CASE REPORT OF ICU ADMISSION DUE TO *LEGIONELLA PNEUMOPHILA* SEVERE PNEUMONIA IN VIET NAM

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Summary

Legionnaires' disease is a serious type of atypical pneumonia caused by Legionella bacteria. In this case study, the first case of ICU admission due to Legionella pneumophila severe infection in Vietnam is reported. A 40-year-old Japanese male patient with a history of hypertension for over 4 years was hospitalized with fever and frequent breathing difficulties. Diagnosis upon hospitalization was sepsis shock and ARDS pulmonary consolidation. The sputum specimen was then tested with multiplex PCR using Film array panel and the result was positive with Legionella pneumophila detection. The patient was medicated according to the results of bacterial identification which gave good response and was discharged after 22 days of treatment.

Keywords: *Legionnaires' disease, pneumonia.*

INTRODUCTION

Legionnaires' disease (LD) is a serious type of pneumonia caused by *Legionella* bacteria[1] with 2 main species named *Legionella pneumophila* and *Legionella longbeachae*. Legionella spp is gram-negative obligate intracellular bacteria and could not be cultured using traditional method[2]. Therefore, although this disease is reported as a common cause of community-acquired pneumonia (CAP) worldwide[3], limited studies in Vietnam investigate the prevalence of such atypical pathogen[4,6]. Several studies described the clinical presentation of severe pneumonia cases caused by *Legionella* bacteria globally[7,8]. In this case report, we describe a first *Legionella pneumophila* severe infection leading to ICU admission in Vietnam.

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CASE REPORT

A 40-year-old male Japanese patient with hypertension history over 4 years was hospitalized with the symptoms of fever and breathing difficulties. Examination upon admission indicated that the patient was conscious, had good interaction, soft abdomen, intangible liver and spleen, stable heartbeat, and frequent breathing difficulties with SpO_2 92%. His clinical features were as follows: pulse 94 times/minute, body temperature 37.5 degree Celcius, blood pressure 190/100 mmHg, breathing rate 27 times/minute, body weight 75 kg, height 170 cm. Patient with oxygen mask 15 litre/minute was admitted to the Emergency department then was ventilated and transferred to ICU immediately. Diagnosis upon hospitalization was sepsis shock and ARDS pneumonia due to unknown pathogen. This foreign patient was admitted to the hospital on 29th June, 2020 after the 1st wave of COVID-19 pandemic in Vietnam, therefore, he was screened for SARS-CoV-2 infection by real-time PCR method. However, his SARS-CoV-2, Dengue, Rickettsia, AFB staining and other traditional bacterial culture gave all negative results. On the 1st July 2020, his sputum sample was tested using multiplex PCR Film array panel and the result was positive with *Legionella pneumophila* (Figure 1).

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Run Information			
Sample ID	TERUO UEHARA	Run Date	01 Jul 2020 12:32 PM
Protocol	SPUTUM v3.3	Serial No.	25801595
Pouch Type	Pneumo*plus* v2.0	Lot No.	901019
Controls	Passed	Operator	hoa le (minhhoa)
Run Status	Completed	Instrument	2FA06200

Detection Summary

Bacteria
Detected: None

Antimicrobial Resistance Genes
Detected: None

Note: Antimicrobial resistance can occur via multiple mechanisms. A Not Detected result for a genetic marker of antimicrobial resistance does not indicate susceptibility to associated antimicrobial drugs or drug classes. A Detected result for a genetic marker of antimicrobial resistance cannot be definitively linked to the microorganism(s) detected. Culture is required to obtain isolates for antimicrobial susceptibility testing and FilmArray Pneumonia Panel *plus* results should be used in conjunction with culture results for the determination of susceptibility or resistance.

Atypical Bacteria
Detected: ✓ *Legionella pneumophila*

Viruses
Detected: None

Figure 1. Laboratory report of detecting *Legionella pneumophila* from sputum sample

The subclinical data of this patient indicated clear infection condition on admission with high number of white blood cells and other inflammatory markers such as CRP and Procalcitonin. Other parameters including liver enzymes (AST, ALT, GGT) or renal function (urea, creatinine) also increased during hospitalization but mostly were reported within the normal range at discharge (Table 1). The patient also suffered from coagulation disorder with the highest value of D-Dimer was nearly 15000 ng/mL and other heart problems with remarkable increase value of proBNP and Troponin Ths (Table 1). Chest radiograph demonstrated pulmonary consolidation with no clear boundary between two lobes of the lung (Figure 2).

