Consent: Written informed consent was obtained

from the patient for publication of this case report.

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