

## **Case Report**

# Weil's disease with multiple organ dysfunction, community-acquired pneumonia and septic shock: The role of rapid diagnosis and management

Berty D. Hermawati<sup>1</sup>, Brigitta DA. Hapsari<sup>2\*</sup>, Evi L. Wulandari<sup>1</sup>, Nurhasan A. Prabowo<sup>1</sup>, Coana Sukmagautama<sup>1</sup>, Desy P. Putri<sup>1</sup>, Hendrastutik Apriningsih<sup>2</sup>, Annisa A. Rahma<sup>3</sup> and Ragil R. Nafila<sup>3</sup>

<sup>1</sup>Department of Internal Medicine, Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia; <sup>2</sup>Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia; <sup>3</sup>Faculty of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia;

\*Corresponding author: brigitta.anindita@staff.uns.ac.id

## Abstract

Leptospirosis is an uncommon infectious illness – a spirochetal zoonosis – caused by Leptospira species and the primary cause of human leptospirosis is exposure to the urine of infected rodents. Clinical manifestations of human leptospirosis are diverse, ranging from asymptomatic infection to severe life-threatening with multiorgan dysfunction. The severe condition is known as Weil's disease, which is characterized by feverish illness with jaundice, acute kidney damage, and bleeding. The aim of this case report was to present a Weil's disease which occurred simultaneously with a community-acquired pneumonia (CAP) resulting in serious complications. A 41-year-old man with Weil's disease, as well as CAP caused by Streptococcus pneumoniae, and septic shock was presented. The patient was treated accordingly after establishing the diagnosis through history taking, physical examination, and laboratory tests. In this instance, the score for diagnosing leptospirosis based on Modified Faine's Criteria was calculated resulting possible diagnoses; and therefore, therapeutic management was initiated. Despite presenting with severe symptoms, the patient recovered completely after receiving antibiotics and supportive care. This study highlights that when a patient has Weil's disease and a CAP infection, which could cause unfavorable consequence, a prompt diagnosis and proper treatment could result satisfied patient recovery.

**Keywords**: Leptospirosis, Weil's disease, multiple organ dysfunction, communityacquired pneumonia, septic shock

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## Introduction

Leptospirosis is an emerging zoonotic disease caused by *Leptospira* sp. [1] and becoming more common all over the world [2]. Each year, 1.03 million cases of leptospirosis are reported, with 58,900 fatalities [3]. Leptospirosis is anticipated to be the primary zoonotic cause of sickness and mortality. Furthermore, illness and death rates were the highest in the world's poorest regions and in regions where monitoring is not frequently done [3]. Cuts and abrasions, as well as mucous membranes such as the conjunctiva, and oral, or vaginal surfaces, may serve as entrance points. Exposure may occur via direct contact with infected animals or by indirect contact with soil or water contaminated with infected animals' urine [4]. Indirect contact with *Leptospira*-contaminated water or soil is much more prevalent, and it may be linked to recreational or

occupational activities [4]. In addition to the dangers associated with outdoor labor, sewage work, military training, and agriculture in tropical locations with considerable rainfall are all recognized, with the last being the most significant in terms of numbers.

The clinical manifestation of leptospirosis ranges from subclinical or asymptomatic, modest indicator, self-limited symptoms to severe lethal presentations. A significant number of patients in endemic locations may have subclinical illness detected only by serology [5]. Leptospirosis may cause life-threatening consequences such as renal failure, meningitis, pulmonary hemorrhage, and multi-organ failure. Weil's syndrome, a severe form of leptospirosis with high mortality, is characterized by liver dysfunctions accompanied by renal failure and hemorrhage [6]. Patients with severe leptospirosis should receive prompt diagnosis and intensive treatment. Although immediate antibiotic therapy may lessen the severity of leptospirosis, diagnosis is often delayed, resulting in a high fatality rate [7].

