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CASE REPORT

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Severe infectious acute respiratory failure mimicking COVID-19 in a healthy adolescent

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Abstract

A 15-year-old male presented with headache, high fever and respiratory distress. Chest computed tomography showed bilateral pneumonia, and antimicrobial therapy was initiated. However, his respiratory condition deteriorated, and he developed respiratory failure requiring intubation. A multiplex polymerase chain reaction (PCR) test and 16S ribosomal RNA gene analysis were done from his intratracheal secretions to determine the causative pathogens, and *Mycoplasma pneumoniae* was detected. He was treated with appropriate antimicrobial therapy, systemic corticosteroid therapy and extracorporeal membrane oxygenation. He also presented with pulmonary thromboembolism and was treated with anticoagulants, to which he responded well. This patient demonstrates the similarities between severe *M. pneumoniae* pneumonia with bilateral pneumonitis and thrombosis, and severe coronavirus disease 2019. Therefore, it is important to identify cases of bilateral pneumonia with severe respiratory dysfunction using multiplex PCR tests to provide appropriate medical management and therapeutic interventions.

KEYWORDS
catastrophic antiphospholipid syndrome, COVID-19, multiplex PCR test, *Mycoplasma pneumoniae*, respiratory dysfunction

INTRODUCTION

Mycoplasma pneumoniae is one of the most common pathogens of community-acquired pneumonia.[1] Most cases are mild, but some are severe with extrapulmonary complications such as thrombosis.[1]

Severe *M. pneumoniae* pneumonia (MPP) with extended consolidation to the bilateral lungs with thrombosis mimics severe coronavirus disease 2019 (COVID-19).[2] However, contrary to COVID-19, MPP necessitates appropriate antimicrobial therapy and therefore requires accurate differentiation during the COVID-19 pandemic.

Herein, we report a patient with severe MPP mimicking severe COVID-19, characterized by rapid-onset respiratory dysfunction and pulmonary embolism.

CASE REPORT

A 15-year-old Japanese male presented with headache, high-grade fever (40.0°C) and general fatigue in December 2019. As repetitive influenza antigen detection tests were all negative and laninamivir treatment was ineffective, he was previously admitted to a hospital. On admission, he showed respiratory failure with respiratory distress, and chest computed tomography (CT) revealed right lower lobe consolidations, right pleural effusion and bilateral diffuse ground-glass attenuations. As his bilateral infiltrations and respiratory conditions were rapidly worsening in a couple of days, he was intubated, mechanically ventilated and then transferred to our hospital, instead of receiving treatment with ceftriaxone (2 g/day) and subsequent tazobactam/

TABLE 1 Results of peripheral blood analysis on admission

Blood cell counts		Blood chemistry		Serology	
WBC	5000/μl	TP	4.1 g/dl	CRP	11.9 mg/dl
Neutrophils	68.6%	Alb	1.9 g/dl	Cold agglutinin	×8192
Lymphocytes	27.8%	AST	112 IU/L	*Mycoplasma pneumoniae* (CF)	×256
Eosinophils	0.0%	ALT	48 IU/L	Blood coagulation	
Monocytes	3.6%	LDH	575 IU/L	PT	16.1 s
Basophils	0.0%	T-bil	0.3 mg/dl	PT%	58.6%
RBC	444 × 10^4/μl	BUN	18 mg/dl	INR	1.29
Hb	13.5 g/dl	Cre	1.07 mg/dl	APTT	37.1 s
Ht	40.4%	CK	1971 IU/L	FDP	89.1 μg/ml
Platelets	11.3 × 10^4/μl	Na	138 mmol/L	D-dimer	41.1 μg/ml
		K	5.4 mmol/L	β2-glycoprotein IgG	<1.2 U/ml
		Cl	103 mmol/L	Anticardiolipin IgG	<8.0
				Lupus anticoagulant	1.46

Abbreviations: Alb, albumin; ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CF, complement fixation; CK, creatine kinase; Cre, creatinine; CRP, C-reactive protein; FDP, fibrinogen/fibrin degradation products; INR, international normalized ratio; LDH, lactate dehydrogenase; Hb, haemoglobin; Ht, haematocrit; PT, prothrombin time; RBC, red blood cell; T-bil, total bilirubin; TP, total protein; WBC, white blood cell.

