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CASE SERIES

Adult Hospitalized Mycoplasma Cases in a Tertiary Hospital in Japan

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Background: Mycoplasma infections have increased globally, including in Japan. Severe pneumonia due to *Mycoplasma pneumoniae* (*M. pneumoniae*) that is resistant to macrolides has been reported in the post-COVID-19 period, but its pathogenesis and detailed treatment regimens are still unclear.

Case Series: Four adult cases of *M. pneumoniae* pneumonia that required admission to the hospital in the 2024–2025 season are presented. Case 1: a 17-year-old male without a specific medical history who was admitted with pneumonia with a severe dry cough. *Mycoplasma. pneumoniae* genes were detected by multiplex PCR from his sputum. The patient's condition improved with minocycline and corticosteroids for 5 days. Case 2: a 88-year-old man with acute kidney injury who was admitted with severe respiratory failure. Mycoplasma antigen was detected in his pharyngeal swab. He received lascufloxacin drip infusion with corticosteroids for 10 days, and soon improved. Case 3: a 38-year-old woman with maxillary carcinoma and a history of aplastic anemia who was admitted with a severe cough. Mycoplasma antigen was detected in her pharyngeal swab. She received minocycline and corticosteroid drip infusion for 1 week, and finally improved. Case 4: a 74-year-old man with multiple systemic atrophies who was admitted with a severe cough and dyspnea. Mycoplasma antigen was detected from his pharyngeal swab and methicillin-susceptible *Staphylococcus aureus* (MSSA) was isolated from his sputum. The patient was diagnosed with co-infection with mycoplasma and MSSA. He was treated with sulbactam/ampicillin drip infusion and oral administration of minocycline for 2 weeks, and improved.

Conclusion: All hospitalized adult patients with mycoplasma pneumonia were treated with antibiotics, such as minocycline and fluoroquinolone, along with corticosteroid co-administration, and all of them ultimately improved, although the chest X-ray findings varied. Antibiotics other than macrolides and corticosteroids may be an effective regimen for the treatment of severe mycoplasma pneumonia with potential macrolide resistance.

Keywords: corticosteroid, *Mycoplasma pneumoniae*, macrolide, minocycline, respiratory quinolone

Introduction

Mycoplasma pneumoniae (M. pneumoniae) is a representative pathogen of respiratory tract infections in adults, as well as in children, and sometimes become life threatening.[1] A characteristic epidemic cycle of approximately 4 years is well known, and a shift in circulating variants has appeared.[2]

Mycoplasma pneumoniae lack cell walls, and decreased metabolic pathways restrict the antibiotic treatment options.[2] Recently, *M. pneumoniae* that has acquired macrolide resistance has emerged around the world, and appropriate antibiotic treatment become issues clinically,[1,3] with >80% of *M. pneumoniae* cases in China now being resistant to macrolides.[2]

In addition, *M. pneumoniae* has several virulence factors, including biofilm formation and toxin production; although it usually has low virulence, it also demonstrates evasion of immunity. Severity is usually defined by physical examination, laboratory data, and radiological data, and it may be predicted by a combination of these data.[4]

This case series presents patients with severe adult mycoplasma pneumonia who required hospitalization. The treatment regimen for potentially macrolide-resistant *M. pneumoniae* is still unclear; however, all of the patients were treated with antibiotics other than macrolides, followed by corticosteroids, and finally improved.

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The Institutional Review Board of Saitama Medical University International Medical Center gave approval for the publication of the details on each mycoplasma patient in this case series, such as their age, sex, underlying diseases, and clinical data (registered as UMIN000047992), and related analyses were conducted in accordance with the principles of the Declaration of Helsinki. All patients whose specimens were used and who participated in this study provided written, informed consent, as part of the comprehensive consent obtained at admission, to have their case details and any accompanying images published. The patients were provided with the means to opt out of these clinical studies in particular.

Case Series

Case 1

A 17-year-old male visited the emergency outpatient division with a severe dry cough. Chest radiography and computed tomography (CT) showed an infiltration shadow with ground-glass opacity (GGO) (Figure 1A and B), suggesting atypical pneumonia. Mycoplasma pneumonia was diagnosed based on positive results for the *M. pneumoniae* gene from his nasopharyngeal swabs by multiplex polymerase chain reaction (PCR) (FilmArray Respiratory Panel 2.1; Biomerieux, Lyon, France). Laboratory data were as follows: white blood cell count (WBC) $5.81\times10^3/\mu L$ and C-reactive protein (CRP) 5.81 mg/dL. He was treated with minocycline 100 mg drip infusion twice and methylprednisolone 60 mg (1 mg/kg/day) for 5 days, and his symptoms and the chest X-ray findings improved (Figure 1C).