Patients infected with *L. interrogans* – one of the species of *Leptospira* – typically suffer from multiorgan dysfunction due to the difficulties in early detection of the disease [7]. A diagnosis based only on clinical examination is not always correct, but a specific diagnosis may only be ascertained after clinical suspicion has been established. The diagnosis of leptospirosis must be confirmed by blood or urine cultures, or serological testing, in addition to the presence of clinical symptoms. The World Health Organization (WHO) has proposed "Faine's criteria" for leptospirosis diagnosis, which now has been modified to improve diagnostic sensitivity [8,9]. Prompt initiation of anti-biotherapy is essential for both disease control and preventing the microorganism's urinary spread [10]. The aim of this case report was to describe a patient who experienced Weil's disease with multiple organ dysfunction and a community-acquired pneumonia (CAP) due to *Streptococcus pneumoniae*. The patient experienced serious complications, including septic shock, but the condition improved with prompt diagnosis and treatments.

## Case

A 41-year-old male from Grobogan, Karanganyar, Central Java, Indonesia, presented to the emergency department of Universitas Sebelas Maret Hospital, Surakarta, Central Java, Indonesia, on March 17, 2023 with a fever of 39°C, headache, malaise, nausea, and vomiting, which he had experienced for three days. The patient had developed jaundice, continual fatigue, and severe calf pain five days before hospital admission. The patient also complained of coughing for the last seven days, coughing up yellow mucus that grew increasingly aggravating. Additionally, the patient had also felt chest tightness for the past three days. The feces were a brownish-yellow color with a soft consistency and no blood or mucus; the urine was a dark color, and the volume was less than usual.

The patient works for the city's sanitation service, scrubbing the drains along municipal streets every day. Approximately three days before complaining the health, an object injured the right leg while was working. The patient confessed that the boots were damaged at the time, but continued to wear them to work and was submerged in the water.

The patient reported having previously smoked. Recent travel, alcohol consumption, recent antibiotic exposure, or contact with sick individuals were denied. The patient also denied taking injectable drugs, engaging in deviant sexual behavior, or having several relationships. The patient experienced an ST-elevation myocardial infarction in 2017 while taking acetylsalicylic acid 1×80mg, atorvastatin 1×20mg, perindopril 1×4mg, and bisoprolol 1x5mg as routine medication. Later, however, the patient discontinued treatment on his own and was no longer routinely monitored by the physician, as no more complaints.

Physical examination at the emergency room revealed somnolence, low blood pressure of 70/30 mmHg with mean arterial pressure (MAP) 43.3 mmHg, bradycardia with a pulse rate of 43 beats per min (bpm), high body temperature (39°C), and tachypnea with a respiratory rate of 50x/min. The initial oxygen saturation was 86% and 10 liters per min non-rebreathing mask (NRM) oxygen was administered resulting the saturation rose to 98%. Conjunctival suffusion and icteric scleral were found in both eyes. Thoracic examination revealed the presence of coarse crackles in both lungs. There was tenderness on the right hypochondriac region of the abdomen, pain in the bilateral gastrocnemius, prolonged capillary refill time (CRT) of the lower

extremities, and warm and sweaty skin. The patient was admitted to the intensive care unit (ICU) with the diagnosis of septic shock, Weil's disease suspicion, and community-acquired pneumonia.

Blood laboratory on the first day of hospitalization showed a hemoglobin (Hb) level of 12 g/dL, thrombocytopenia with platelet counts of  $51,000/\mu$ L, and leukocytosis ( $15,510/\mu$ L) with lymphocytopenia (4.2%) and neutrophilia (87.4%) (Table 1). Blood biochemical examinations revealed abnormal liver function with an increase of total bilirubin (2.04 mg/dL), direct bilirubin (1.32 mg/dL), aspartate transaminase (AST) (189 U/L), and alanine transaminase (ALT) (92 U/L). A rise in blood urea nitrogen (148 mg/dL) and serum creatinine (5.66 mg/dL) indicated impaired renal function were also found. Moreover, laboratory findings also showed electrolyte imbalance with severe hyponatremia (121.81 mmol/L) and hypocalcemia (1.01 mmol/L). Immuno-serological test for anti-Leptospira IgM was negative on the first day of hospitalization. Arterial blood gas analysis showed partially compensated metabolic acidosis with pH 7.310, PCO<sub>2</sub> 24 mmHg, PO2 119 mmHg, HCO3 12.3 mmHg, and lactate 4.20 mmol/L. Urinalysis test revealed deep vellow and slightly cloudy urine with hematuria (3+). Cultures on the patient's sputum and blood were also conducted, in which blood culture did not show any growth of bacteria. Sputum culture results that came out five days after the examination yielded S. pneumoniae as the cause of pneumonia. Various serologic tests were also performed with anti-HAV, anti-HBsAg, anti-HCV, and anti-HIV were all negative. The test of dengue IgM and Salmonella typhi IgM were also negative (Table 1).

