Severe Weil's Disease Complicated by Symmetrical Peripheral Gangrene

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ABSTRACT

A man in his 70s presented with fever, jaundice, myalgia, and shortness of breath, which rapidly progressed to septic shock, acute kidney injury (AKI), and acute respiratory distress syndrome (ARDS). The diagnosis of Weil's disease was confirmed by a positive urine Polymerase Chain Reaction (PCR) for pathogenic Leptospira. A rare and severe complication of symmetrical peripheral gangrene developed in all four extremities. Intensive care management included mechanical ventilation, vasopressors, antibiotics, and hemodialysis. Despite initial stabilization and confirmation of the underlying infection, the patient's condition ultimately deteriorated, leading to his death on the 25th day of hospitalization. This case highlights symmetrical peripheral gangrene as a devastating vascular complication of severe leptospirosis and underscores the importance of early, aggressive, multidisciplinary management.

Keywords: Acute Kidney Injury; Gangrene; Leptospirosis; Sepsis; Weil Disease

INTRODUCTION

Leptospirosis is a globally significant zoonotic disease caused by pathogenic spirochetes of the genus Leptospira [1]. It is estimated to cause over one million severe cases and nearly 60,000 deaths annually, establishing it as a leading zoonotic cause of morbidity and mortality worldwide [2]. The disease burden is disproportionately high in tropical and subtropical regions, where environmental conditions such as heavy rainfall and flooding facilitate the transmission of the bacteria from animal reservoirs to humans through contaminated water and soil [3].

The clinical presentation of leptospirosis ranges from a mild, self-limiting febrile illness to a severe, life-threatening condition known as Weil's disease [4]. This severe form occurs in approximately 5-15% of infected individuals and is classically defined by a triad of jaundice, acute kidney injury (AKI), and hemorrhagic manifestations [5]. The mortality rate for Weil's disease can be as high as 40%, particularly when complicated by multi-organ failure, including severe pulmonary hemorrhage syndrome and septic shock [6, 7].

A rare but devastating complication associated with severe systemic infections and shock is Symmetrical Peripheral Gangrene (SPG). SPG is characterized by ischemic damage and necrosis of two or more distal extremities in the absence of major thrombo-occlusive vascular disease [8]. The pathogenesis is often linked to disseminated intravascular coagulation (DIC) and a low-flow state induced by septic shock and the use of vasopressors [9]. While SPG has been described in various septic conditions, its association with leptospirosis is exceedingly rare, with only a few cases reported in the literature [10].

This report describes the case of a geriatric patient who presented with severe Weil's disease and subsequently developed SPG in all four extremities, highlighting the diagnostic challenges and complex management of this unusual and fatal complication.

CASE PRESENTATION

Patient Information and Presentation

A man in his 70s, a farmer by occupation, was referred from a regional hospital to our tertiary care center's emergency department with a chief complaint of worsening shortness of breath that began one day prior to admission. The illness had started four days earlier with continuous fever, followed by yellowing of the eyes (jaundice), headache, and severe bilateral calf pain that made walking difficult. He also experienced nausea and reddish vomitus. Two days before admission, his family noticed a bluish discoloration of his hands and feet, and his urine output had significantly decreased.

Prior to referral, he was managed in an intensive care unit (ICU) for hypotension and respiratory distress. Serology from the referring hospital was positive for Leptospira IgG. His occupational history was significant for farming without protective footwear, with recent exposure to an increased rat population. A neighbor had recently been treated for a similar illness.

Physical Examination and Initial Investigations

On arrival, the patient was severely ill and somnolent. Vital signs were indicative of shock, with a blood pressure of 88/50 mmHg, a heart rate of 135 beats/minute, and a respiratory rate of 28 breaths/minute. His oxygen saturation was 78% on a high-flow non-rebreathing mask. Physical examination revealed deep jaundice with icteric sclerae and conjunctival suffusion. His extremities were cold with marked peripheral cyanosis. There was tenderness in the epigastrium, right hypochondrium, and bilaterally over the gastrocnemius muscles. Respiratory examination noted intercostal retractions and bilateral crackles.