Case 2

An 88-year-old male with severe respiratory failure and septic shock was admitted to the emergency division. Chest radiography and CT revealed massive GGO in the right lung (Figure 2A and B). He was diagnosed with mycoplasma pneumonia based on positive results for *M. pneumoniae* antigen from nasopharyngeal swabs using a rapid detection kit (Quick Caser Myco; Mizuho Medy, Tokyo, Japan). Laboratory data were as follows: WBC $7.92\times10^3/\mu L$ and CRP 10.81 mg/dL. He was treated with lascufloxacin (LSFX) 300 mg × 1/day on the first day, followed by 150 mg × 1/day intravenously and methylprednisolone 50 mg (1 mg/kg/day) intravenously for 10 days. His respiratory status and chest radiographic findings finally improved (Figure 2C).

Case 3

A 38-year-old female with maxillary cancer and a history of aplastic anemia was admitted to the ear, nose, and throat department with a severe cough. Chest radiography and CT showed GGO and slight bronchial thickness (Figure 3A and B).

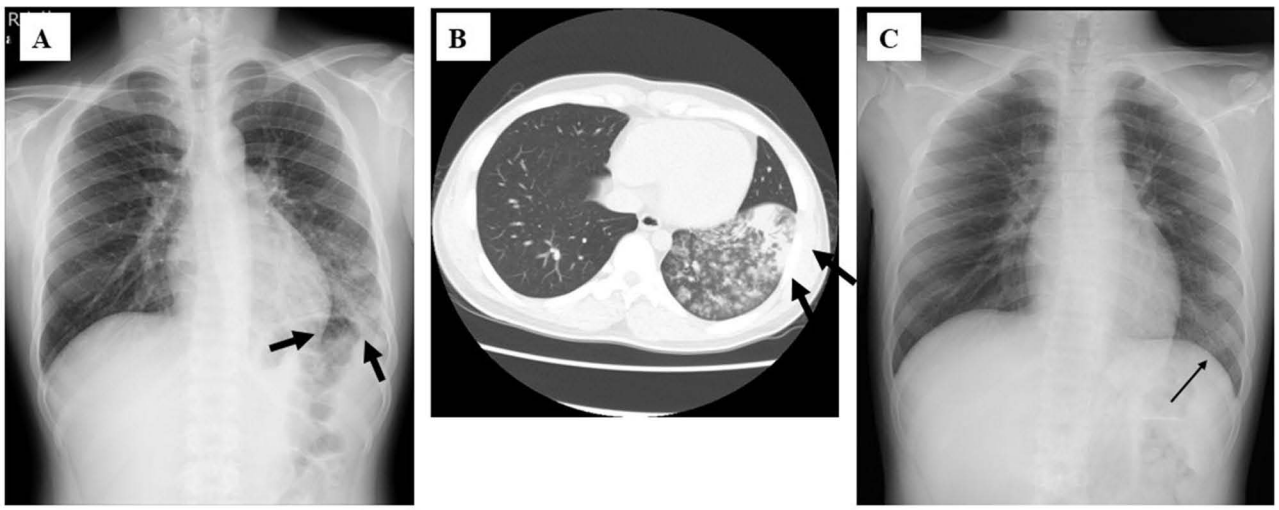

Figure 1 Chest X-rays (**A** and **C**) and computed tomography (**B**) of the Case 1 patient. At admission, there are abnormal shadows on the chest X-ray (**A**) and computed tomography (**B**), but these shadows improve after treatment (**C**). Arrows indicate the abnormal shadows.