#### Table 1. Serial results of blood tests

Indicator	Normal	Day 1	Day 2	Day 3	Day 5	Day 7
	value					
Hematology						
Leukocytes (10 <sup>3</sup> /mm <sup>3</sup> )	4.2-9.3	15.51	15.68	8.69	10.13	9.2
Thrombocytes (10 <sup>3</sup> /mm <sup>3</sup> )	150-450	51	13	26	45	98
Erythrocytes (10 <sup>6</sup> /mm <sup>3</sup> )	4-5	3.94	3.85	4.25	4.16	4.45
Hemoglobin (g/dL)	12 - 15	12.0	11.6	12.8	12.4	12.8
Hematocrit (%)	37-43	31	30	33	33	37
MCV (µm <sup>3</sup> )	80-100	79.4	78.2	78.1	79.6	80.1
MCH (pg)	26-34	30.5	30.1	30.1	29.8	30.6
MCHC (g/dL)	32-36	38.3	38.5	38.6	37.5	35.6
Diff count						
Lymphocytes (%)	20-40	4.2	3.8	5.5	16.3	19.1
Monocytes (%)	4-12	4.6	6.0	5.9	14.8	12.9
Neutrophil (%)	50-70	87.4	89.8	88.4	68.1	65
Eosinophil (%)	0.5-7	3.5	0.1	0.0	0.6	0.6
Basophil (%)	0-2	0.3	0.3	0.2	0.2	0.2
Liver function						
ALT (IU/L)	<31	189			64	29
AST (IU/L)	9–36	92			38	35
Indirect bilirubin mg/dl	0.20-0.80	0.72				
Total bilirubin mg/dl	0.10-1.00	2.04				
Direct bilirubin mg/dl	0.00 - 0.20	1.32				
Kidney function						
Urea (mg/dL)	10-45	148	206		139	40
Creatinine (mg/dL)	0.5 - 1.2	5.66	4.83		1.67	1.1
Transient blood glucose (mg/dL)	75-200	109	125		130	
Electrolyte serum						
Sodium mmol/L	135-145	121.81	126.08	135.90		
Potassium mmol/L	3.50 - 5.50	3.89	3.51	3.55		
Calcium mmol/L	1.10 - 1.35	1.11	1.10	1.12		
Chloride	96–106	104.06	113.80	100		

Chest X-ray showed prominent broncho vascular marking, right para cardiac infiltrates, and an increased cardiothoracic ratio, suggesting cardiomegaly and bronchopneumonia (**Figure 1A**). Electrocardiography (ECG) of day 2 of admission showed borderline 1<sup>st</sup> degree AV block and lateral ST elevation, thus, acute ST-elevation myocardial infarction (STEMI) was considered (**Figure 1B**).



Figure 1. Chest radiograph on the first day of hospitalization (A) and electrocardiography (ECG) on day 2 of admission (B). The chest radiograph reveals right paracardial infiltrates, a higher cardiothoracic ratio, and significant broncho vascular marking and the ECG suggests borderline 1<sup>st</sup> degree AV block and lateral ST elevation.

On the first day of hospital admission, the patient was promptly transported from the emergency department to the ICU for continuous monitoring. The patient was diagnosed with septic shock, suspected leptospirosis, CAP with a pneumonia severity index score of 91 and a risk class of 4, and cardiogenic pulmonary edema. Nutritional therapy in addition to oxygen therapy was initiated. Rapid administration of 30 mL/kg 0.9% NaCl intravenous fluid with attention to the presence of overhydration, infusion of norepinephrine 0.2 mcg/kg/min, and dobutamine 5 mcg/kg/min were administered. A 3% NaCl infusion over 18 h was also given to correct severe hyponatremia. The patient was given 750 mg of levofloxacin on the first day, followed by 500 mg every 48 h, 2 g of ceftriaxone every 24 h, and 300 mg acetylcysteine infusion 1 g every 8 h (if necessary), folic acid 800 mcg once daily, and curcuma one tablet every 8 hours were also initiated. This patient was also prescribed oral atorvastatin 20 mg once daily due to the possibility of acute STEMI.