Initial laboratory investigations, summarized in Table 1, revealed leukocytosis (25,600/µL) with neutrophilia, severe thrombocytopenia (20,000/µL), and coagulopathy (INR 1.78). There was evidence of severe acute kidney injury (Ureum 208 mg/dL, Creatinine 5.4 mg/dL), liver dysfunction (SGOT 163 U/L, SGPT 141

U/L), hypoalbuminemia (2.7 g/dL), and severe hypocalcemia (0.97 mmol/L). Arterial blood gas analysis showed metabolic acidosis.

Table 1. Hematology and Clinical Chemistry Laboratory Results, as found in the case report. This table shows the patient's initial laboratory findings upon admission

Test)	Result	Normal Range	Unit
Hematology			
Hb (Hemoglobin)	13.1	11.8-17.5	g / dl
Hct (Hematocrit)	42	35-45	%
Eritrosit (Erythrocytes)	4.75	4.50-5.90	10^6 /uL
Leukosit (Leukocytes)	25.6	4.5-11.0	10^3 /uL
Trombosit (Platelets)	20	150-450	10^3 /uL
MCV	87.4	80.0-96.0	/um
MCH	27.5	28.0-33.0	Pg
MCHC	31.5	33.0-36.0	g/dl
RDW	15.0	11.6-14.6	%
MPV	11.2	7.2-11.1	FL
PDW	16	25-65	%
Eosinofil (Eosinophils)	0.10	0.00-4.00	%
Basofil (Basophils)	0.50	0.00-2.00	%
Netrofil (Neutrophils)	89.20	55.0-80.00	%
Limfosit (Lymphocytes)	6.40	22.00-44.00	%
Monosit (Monocytes)	3.80	0.00-7.00	%
PT (Prothrombin Time)	23.5	10.0-15.0	detik (seconds)
APTT	47.5	20.0-40.0	detik (seconds)
INR	1.780		
Clinical Chemistry			
GDS stik (Random Blood Sugar)	14	60-140	Mg/dl
SGOT	163	<35	U/L
SGPT	141	<45	U/L
Albumin	2.7	3.2-4.6	g/dl
Ureum	208	<50	mg/dl
Kreatinin (Creatinine)	5.4	0.8-1.3	mg/dl
Natrium (Sodium)	134	136-145	mmol/L
Kalium (Potassium)	4.6	3.3-5.1	mmol/L
Kalsium (Calcium)	0.97	1.17-1.29	mmol/L
Arterial Blood Gas Analysis			
PH	7.248	7.310-7.420	
BE (Base Excess)	-13.4	-2-+3	mmol/L
PCO2	32.0	27.0-41.0	mmol/L
PO2	73.8	71.0-104.0	mmHg
Hematokrit	36	37-50	%
HCO3	14.1	21.0-28.0	mmol/L
Total CO2	15.1	19.0-24.0	mmol/L
O2 saturasi (O2 Saturation)	92.2	94.0-98.0	%
Serology			
HbSAg Rapid	Non reaktif	Non reaktif	

An anteroposterior chest radiograph, seen in Figure 1, demonstrated bilateral perihilar haziness and infiltrates consistent with bilateral pneumonia and pulmonary edema, along with minimal bilateral pleural effusions. The patient's initial clinical state, including the prominent jaundice and peripheral cyanosis, is documented in the clinical photographs in Figure 2. An initial electrocardiogram (ECG) showed sinus tachycardia at 133 beats/minute.