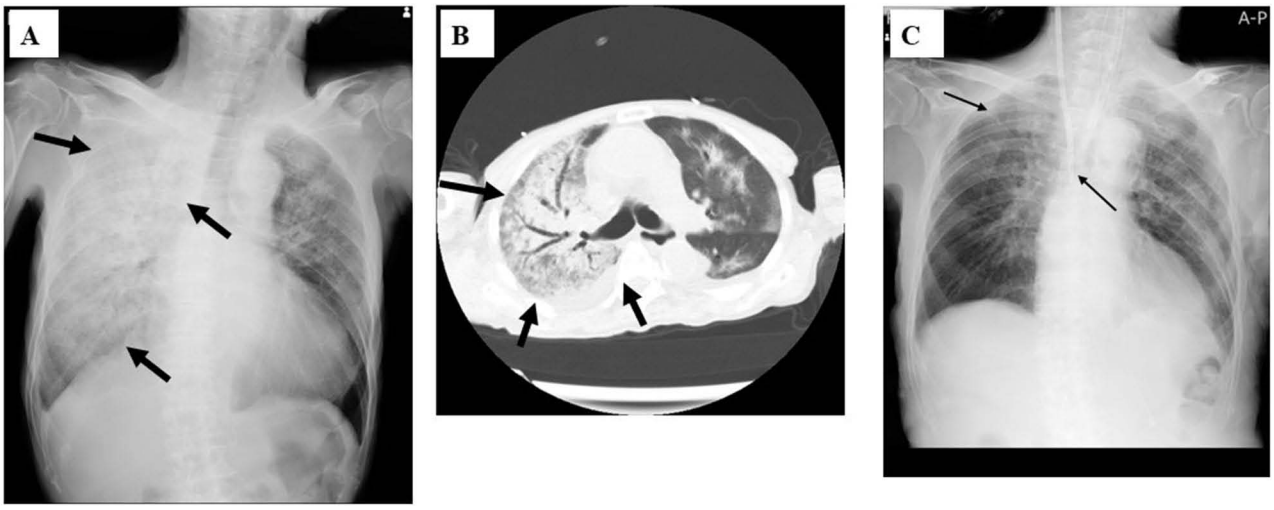

Figure 2 Chest X-rays (**A** and **C**) and computed tomography (**B**) of the Case 2 patient. At admission, there are abnormal shadows on the chest X-ray (**A**) and computed tomography (**B**), but these shadows improve after treatment (**C**). Arrows indicate the abnormal shadows.

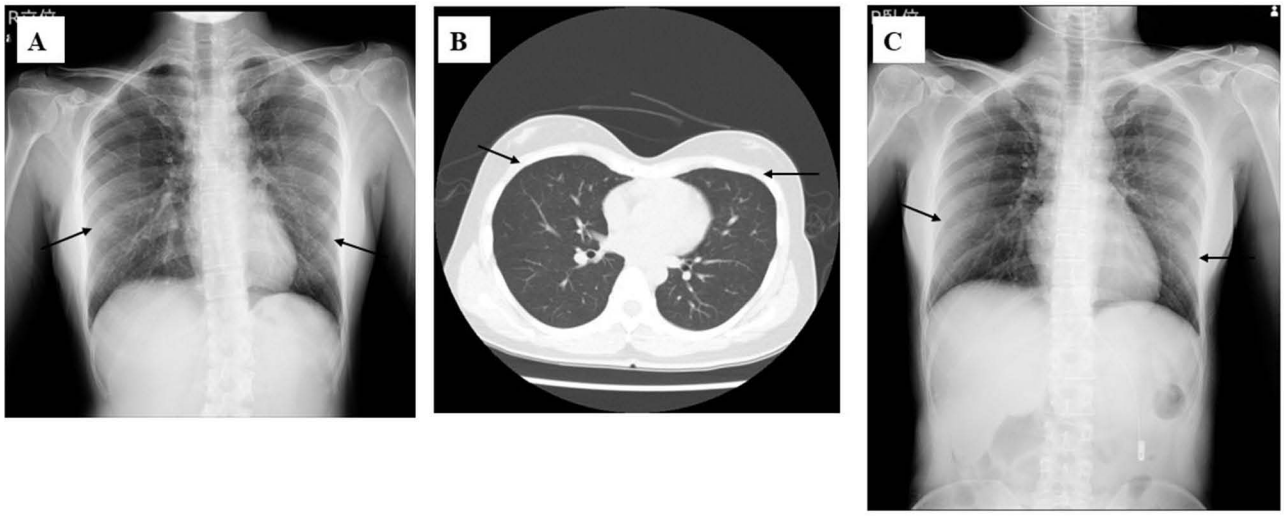

Figure 3 Chest X-rays (**A** and **C**) and computed tomography (**B**) of the Case 3 patient. At admission, there are abnormal shadows on the chest X-ray (**A**) and computed tomography (**B**), but these shadows improve after treatment (**C**). Arrows indicate the abnormal shadows.