On the second day of admission, blood tests revealed a decrease in platelets to 13,000/L. Due to the patient's severe thrombocytopenia and hematuria, four units (200 ml) of thrombocyte concentrate were administered. Post-transfusion blood exam showed an increase in platelet counts to 26,000/L. After serum electrolytes were corrected and re-examined, sodium levels increased to 126.08 mmol/L. A 3% NaCl drip over 18 h was administered to achieve normal sodium levels the following day. On the fourth day of admittance, hemodialysis was performed as the patient was diagnosed with stage 3 acute kidney injury, with a 24-h decrease in urination output of only 0.2 mL/kg/hour. The patient's consciousness improved after hemodialysis, and the urine output increased to 0.5 cc/kg/h. Due to the suspected leptospirosis, the Leptospira IgM test was repeated on the fifth day and yielded positive. Following ICU treatment and monitoring for a duration of 5 days, which involved oxygenation therapy, fluid and nutritional therapy, electrolyte correction, administration of antibiotics based on clinical conditions, administration of vasopressors, transfusion of thrombocyte concentrate, and one session of hemodialysis due to a 24-hour urine output of 0.2 mL/kg/hour, the patient's condition progressively stabilized and improved. On the sixth day of treatment, the patient was transferred from the ICU to the general ward.

A transthoracic echocardiogram performed on the eighth day of admission revealed grade 1 diastolic dysfunction, mild pulmonic regurgitation, and mild tricuspid regurgitation, with a low likelihood of pulmonary hypertension (**Figure 2A**). The liver, gallbladder, spleen, pancreas, kidneys, and bladder were all normal, according to the abdominal ultrasound results (**Figure 2B-D**).

The patient's condition improved after eight days of hospitalization as his complaints of fever, tightness, jaundice, myalgia, and gastrointestinal issues diminished. His vital signs were stable, and he could communicate and eat normally. The patient was then discharged after eight days of hospitalization.



Figure 2. Transthoracic echocardiography (A) and ultrasound (USG) of the abdomen (B-D) of the patient on the eighth day of hospital admission. The transthoracic echocardiography reveals grade 1 diastolic dysfunction, mild pulmonic regurgitation, and mild tricuspid regurgitation, with a low likelihood of pulmonary hypertension (A) and abdominal USG within normal limits (B-D).

## Discussion

In this report, a case of severe leptospirosis, also known as Weil's disease, accompanied by CAP and *S. pneumonia* and a septic shock was described. On admission, the patient had a fever, headache, conjunctival suffusion, dark urine, myalgias, leukocytosis, thrombocytopenia, acute kidney injury, liver failure, hyperbilirubinemia, and shortness of breath. The patient also encountered septic shock and was treated according to the guidelines for septic shock management. The following treatments were administered: oxygenation, nutritional therapy, aggressive hydration, electrolyte imbalance therapy, vasopressors, and antibiotics. Due to severe thrombocytopenia and hematuria, the patient was administered a thrombocyte concentrate transfusion. Moreover, the patient underwent a single hemodialysis treatment due to a 24-hour urine output of 0.2 cc/kg. Strict hemodynamic, respiratory, hematological, hepatic, and kidney monitoring was performed. The patient's condition improved with the treatment, and recovered after eight days.

Leptospirosis is a zoonosis that is prevalent in tropical countries and poses a considerable public health risk, with an estimated annual morbidity of 39.2 cases per 100.000 people in Indonesia [3,11]. Mud fever, slime fever, swamp fever, autumnal fever, infectious jaundice, field fever, and cane fever are all names for Leptospirosis. Leptospirosis is caused by spirochetes bacteria of the genus *Leptospira*, family Treponema. *Leptospira* infection may occur in humans either through direct contact (blood, urine, or other bodily fluids exchange) or indirect contact with the urine of infected animals that usually live in stagnant water, rivers, lakes, ditches, or feces. *Leptospira* can enter the human circulation via intact mucosa, and systemic vasculitis may be seen in both major and small blood vessels in addition to other organs [6]. According to the patient's account, he was working hard to clear ditches when he sustained an injury on his right limb and accidentally immersed it in the water that was in the ditch.