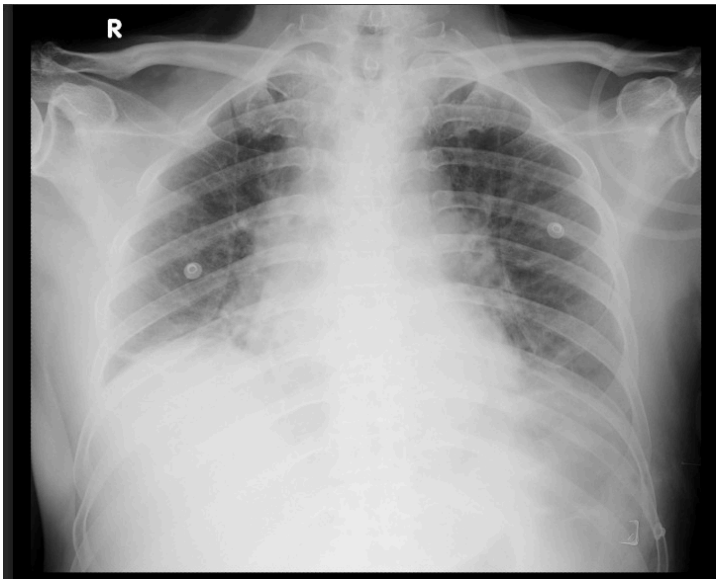

Figure 1. Anteroposterior (AP) Chest X-ray showing bilateral perihilar haziness and infiltrates with air bronchograms, consistent with bilateral pneumonia and pulmonary edema.

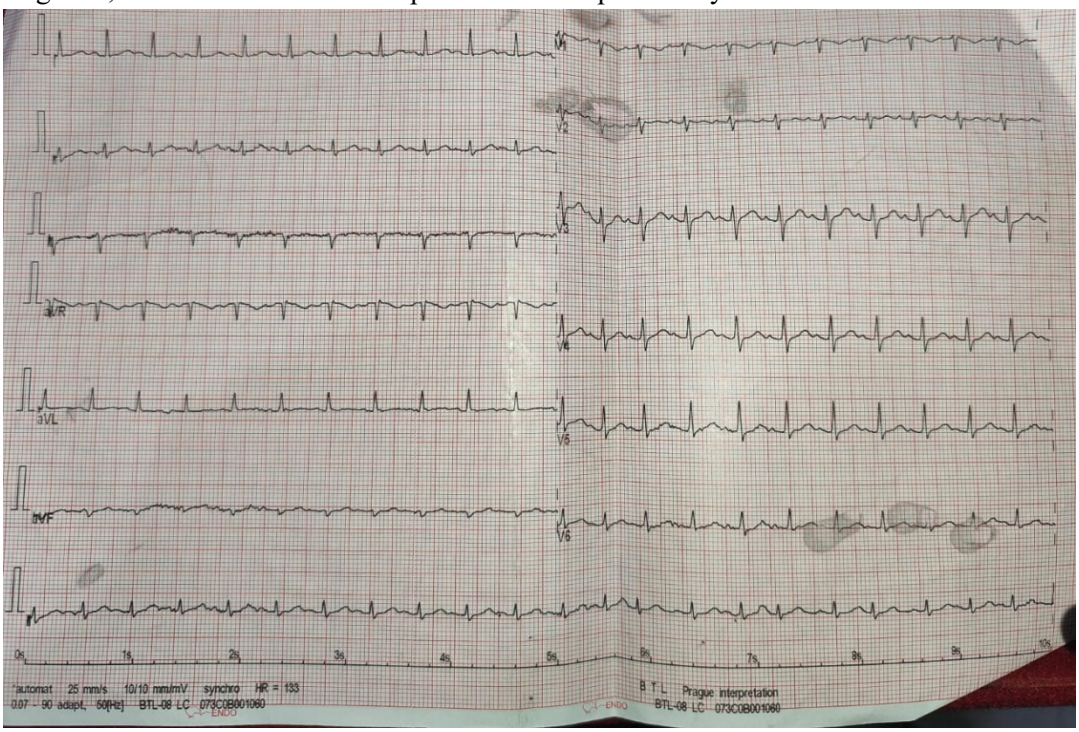

Figure 2. Electrocardiogram (ECG), showing Sinus Tachycardia with a heart rate of 133 beats per minute

Hospital Course

The patient was admitted to the ICU and intubated for acute respiratory distress syndrome (ARDS) and septic shock. During intubation, he developed an episode of atrial fibrillation with a rapid ventricular response of 174 beats/minute, which subsequently converted back to sinus rhythm. He was started on vasopressor support (norepinephrine), broad-spectrum antibiotics (Ceftriaxone), and supportive care. Due to severe AKI (AKIN stage III) and uremia, he was initiated on hemodialysis on the third day of admission.

Over the following days, despite aggressive resuscitation and organ support, the cyanosis in his extremities progressed dramatically. By day six, there was established dry gangrene affecting the distal fingers and toes of all four limbs, consistent with a diagnosis of Symmetrical Peripheral Gangrene (SPG). A Doppler ultrasound of the extremities revealed features of peripheral artery disease with decreased blood flow but no major vessel occlusion .