She was diagnosed with mycoplasma pneumonia based on positive results for *M. pneumoniae* antigen from nasopharyngeal swabs using a rapid detection kit (Quick Caser Myco). Laboratory data were as follows: WBC 3.99×10^3/μL and CRP 4.88 mg/dL. She was treated with minocycline 100 mg drip infusion twice and methylprednisolone 40 mg (1 mg/kg/day) intravenously for 1 week, after which her respiratory status and chest radiographic findings improved (Figure 3C).

Case 4

A 74-year-old male with multiple systemic atrophy was admitted to the emergency department with a severe cough. Chest radiography and CT revealed an infiltration shadow with GGO in the left lower field of the lung (Figure 4A and B). The patient was diagnosed with mycoplasma pneumonia co-infected with methicillin-susceptible *Staphylococcus aureus* (MSSA) pneumonia, based on positive results for the *M. pneumoniae* antigen from his nasopharyngeal swabs using a rapid detection kit (Quick Caser Myco) and isolation of MSSA from his sputum. Laboratory data were as follows: WBC 9.83×10^3/μL and CRP 3.73 mg/dL. He was treated with sulbactam/ampicillin (1.5 g) intravenously three times,

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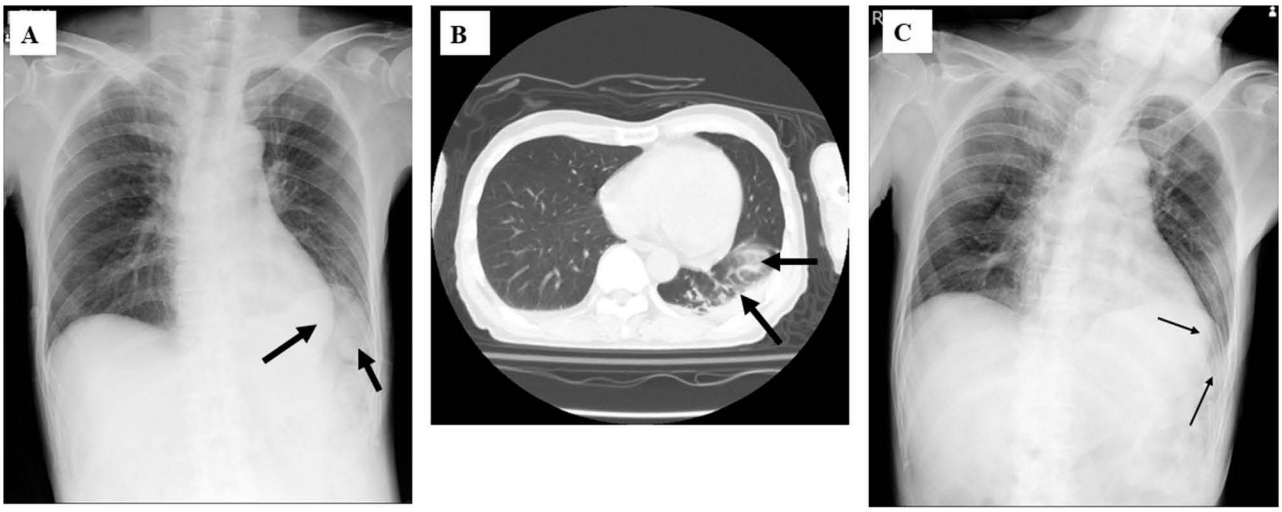

Figure 4 Chest X-rays (**A** and **C**) and computed tomography (**B**) of the Case 4 patient. At admission, there are abnormal shadows on the chest X-ray (**A**) and computed tomography (**B**), but these shadows improve after treatment (**C**). Arrows indicate the abnormal shadows.

minocycline 100 mg orally twice, and methylprednisolone 1 mg/kg/day (40 mg) intravenously for 2 weeks, and his respiratory status and chest X-ray findings improved (Figure 4C).