The progression of the disease is comprised of two distinct clinical phases, septicemic and immune [12,13]. In the initial phase, humans exposed to the bacteria may exhibit flu-like symptoms 7 to 14 days after exposure [12]. During this time frame, patients may appear with conjunctival suffusion, a symptom that normally does not occur with other nonspecific tropical

febrile infections such as dengue, typhoid, or malaria. Patients may also come with a fever [12,13]. After one month of contact with the bacteria second phase of leptospirosis may continue [12,14]. During this phase, the immune system responds to bacterial infection by unleashing and regulating cytokines 3 and 7. The body effectively balances these responses in moderate cases, resulting in asymptomatic resolution [12,15]. In extreme circumstances, however, the immune system would react more forcefully, resulting in a cytokine storm that damages many organs, including the liver, kidney, and heart [15]. Cytokine storms are caused when the immune system releases a large number of cytokines all at once. As a consequence of this phenomenon, abnormal laboratory findings such as higher levels of bilirubin, liver enzymes, renal function, and thrombocytopenia could be observed [12,16].

People who are infected with leptospirosis may present with asymptomatic illness, a selflimiting systemic infection, or severe and possibly deadly clinical manifestations. The clinical symptoms of leptospirosis span a wide spectrum and include all of these possibilities [14]. Headache, fever, malaise, myalgia, conjunctival suffusion, and a fleeting rash are among the symptoms that suddenly appear after the commencement of the condition [6,17]. Research has shown that only a small percentage of exposed people acquire severe types of diseases like Weil's illness, whereas the vast majority merely have mild symptoms [6,17].

Weil's disease is a severe type of leptospirosis that has a high death rate, characterized by hepatic dysfunctions associated with renal failure and hemorrhages. Weil's disease accounts for 10% of all cases of leptospirosis [6]. Patients suffering from Weil's disease should get an early diagnosis and comprehensive medical therapy as soon as possible. At this time, neither the pathophysiology of leptospirosis nor the variables that lead to severe leptospirosis are completely understood [18]. Like this patient, leptospirosis was characterized by severe manifestations, including jaundice, AKI, and hemorrhage [19,20].

The polymerase chain reaction (PCR) test is now considered to be the most accurate method for detecting leptospirosis [21,22]. A quick serology test using microscopic agglutination test (MAT) may be used as an alternative in secondary healthcare institutions that are unable to execute the test [13,21]. Therefore, early diagnosis and prompt treatment are pivotal to avoid illness development, which might lead to multiple organ failures and ultimate fatality [13,23].

Clinical history (Part A), epidemiological history (Part B), and laboratory parameters (Part C) make up the three parts of the Faine's criteria that the WHO created for the diagnosis of leptospirosis [2]. Since then, Faine's criteria have seen an improvement in their diagnostic sensitivity [8]. The patient in this case, had a fever of 39°C (2), headache (2), conjunctival suffusion (4), myalgia (4), jaundice (1), and dyspnea (2), according to the Modified Faine's Criteria (**Table 2**). Epidemiological factors revealed contact with a contaminated environment (4), and bacteriological and laboratory findings revealed the presence of IgM antibodies to *Leptospira* (15). The total Modified Faine's Criteria score for this patient was 34, which indicated leptospirosis as a possible diagnosis.

The vast majority of leptospirosis is considered to be minor and self-limiting. The development of illness might be avoided in some individuals by starting antibiotic treatment early. As soon as there is a reason to think that a patient has leptospirosis, empirical therapy should be initiated. Patients diagnosed with severe leptospirosis are often given intravenous penicillin (1.5 million units IV every six hours), ampicillin (0.5–1 g IV qid), ceftriaxone (1 g IV daily), or cefotaxime (1 g IV qid) as part of their treatment. It has been established that ceftriaxone is just as effective as penicillin in treating severe leptospirosis [6,17].

Additionally, the patient, in this instance, has experienced chest tightness for the past three days. The patient also complained of coughing with increasingly yellow mucous for seven days. Upon examination of the chest, the pulmonary fields of both lungs revealed coarse crackles. The chest x-ray showed prominent broncho vascular signs and right pericardiac infiltration, suggesting CAP. *S. pneumonia* is a common cause of CAP, as indicated by the sputum culture results in this patient. The antibiotic sensitivity test revealed that the organism was susceptible to ceftriaxone and levofloxacin, administered a few days prior.