The diagnosis of leptospirosis was confirmed when a polymerase chain reaction (PCR) test on a urine sample collected on day 15 was positive for pathogenic Leptospira. A Microscopic Agglutination Test (MAT) performed on day nine was negative.

The patient remained in the ICU for 16 days, requiring prolonged mechanical ventilation and multiple sessions of hemodialysis. He was successfully extubated on day nine and transferred to a high-care unit on day 16. His renal and hepatic functions showed slow improvement. However, the gangrene of his extremities showed no improvement, progressing to mummification, as seen in Figure 6. On the 25th day of hospitalization, the patient experienced a sudden cardiac arrest with asystole on the monitor. Resuscitation efforts were unsuccessful, and he was declared deceased.

DISCUSSION

This report details a fatal case of severe leptospirosis, or Weil's disease, in a geriatric patient, which was complicated by the exceptionally rare development of Symmetrical Peripheral Gangrene (SPG). The case underscores the diagnostic complexities, the severe multi-organ pathophysiology of the disease, and the devastating consequences of its rare vascular complications.

Diagnostic Pathway and Challenges

The initial diagnosis of leptospirosis was challenging, as its early symptoms—fever, myalgia, and headache—are non-specific and mimic other endemic tropical diseases [7]. The patient's occupational exposure as a farmer working without protective footwear in a rat-infested area, a known risk factor [10], and a local outbreak provided a strong epidemiological link. The presentation with the classic triad of jaundice, acute kidney injury, and hemorrhagic manifestations strongly suggested Weil's disease, the severe icteric form of leptospirosis [11].

The Modified Faine's Criteria yielded a score of 24, placing him in the "Possible Leptospirosis" category [1]. This highlights a limitation of scoring systems in the acute phase, especially when definitive laboratory results are pending. Serological testing often yields false negatives in the first week of illness, as antibody titers may not have risen sufficiently [3]. Indeed, while the initial Leptospira IgG from the referring hospital was positive, the Microscopic Agglutination Test (MAT)—the gold standard for serodiagnosis [4]—was negative when performed on day nine of the illness. This is not unexpected, as MAT conversion can be delayed, with antibody levels typically peaking in the third to fourth week of illness [5]. The definitive diagnosis was ultimately established by a positive Polymerase Chain Reaction (PCR) test on the patient's urine, which detected pathogenic Leptospira DNA. This underscores the critical role of molecular diagnostics like PCR for early and accurate confirmation [2, 8], as it can detect bacterial DNA in the blood for up to 10 days post-infection and subsequently in the urine, offering a diagnostic window before the immune response is fully established [3].

Pathophysiology of Multi-Organ Failure in Weil's Disease

The patient's rapid deterioration into multi-organ failure is characteristic of severe leptospirosis. The underlying pathology is believed to be a widespread vasculitis caused by damage to the endothelial lining of small blood vessels. This is mediated by bacterial components, such as lipoproteins and lipopolysaccharide (LPS) [9], and a subsequent overwhelming inflammatory response or "cytokine storm" involving high levels of TNF-α, IL-6, and IL-10 [12]. This systemic inflammation drives the cascade of organ failures observed.

Acute Kidney Injury (AKI): The patient presented with severe AKI, classified as AKIN stage III, with a creatinine of 5.4 mg/dL and oliguria. In leptospirosis, AKI is primarily caused by acute tubulointerstitial nephritis resulting from the direct invasion of the renal tubules by leptospires and the ensuing inflammatory response [13]. The severity is associated with this uncontrolled cytokine production and elevated levels of Kidney Injury

Molecule-1 (KIM-1), which correlate with the degree of renal damage [13]. The severe uremia (208 mg/dl) in this patient warranted initiation of hemodialysis on the third day of admission, in line with KDIGO guidelines [14], which recommend considering renal replacement therapy when Glomerular Filtration Rate (GFR) is below 15 ml/min/1.73m2, as was the case here (GFR 10.3 ml/min/1.73m2) [15].

