

[ CASE REPORT ]

## Multiple Pulmonary Nodules in Leptospirosis

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### Abstract:

A 21-year-old man presented with the chief complaints of fever and sore throat after visiting Cambodia and Thailand. Computed tomography revealed multiple pulmonary nodules. After performing antibiotic therapy, the pulmonary nodules without bacteremia disappeared completely. Paired microscopic agglutination tests revealed seroconversion against *Leptospira* serogroup Autumnalis. Thus, he was diagnosed with multiple pulmonary nodules caused by leptospirosis. Leptospirosis is a common zoonosis that occurs in tropical and subtropical areas. Its various clinical features include unspecified fever and Weil's disease. Although diffuse alveolar hemorrhaging is known to occur in severe leptospirosis, multiple pulmonary nodules resembling septic emboli or vasculitis are a rare complication.

**Key words:** multiple pulmonary nodules, leptospirosis, *Leptospira*

(Intern Med 59: 2941-2944, 2020)

(DOI: 10.2169/internalmedicine.4305-19)

### Introduction

Leptospirosis is a common zoonosis worldwide, particularly in tropical and subtropical regions, often presenting with non-specific clinical features (1, 2). Alveolar hemorrhaging is common in severe infections (2-4). The frequency of pulmonary complications in mild-to-moderate leptospirosis is largely unknown, although small nodular opacities, consolidation, or ground glass opacities are noted on chest radiographs in some patients (5, 6). In the case described herein, the pulmonary lesions caused by leptospirosis showed atypical findings, including bilateral peripheral pulmonary nodules characteristic of septic emboli or vasculitis on high-resolution computed tomography (HRCT) of the chest.

### Case Report

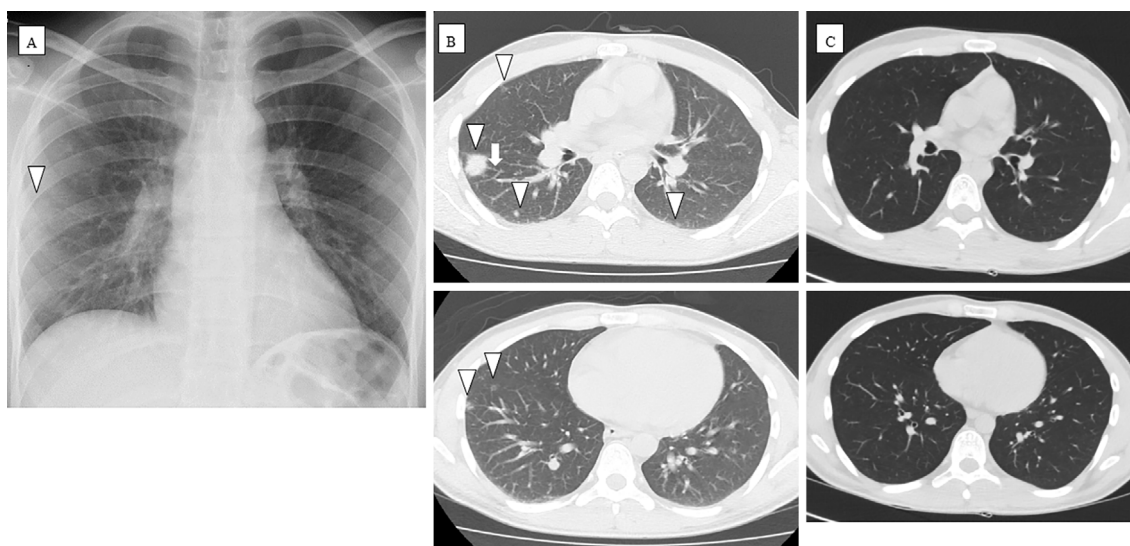
A 21-year-old previously healthy man from the Netherlands arrived in Japan following a 22-day trip to Cambodia and Thailand and was admitted to a hospital 6 days after arrival. He complained of a 3-day history of fever followed by a 2-day history of sore throat, hoarseness, headache, and di-