Based on the 2007 IDSA/ATS CAP guidelines one significant or three minor criteria are needed to define severe pneumonia requiring ICU admission [24]. One primary criterion found in this patient was septic shock with the need for vasopressors. Besides, three minor criteria were

also found, including the respiratory rate of more than 30 breaths/min, uremia (148 mg/dL), and thrombocytopenia ( $51,000/\mu$ l). Thus, the patient needed to be admitted to the ICU. CAP patients with ICU admission are given beta-lactam antibiotics (ampicillin-sulbactam, cefotaxime, or ceftriaxone) plus either a macrolide or a fluoroquinolone including levofloxacin.

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Criteria	Score	Patient
		score
Part A: Clinical data		
Headache	2	2
Fever	2	
Fever >39°C	2	2
Conjunctival suffusion	4	4
Meningism	4	
Myalgia	4	4
Conjunctival suffusion with meningism and myalgia	10	
Jaundice	1	1
Albuminuria/nitrogen retention	2	
Hemoptysis/dyspnea	2	2
Part B: Epidemiological factors		
Rainfall	5	
Contact with contaminated environment	4	4
Animal contact	1	
Part C: Bacteriological and laboratory findings		
Isolation of Leptospira in culture-Diagnosis certain		
Polymerase chain reaction	25	
Positive serology		
Enzyme-linked Immunosorbent assay Ig M positive	15	15
Slide Agglutination test positive	15	
Other rapid test-latex agglutination tests	15	
Microscopic agglutination test-single positive in high titer	15	
Microscopic agglutination test-rising titer/seroconversion (paired sera)	25	
Presumptive diagnosis of leptospirosis is made of:		
Part A or Part A and Part B score: 26 or more		
Part A, B, C (total): 25 or more		34
A score between 20 and 25 suggest leptospirosis as a possible diagnosis		

In 2017, the patient had an ST-elevation myocardial infarction. Additionally, the chest X-ray revealed a heightened cardiothoracic ratio. During this hospitalization, the patient also encountered shortness of breath. The ECG showed an anomalous ECG with probable first-degree AV block and lateral ST elevation. Therefore, acute STEMI should be considered. Later conducted serial ECGs demonstrated that acute STEMI was ruled out. A transthoracic echocardiogram on the eighth day revealed grade 1 diastolic dysfunction, mild pulmonic regurgitation, and mild tricuspid regurgitation, with a low likelihood of pulmonary hypertension.

The patient was also treated for septic shock with rapid administration of NaCl intravenous fluid, norepinephrine, and dobutamine. Sepsis and septic shock are medical emergencies requiring early fluid resuscitation as the first-line therapy. The resuscitation requires at least 30 mL/kg of crystalloid fluid (including NaCl) within the first three hours [25,26]. Fluid resuscitation in septic shock is given to correct hypotension associated with hypovolemia. The mechanism of action of vasopressors, including norepinephrine, is to increase peripheral vascular resistance to increase blood pressure in patients with hypotension despite adequate fluid resuscitation or cardiogenic pulmonary edema [26,27]. Inotropes, such as dobutamine, can be administered in cases of myocardial dysfunction to increase cardiac output by increasing cardiac contractility. Patients with persistent hypoperfusion and low cardiac output despite adequate fluid resuscitation and the use of vasopressor agents may be given dobutamine.

## Conclusion

This is a case report of a 41-year-old man with severe manifestations of leptospirosis (Weil's disease), along with CAP *S. pneumonia*, and septic shock. Leptospirosis was diagnosed using the Modified Faine's Criteria assessment, which confirmed the possibility of infection. The disease was diagnosed based on clinical data, epidemiological factors, bacteriological and laboratory

findings, and then antibiotics and other symptomatic treatments were administered. Despite presenting with severe symptoms, the patient recovered completely after eight days, highlighting the importance of early diagnosis and prompt treatment.

## **Ethics approval**

The patient provided written informed consent to be published as case report.

#### **Competing interests**

The authors declare that there is no conflict of interest.

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#### **Underlying data**

All data underlying the results are available as part of the article and no additional source data are required.

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