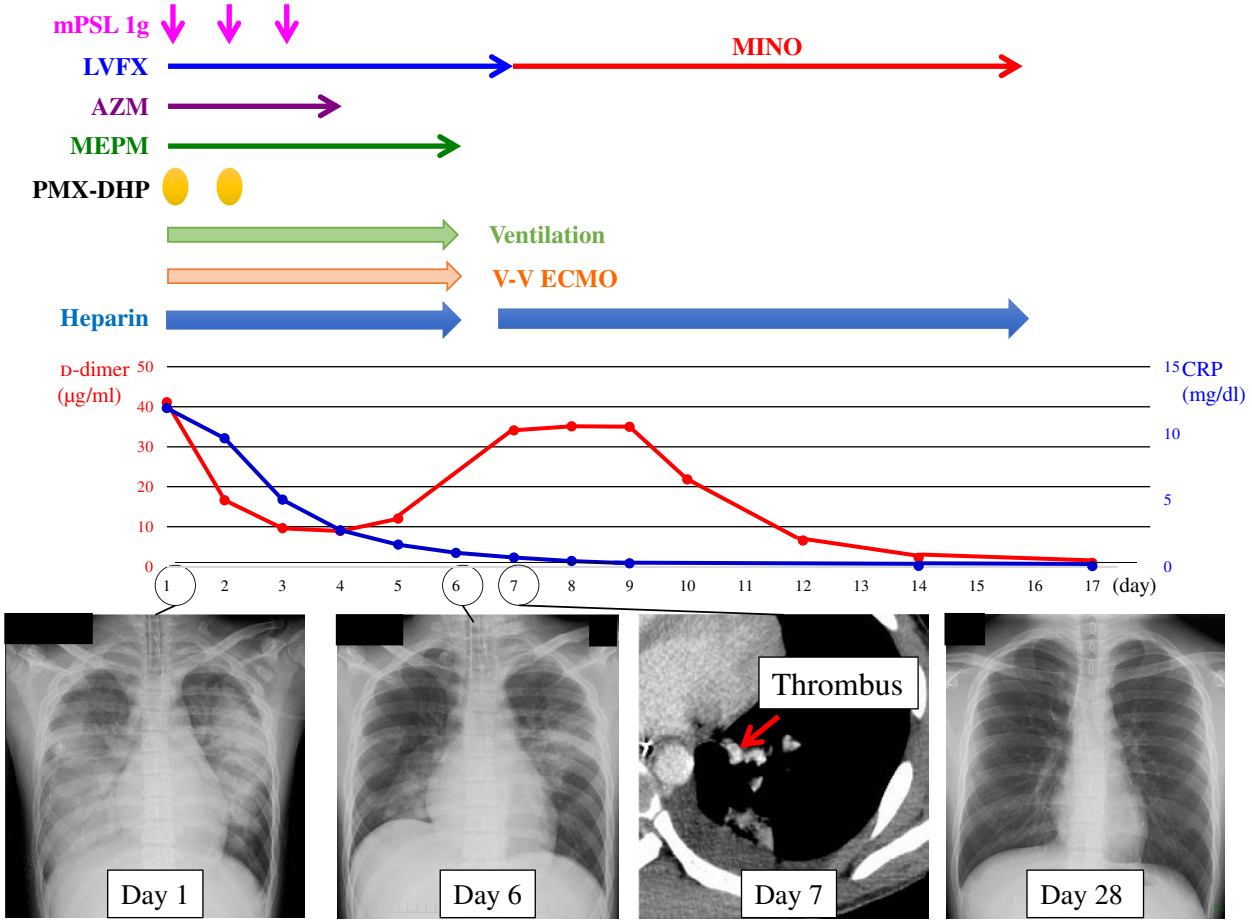

FIGURE 1 Clinical course. AZM, azithromycin; CRP, C-reactive protein; LVFX, levofloxacin; MEPM, meropenem; MINO, minocycline; mPSL, methylprednisolone; PMX-DHP, direct hemoperfusion with a polymyxin B-immobilized fibre column; V-V ECMO, veno-venous extracorporeal membrane oxygenation