arrhea. He had visited the emergency room of another hospital the previous day, where investigations showed his serum creatinine level to be elevated at 1.96 mg/dL (reference range, 0.60-1.10 mg/dL). In addition, the alanine transaminase levels were slightly elevated, at 58 IU/L (reference range, 8-42 IU/L), and the C-reactive protein level was elevated at 14.3 mg/dL (reference range, 0-0.3 mg/dL). A chest radiograph showed faint small nodules in the right lung (Figure A). HRCT revealed several bilateral random hypervascular nodules (measuring 5-20 mm in diameter) (Figure B). Ceftriaxone (2 g) was administered intravenously. After the administration of antibiotics, his symptoms, such as chills and rigor worsened and oliguria appeared, thus suggesting a Jarisch-Herxheimer reaction. On the following day, he was referred to our hospital with these symptoms. He had not been exposed to any animals or fresh water in Cambodia, except water from a swimming pool. He strongly denied using illicit drugs intravenously. On examination, his body temperature was elevated to 38.2°C, and he looked slightly sick. His throat looked normal except for some faint redness, with disseminated stomatitis on his soft palate. A blood test showed that serum creatinine and urea nitrogen levels were elevated at 3.58 mg/dL (reference range, 0.60-1.10 mg/dL) and 25.5 mg/dL (reference range, 8.0-22.0 mg/

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Received: December 23, 2019; Accepted: June 7, 2020; Advance Publication by J-STAGE: July 21, 2020

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**Figure.** Radiological image findings. A: Chest radiograph on 4th day of illness shows a nodular lesion (arrow head). B: Chest computed tomography (CT) on 4th day of illness showing bilateral multiple random nodular lesions (white arrow head) with an effluent pulmonary artery (white arrow). C: Chest CT 20 days after discharge showing no nodular lesions.

**Table.** Laboratory Findings on Admission.

WBC	8.40×10 <sup>3</sup> /μL	Alb	2.7 g/dL	K	3.7 mEq/L
Neutrophil	87.6 %	T-bil	0.3 g/dL	Cl	95 mEq/L
Lymphocyte	6.7 %	AST	41 U/L	Glucose	113 mg/dL
Monocyte	5.5 %	ALT	40 U/L	CRP	13.05 mg/dL
Eosinophil	0.1 %	LDH	263 U/L		
RBC	4.49×10 <sup>6</sup> /μL	γGTP	36 U/L	<Urinalysis>	
Hb	12.8 g /dL	ALP	123 U/L	Protein	1+
Ht	37.2 %	CK	795 mg/dL	Glucose	3+
Platelet	17.8×10 <sup>4</sup> /μL	BUN	25.5 mg/dL	Blood	3+
		Cr	3.58 mg/dL	Nitrate	-
		Na	128 mEq/L	Leukocyte esterase	1+

WBC: white blood cells, RBC: red blood cells, Ht: hematocrit, Hb: hemoglobin, BUN: blood urea nitrogen, Cre: serum creatinine, Alb: albumin, T-Bil: total bilirubin, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, γGTP: γ-glutamyl transpeptidase, ALP: alkaline phosphatase. Na: serum sodium, K: serum potassium, Cl: serum chloride, CRP: C-reactive protein

dL), respectively (Table). The results of a rapid antigen test for dengue (BIOLINE Dengue Duo NS1Ag+IgG/IgM, Standard Diagnostics, Gyeonggi-do, Republic of Korea) and smears for malaria were negative. Urine analysis revealed proteinuria and pyuria. Two sets of blood cultures collected from two different sites before starting antibiotics and urine culture were negative. On the following day, his urine output normalized after adequate hydration. The creatinine levels decreased to 1.22 mg/dL, 5 days after admission. A transthoracic echocardiogram showed no vegetations on the tricuspid valve and pulmonary valve, and no valve destruction was seen. There was no ventricular septal defect that could have caused infective endocarditis of the right heart.

We continued ceftriaxone (2 g/day intravenously) for suspected pulmonary septic emboli of unknown etiology. He subsequently became afebrile, and the pulmonary lesions

improved, as noted on the chest radiograph. Owing to the patient's requests for urgent discharge, the antibiotic was changed to oral amoxicillin/clavulanic acid on day 6 of his illness, and he was discharged on day 10.