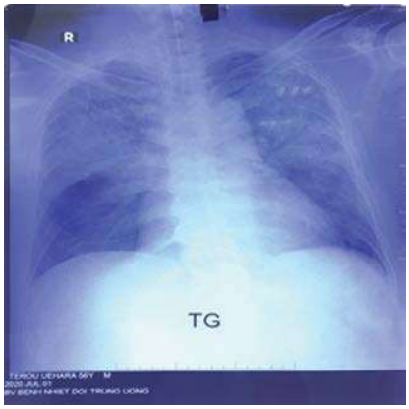

Figure 2. Radiograph showing the pulmonary consolidation in both lung lobes

Before admitting to NHTD, the patient was treated with Rocephine and Avelox at the primary health care centre. However, after 2 days of treatment, the disease was still deteriorated, and his antibiotic was changed to a combination of tienam (imipenem), linezolid and tamiflu at admission. NHTD doctors prescribed Tamiflu as they suspected this patient contracted influenza leading to ARDS pneumonia. They also used broad-spectrum antibiotic and linezolid to cover for potential bacterial co-infection including Staphylococci. After 3 days of treatment, the bacterial identification result was reported with *Legionella pneumophila* positive, therefore moxifloxacin was added to the antibiotic regime. Due to the more complicated pneumonia condition and suspected nosocomial infection, the patient was treated with meropenem and colistin with dose adjusted according to body weight. However, the patient was then detected with renal failure at the day 10 of treatment, so tigecycline was included in the combination with meropenem. He was discharged after 22 days of hospitalization under a stable condition, with an appointment of re-examination after 15 days.

Table 1. The highest value, value on admission and on discharge date of several laboratory parameters

		Date of test		
No	**Test name**	**Admission**	**Highest value**	**Discharge**
1	CRP	391 mg/L	391 mg/L	7.2 mg/L
2	Lactate	4.6 mmol/L	4.6 mmol/L	1.34 mmol/L
3	Urea	5.6 mmol/L	39.8 mmol/L	4.7 mmol/L
4	Glucose	5.4 mmol/L	9.7 mmol/L	5.7 mmol/L
5	Creatinine	80.8 mmol/L	199.8 mmol/L	72.4 mmol/L
6	AST	38.7 U/L	189.5 U/L	43.9 U/L
7	ALT	29.4 U/L	234.4 U/L	103.2 U/L
8	GGT	61.8 U/L	123.4 U/L	77.9 U/L
9	Na+	140 mmol/L	154 mmol/L	143 mmol/L
10	K+	3.7 mmol/L	3.0 mmol/L	3.9 mmol/L
11	Cl-	103 mmol/L	115 mmol/L	107 mmol/L
12	Acid uric	230.8 µmol/L		
13	Total bilirubin	16.1 µmol/L	32.8 µmol/L	24.7 µmol/L
14	Direct bilirubin	6.1 µmol/L	16.3 µmol/L	10.3 µmol/L
15	Albumin	36 g/L	43 g/L	34 g/L
16	White blood cells	13.82 (10^9/L)	17.1 (10^9/L)	12.39 (10^9/L)
17	% Neutrophils	89.8%	84%	61%
18	% Lymphocytes	5.9%	7.6%	25.5%
19	Platelet	179 (10^9/L)	516 (10^9/L)	400 (10^9/L)
20	Hemoglobin	106 (g/L)	106 (g/L)	91 (g/L)
21	PT	51%	68%	57%
22	INR	1.58	1.68	1.45
23	APTT	1.11	1.66	1.2
24	Fibrinogen	7.08 g/L	7.08 g/L	2.81 g/L
25	D-Dimer	2256 ng/mL	14931 ng/mL	1463 ng/mL
26	Procalcitonin	7.66 ng/mL	14.01 ng/mL	0.241 ng/mL
27	proBNP	195.3 pg/mL	1119pg/mL	120.8 pg/mL
28	Troponin Ths	17.2 pg/mL	32 pg/mL	19.46 pg/mL

DISCUSSION

This is the first clinical case report of *Legionella pneumophila* severe infection leading to ICU admission in Vietnam. There are only a few similar reports over the world, in which *L. pneumophila* related to ICU admission is detected in old-aged patients[9]. The symptoms of this Legionnaires' disease case was also in concordance with diseases caused by other pathogen including pneumonia, fever and sputum production. Therefore, without accurate diagnostic approach, such incorrect treatment could result in serious clinical complications requiring hospitalization.

The microbiological method used to detect *Legionella pneumophila* is multiplex PCR Film array panel. This state-of-the-art approach is very accurate with the capacity of detecting 34 respiratory pathogens simultaneously in 1-hour of turn-around time[10]. However, this method is only suitable for tertiary hospital due to its cost-effective issue. Some studies suggested the utility of single PCR reaction to detect *Legionella pneumophila* and other atypical pathogen[4-6], however this method is only limited for research purpose. Other approach is to detect *Legionella pneumophila* antigen through immune complex in

urine samples11 but this test is still not available in routine practice of clinical laboratory in Vietnam.

The study has several limitations. First, we could not explore more about the transmission model of this case, i.e. where and how this foreign patient contracted with *Legionella pneumophila*. Although, literature review suggest the main transmission route of this bacteria is waterborne, we could not find the association between the epidemiological data and the clinical outcome. Second, the laboratory could not provide the antibiotic susceptibility result of this atypical pathogen, therefore, the clinical treatment decision was only based on empirical guideline. Finally, the multiplex PCR using Film array panel was performed solely at admission and the test was not be done at discharge to confirm the clearance of this bacteria from the patient.

CONCLUSION

In conclusion, In this case report, we describe a first Legionella pneumophila severe infection leading to ICU admission in Vietnam. Early and accurate diagnostic approach plays an important role in the outcome of clinical treatment. With such modern multiplex PCR technique, more atypical pathogen can be detected and therefore, the effective treatment of acute respiratory tract infection within ICU setting could be enhanced.

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