piperacillin (13.5 g/day) with levofloxacin (500 mg/day) with right chest tube drainage. On the day of transfer (early January 2020), he had severe hypoxaemia [partial pressure of arterial oxygen (PaO_2), 47 mmHg; inspired oxygen fraction (FiO_2), 1.0], subconjunctival haemorrhage, low white blood cell count (2900/μl) and increased serum lactate dehydrogenase (575 IU/ml), C-reactive protein (11.9 mg/dl), fibrin degradation product (FDP; 89.1 μg/ml) and D-dimer (41.1 μg/ml) levels (Table 1). His echocardiography findings showed no evidence of heart impairment (ejection fraction: 60%), and venous thrombosis was not apparent on his lower extremity ultrasonography. Extracorporeal membrane oxygenation (ECMO) with heparinization (12,000–24,000 units/day), methylprednisolone (1000 mg/day), levofloxacin (500 mg/day), meropenem (3 g/day) and azithromycin (500 mg/day) were initiated, and his hypoxaemia, laboratory data and chest radiographic findings drastically improved in several days. ECMO was withdrawn 6 days after admission. Analyses of the 16S ribosomal RNA (16S rRNA) gene and a multiplex polymerase chain reaction (PCR) test (FilmArray Respiratory Panel [bioMérieux, BioFire Diagnostics, Inc., Salt Lake City, UT]) of his intratracheal secretions were both positive for *M. pneumoniae*, and negative for influenza antigen. PCR test for SARS-CoV-2 was not performed because his admission was 2 months before the start of the COVID-19 pandemic. Heparinization was discontinued; therefore, his FDP and D-dimer levels re-increased, and enhanced CT on the seventh day after the transfer revealed a left pulmonary venous thrombus, and heparinization (27,000 units) was reinitiated. His serum was positive for antiphospholipid antibody (lupus anticoagulant 1.46 U/ml), and his physical findings and family history were not indicative of causing connective tissue disease. Therefore, he was diagnosed with catastrophic antiphospholipid syndrome (CAPS) associated with severe MPP and pleuritis. Heparin was then discontinued on the 16th day of the transfer, and he was discharged 27 days after the transfer with normal chest radiographic findings (Figure 1). Six months after his CAPS diagnosis, his serum lupus anticoagulant level turned to be normal at 1.26 U/ml (normal range: <1.30 U/ml).

DISCUSSION

Here, we present the patient who developed rapid-onset respiratory dysfunction and pulmonary embolism due to CAPS associated with MPP.

Mycoplasma pneumoniae is a respiratory pathogen that causes community-acquired pneumonia, which presents with symptoms such as fever, cough and general malaise similar to common cold symptoms.[1] MPP occasionally presents with extrapulmonary complications such as coagulopathy with thrombosis,[1] and like our patient who had MPP with severe respiratory dysfunction due to left pulmonary venous thrombus. His laboratory data showed coagulopathy with elevated FDP and D-dimer levels and positive for serum antiphospholipid antibody. Antiphospholipid syndrome (APS) is an autoimmune disease that causes repetitive arteriovenous thrombosis and failure to thrive in the presence of antiphospholipid antibodies and lupus anticoagulants.[3] CAPS is APS that causes rapid development of thrombosis of microvessels in multiple organs.[3] Approximately 20% of CAPS cases are caused by viral infections, and transient elevation of antiphospholipid antibodies is observed in patients with CAPS associated with viral infections.[3] Transient elevation of serum antiphospholipid antibodies and thrombosis are more common in patients with MPP than in other bacterial pneumonia.[3,4] The comprehensive mechanism of thrombosis in patients with severe MPP remains unclear so far, but transient hypercoagulability in response to extensive *M. pneumoniae* infection and direct damage to vascular endothelial cells, similar to bronchial epithelial cell damage, may cause thrombosis with elevated antiphospholipid antibody.[3,4] Treatment for CAPS includes anticoagulation, high-dose corticosteroid therapy and plasma exchange. The survival rate of patients with CAPS is reported to be 63% if appropriate treatment is provided.[3]

Our patient presented with bilateral pneumonia, right pleuritis and severe respiratory dysfunction, like the symptoms of COVID-19.[2] It is difficult to precisely differentiate severe MPP with CAPS from severe COVID-19 using only chest CT findings. Multiplex PCR tests have recently been reported to be useful for differentiating severe COVID-19 from severe MPP that require antimicrobial therapy with or without anticoagulation treatment.[5] Multiplex PCR tests and the 16S rRNA gene analysis using bronchoalveolar lavage fluid were useful for confirming *M. pneumoniae* in our patient, which allowed us to initiate appropriate antimicrobial therapy.

We herein present an MPP patient with rapid-onset respiratory dysfunction and pulmonary embolism due to CAPS who was successfully treated with proper antimicrobial treatment due to precise microbiological diagnosis and anticoagulation treatment with ECMO. The manifestations of severe MPP are very similar to severe COVID-19, and proper and prompt microbiological diagnosis is critical in these patients for appropriate antimicrobial therapies, especially in patients presenting with severe bilateral pneumonia in the COVID-19 era.

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CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTION

Kohei Hashimoto and Takako Kawaguchi wrote the draft of the manuscript. Hiroaki Ikegami, Toshinori Kawanami, Kei Yamasaki and Kazuhiro Yatera critically revised the manuscript. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

Research data are not shared.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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