Discussion

Mycoplasma pneumoniae causes pneumonia in both children and adults, and its pathogenesis and chest X-ray findings may be diverse. Its severity also varies from mild to very severe.[1]

In this case series, the four mycoplasma pneumonia patients ranged in age from young to elderly, and severity ranged from mild to extremely severe. Since *M. pneumoniae* lacks cell walls, beta-lactams are ineffective against this pathogen. Antibiotics that act on the bacterial ribosome to inhibit protein synthesis, such as macrolides and tetracyclines, and antibiotics that inhibit DNA gyrases, such as fluoroquinolones, are the main drug classes used for *M. pneumoniae* management.[1]

Macrolides, especially azithromycin and clarithromycin, have been used worldwide as antibiotics against community-acquired bacterial pneumonia. However, in vitro studies have suggested that point mutations in the peptidyl transferase loop of 23S rRNA, as well as insertions or deletions in ribosomal proteins, can result in macrolide resistance in *M. pneumoniae*.[1,5] Over 90% of *M. pneumoniae* are now resistant to macrolides in several areas of Japan and China, although the prevalence in Europe is substantially lower than that in Asia and varies from country to country.[3] Therefore, alternative agents, such as tetracyclines and fluoroquinolones, have been used in Japan.

In the present case series, all four patients received tetracyclines and fluoroquinolones, such as minocycline and lascufloxacin, and finally improved. These data suggest that alternative agents to macrolides, such as tetracyclines and fluoroquinolones, may be effective and should be considered as treatment for *M. pneumoniae* pneumonia in resistant strain-dominant areas, including Japan and China.[3] Furthermore, in cases of co-infection, such as with *M. pneumoniae* and other common bacteria, similar to Case 4 in this case series, we should select the antibiotics more carefully. Penicillin and minocycline were used in Case 4; however, fluoroquinolone alone may be a better option because fluoroquinolone could cover both MSSA and *M. pneumoniae*.

In addition, all four patients in the present case series were co-administered corticosteroids and showed good improvement. Corticosteroids have shown good results in the treatment of refractory *M. pneumoniae* pneumonia in combination with appropriate antibiotics.[6] Usually, *M. pneumoniae* pneumonia shows inflammation-dominant pathogenesis due to cytokine storm, rather than direct tissue damage caused by the pathogen, and the usefulness of immunosuppressive therapy, such as corticosteroids, has been suggested.[1] It has been reported that children with refractory *M. pneumoniae* who received prednisolone combined with macrolides improved more quickly, both clinically and radiologically, than children who received only macrolides.[7] It has also been reported that combination treatment with

macrolides and high-dose methylprednisolone pulse therapy for children with severe systemic macrolide-resistant *M. pneumoniae* led to recovery, although no response was seen with azithromycin and methylprednisolone at standard dosage. Six additional patients received glucocorticoids combined with ciprofloxacin for refractory *M. pneumoniae* infections and finally improved.[8] Rapid and good responses to corticosteroids in children with severe pneumonia with hyperactive immune reactions have been suggested.[1,9,10] More detailed studies are needed to clarify the benefits of combinations of antibiotics and corticosteroids in the treatment of severe mycoplasma infections, including both macrolide-susceptible and macrolide-resistant infections, and in both adults and children. The optimal dose and timing of pulse corticosteroid treatment should be also investigated. The adult patients in the present series ranged from young to elderly and showed various findings, including infiltration shadows with GGO, immunological pathogenic mechanisms, and bacterial co-infections. Therefore, we also need to re-investigate appropriate regimens consisting of antibiotics and corticosteroids.

A limitation of this study is that detailed and genetic assessments for macrolide resistance could not be performed in every patient; therefore, there may be cases of macrolide-susceptible *M. pneumoniae* infection. Furthermore, diagnostic tools, especially mycoplasma antigen testing, do not always show high sensitivity; however, the specificity is very high, and clinical and radiological findings were typical for severe mycoplasma pneumonia. These data suggest that the antibiotics and diagnostic methods used in this case series would be useful at the bedside level in Japan and in similar countries.

In conclusion, since macrolide-resistant *M. pneumoniae* should be considered in Japan, all adult hospitalized patients with mycoplasma pneumonia in this hospital were successfully treated with tetracycline and fluoroquinolones with corticosteroids. The pathogenesis and chest radiographic findings varied. However, we need to establish detailed regimens for the control of severe *M. pneumoniae* pneumonia according to the microbiological and pathophysiological conditions of the patients. Since this pathogen has been suggested to be resistant to macrolides, antibiotics other than macrolides could be used for severe *M. pneumoniae* pneumonia, when used appropriately with corticosteroids.

Disclosure

The author reports no conflicts of interest in this work.

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