Hepatic and Pulmonary Failure (ARDS): Jaundice is a hallmark of Weil's disease and was a prominent feature in this patient. This was reflected in the laboratory findings, which showed significantly elevated transaminases (SGOT 163 U/L, SGPT 141 U/L). Pulmonary complications are a leading cause of death in leptospirosis, with mortality rates for leptospirosis-associated ARDS reaching up to 70% [29]. The patient developed severe ARDS, requiring immediate intubation and mechanical ventilation. The pathophysiology involves damage to the alveolar-capillary barrier, leading to non-cardiogenic pulmonary edema and, in severe cases, diffuse alveolar hemorrhage [29, 30].

Septic Shock and Coagulopathy: The patient was in septic shock upon admission, with profound hypotension requiring high-dose vasopressor support. This systemic response is driven by bacterial components triggering a massive release of inflammatory cytokines, leading to vasodilation, capillary leakage, hypoalbuminemia, and myocardial dysfunction [27, 28]. The coagulopathy, evidenced by a prolonged PT/APTT and severe thrombocytopenia (20,000/µL), is also a key feature [16]. Thrombocytopenia is found in up to 80% of leptospirosis patients and is an independent risk factor for clinical bleeding [17].

Electrolyte Imbalances: The severe hypocalcemia seen in this patient (0.97 mmol/L) is a notable finding. It can occur in leptospirosis due to multiple mechanisms, including renal tubular damage impairing vitamin D activation, hyperphosphatemia from renal failure, and systemic inflammation [24]. Furthermore, hypoalbuminemia (2.7 g/dl), which this patient had, can also contribute to lower total calcium levels, as a significant portion of calcium is bound to albumin [25, 26].

Symmetrical Peripheral Gangrene: A Rare and Devastating Complication

The most striking and unusual feature of this case was the development of SPG, with dry gangrene affecting the distal aspects of all four extremities. SPG is a rare syndrome of distal ischemic necrosis in two or more limbs that occurs in the absence of major vessel obstruction [31]. First described by Hutchinson in 1891 [32], it is most commonly seen in the context of septic shock with DIC and the use of vasopressive agents [34].

The pathogenesis of SPG in this patient was likely multifactorial. First, the profound septic shock from leptospirosis itself created a severe low-perfusion state. Second, the underlying coagulopathy and likely DIC led to widespread microvascular thrombosis in the distal arterioles, occluding blood flow. Third, the necessary use of high-dose norepinephrine to maintain vital organ perfusion would have exacerbated peripheral vasoconstriction, further compromising blood flow to the extremities. A characteristic finding in SPG is the presence of palpable peripheral pulses, which suggests the pathology is at the microvascular level rather than due to large vessel occlusion [33]. The Doppler ultrasound findings in this patient, which showed diffuse arterial wall irregularities and decreased flow velocity without a specific point of occlusion, support this microvascular hypothesis.

The association of SPG with leptospirosis is exceedingly rare, with a 2024 review identifying only two prior case reports linking the infection to digital gangrene [35]. This case adds to that limited body of evidence, highlighting that Leptospira infection should be considered in the differential diagnosis of sepsis leading to this devastating vascular outcome, particularly in endemic regions. Management of SPG is incredibly challenging; the primary goal is to treat the underlying cause of shock and DIC. However, once gangrene is established, the tissue damage is irreversible, and amputation often becomes the only viable option, presenting significant clinical and ethical challenges, especially in a critically ill, elderly patient.

CONCLUSION

This case reports the fatal outcome of Weil's disease in a geriatric patient complicated by septic shock, multi-organ failure, and the rare entity of Symmetrical Peripheral Gangrene. It tragically illustrates that even with

definitive diagnosis via PCR and aggressive intensive care support—including appropriate antibiotics like ceftriaxone and supportive therapies like hemodialysis—the mortality of severe leptospirosis remains high, with rates approaching 80%. The development of SPG represents a catastrophic vascular complication driven by the convergence of septic shock, DIC, and vasopressor therapy. This report contributes to the sparse literature on this specific complication and serves as a reminder of the potentially devastating systemic effects of leptospirosis. Early detection and multidisciplinary management are crucial to mitigate these severe outcomes.

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Informed Consent Statement

Written informed consent has been obtained from the patients to publish this paper.

Conflicts of Interest

The authors declare no conflict of interest

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