We suspected that his symptoms may have been caused by leptospirosis based on the negative blood cultures, the fact that he swam in a pool in a rural area of Cambodia, one of the endemic areas for leptospirosis, and the transient deterioration in the symptoms just after initiating antibiotic administration similar to a Jarisch-Herxheimer reaction. The microscopic agglutination test (MAT) for *Leptospira* serogroups on paired serum samples collected on days 6 (titer less than 1:10) and 10 (titer 1:100) of illness revealed seroconversion for serogroup Autumnalis strains (*L. interrogans* serovars Autumnalis and Rachmati). The pulmonary nodules disappeared after 2 weeks of antibiotic therapy, which was

confirmed by HRCT, 20 days after discharge from our hospital (Figure C).

## Discussion

Respiratory symptoms are found in 20-55% of patients with leptospirosis (3). Pulmonary hemorrhaging is a well-known complication of severe leptospirosis. Pulmonary abnormalities are found in around 68% of chest radiographs of leptospirosis patients, with the commonest being randomized multiple small nodules (57%), large combined shadows (16%), and ground glass opacities (27%) (5). Typical findings of leptospirosis on HRCT are bilateral ground-glass opacities, areas of consolidation, air-space nodules distributed on the bronchi, and small pleural effusions (6-11). In our case, randomly scattered peripheral nodules of various sizes were revealed on HRCT, with no typical findings of leptospirosis.

The HRCT findings in our case were similar to those found in vasculitis, such as granulomatosis with polyangiitis or in septic pulmonary embolism (12-14). Vascular endothelial injuries, which are associated with systemic inflammation in leptospirosis, may cause pulmonary vasculitis similar to that caused by other infectious pathogens (15). However, acute leptospirosis can cause diffuse activating endothelial disorder which is similar to the pathogenesis of sepsis rather than classical systemic vasculitis such as granulomatosis with polyangiitis (15). Moreover, there are no reports of multiple vasculitic nodular lesions associated with leptospirosis (16). Multiple nodules were continuous from the pulmonary artery, and continuity in more than one direction was confirmed. Although this finding suggested that these pulmonary lesions were likely hypervascular lesions, it was unclear whether these findings were feeding vessel signs of septic emboli (17) because an enhanced chest CT scan was not performed. Septic pulmonary embolism is caused by the vegetation of bacteria or fungus, which acts as an emboli. Some cases were associated with right-sided infective endocarditis (13, 14). Although, to our knowledge, there are no reports on septic pulmonary embolism caused by *Leptospira* spp., however, they have been reported to form vegetation functioning as emboli, and thus cause infective endocarditis (18). In the present case, except for pulmonary lesions, there was no clear evidence of endocarditis. There was no evidence of massive pulmonary embolism in the pulmonary artery. Unfortunately, we could not confirm the etiology of the pulmonary nodules because a lung biopsy was not conducted.

Although the source of infection remains unknown in 16% of patients with leptospirosis, almost all patients have a history of contact with animals or swimming in fresh water (4). *L. interrogans* has been detected in inadequately disinfected swimming pools (19). However, infection from this water source is uncommon.

In conclusion, multiple pulmonary nodules resembling septic emboli or vasculitis were caused by leptospirosis.

When the patient experienced multiple pulmonary nodules along with fever after traveling to a leptospirosis endemic area, leptospirosis was considered in the differential diagnosis. Pulmonary complications including multiple nodules in patients with mild-to-moderate leptospirosis are not well documented because these patients do not require HRCT unless they exhibit serious respiratory symptoms. Moreover, the pathology of these nodules remained unclear because a lung biopsy was not performed. Further reports are required on HRCT findings of pulmonary lesions in mild-to-moderate cases of leptospirosis, in order to elucidate the pathology of pulmonary nodules, and to assess their clinical significance.

**The authors state that they have no Conflict of Interest (COI).**

## Financial Support

This study was supported in part by research grants from the Emerging/Re-emerging Infectious Diseases Project of Japan from the Japan Agency for Medical Research and Development, AMED (18fk0108009h0003), and a grant from Japan's National Center for Global Health and Medicine (grant no. 29-1018).

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