MANAGEMENT OF LEPTOSPIROSIS WITH COMPLICATIONS - CASE REPORT

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ABSTRAK

Laporan kasus ini menyajikan seorang pria berusia 54 tahun dengan leptospirosis ikterik dan dugaan gangguan ginjal. Leptospira adalah bakteri penyebab leptospirosis, penyakit zoonosis yang sering terjadi selama musim banjir. Leptospirosis memiliki berbagai manifestasi klinis, dari gejala ringan seperti sakit kepala dan mialgia hingga bentuk berat yang dikenal sebagai sindrom Weil, ditandai dengan jaundice, gangguan ginjal, dan perdarahan. Indonesia memiliki insiden leptospirosis yang tinggi, menempati peringkat ketiga di dunia untuk angka kematian. Pasien, berasal dari daerah yang baru-baru ini terkena banjir, datang dengan keluhan utama demam naik-turun selama satu minggu, disertai sesak napas, ketidaknyamanan epigastrium, mual tanpa muntah, dan tinja berwarna teh. Riwayat medisnya termasuk hipertensi yang dikelola dengan amlodipine. Pemeriksaan fisik menunjukkan sklera ikterik dan tinea pedis. Tes laboratorium menunjukkan peningkatan kadar nitrogen urea darah, meskipun kreatinin serum normal, menunjukkan cedera ginjal akut yang memerlukan pemantauan lebih lanjut. Diagnosis leptospirosis didasarkan pada presentasi klinis dan riwayat paparan banjir. Pasien menerima terapi antibiotik dengan cefotaxime, serta agen gastroprotektif dan anti-inflamasi. Setelah lima hari pengobatan, ia menunjukkan perbaikan signifikan dan dipulangkan dalam kondisi stabil. Leptospirosis sering terjadi di daerah tropis dan berisiko tinggi bagi individu yang tinggal di daerah rawan banjir atau terpapar lingkungan yang mungkin terkontaminasi oleh urine tikus. Diagnosis dini dan terapi yang tepat sangat penting untuk mencegah komplikasi berat seperti gagal ginjal dan kematian. Leptospirosis adalah penyakit yang dapat dicegah dan diobati dengan diagnosis dini dan manajemen yang tepat. Perawatan medis dengan antibiotik dan perawatan suportif sangat penting untuk mencegah perkembangan penyakit yang parah.

Kata kunci **:** leptospirosis, sindrom weil, ikterik, gangguan ginjal, banjir, faktor risiko

ABSTRACT

This case report presents a 54-year-old man with icteric leptospirosis and suspected renal impairment. Leptospira is the causative agent of leptospirosis, a zoonotic disease that frequently occurs during flooding seasons. Leptospirosis has a wide range of clinical manifestations, from mild symptoms such as headache and myalgia to a severe form known as Weil's syndrome, characterized by jaundice, renal impairment, and bleeding. Indonesia has a high incidence of leptospirosis, ranking third in the world for mortality. The patient, who was from a recently flooded area, presented with a chief complaint of a one-week history of high-grade fever, accompanied by shortness of breath, epigastric discomfort, nausea without vomiting, and tea-colored stools. His medical history included hypertension managed with amlodipine. Physical examination revealed icteric sclera and tinea pedis. Laboratory tests showed an elevated blood urea nitrogen level, despite a normal serum creatinine, suggesting acute kidney injury that warrants further monitoring. The diagnosis of leptospirosis was based on the clinical presentation and history of flood exposure. The patient received antibiotic therapy with cefotaxime, as well as gastroprotective and anti-inflammatory agents. After five days of treatment, he showed significant improvement and was discharged in stable condition. Leptospirosis is common in tropical areas and is at high risk for individuals living in flood-prone areas or exposed to environments that may be contaminated by rat urine. Early diagnosis and appropriate therapy are essential to prevent severe complications such as kidney failure and death. Leptospirosis is a preventable and treatable disease with early diagnosis and appropriate management. Medical treatment with antibiotics and supportive care are essential to prevent severe disease progression.

Keywords ***:*** *leptospirosis, weil's syndrome, jaundice, kidney disorders, flooding, risk factors*

INTRODUCTION

Leptospirosis is a zoonotic disease caused by the bacterium Leptospira interrogans, which includes various serotypes. It is commonly associated with flood-prone areas, earning it the nickname "flood fever." The disease spreads when humans come into contact with water or soil contaminated with the urine of infected animals, particularly rats. Leptospira can penetrate the skin through cuts or abrasions, making floodwaters a significant risk factor for infection. Due to the environmental conditions in tropical regions, leptospirosis is particularly prevalent in countries like Indonesia. (Direktorat Jenderal Pengendalian Penyakit Dan Penyehatan Lingkungan, 2014)

Indonesia ranks among the highest in the world for leptospirosis incidence and mortality rates. The clinical manifestations of leptospirosis are diverse, ranging from mild, flu-like symptoms to severe, life-threatening conditions. In its mild form, leptospirosis may present with symptoms similar to the flu, such as headache, muscle pain, and fever. However, in severe cases, known as Weil's syndrome, patients can develop jaundice, renal impairment, and bleeding tendencies, which can lead to multi-organ failure and death if not treated promptly. (Direktorat Jenderal Pengendalian Penyakit Dan Penyehatan Lingkungan, 2014; Jiménez et al., 2018; Russell et al., 2018)

Leptospirosis is challenging to diagnose due to its wide range of symptoms and the overlap with other febrile illnesses common in tropical regions. Early diagnosis and appropriate treatment are critical to managing the disease effectively and preventing complications.2,5,6 In this report, a case of icteric leptospirosis with suspected renal impairment in a 54-year-old male patient from a flood-affected area in East Jakarta is presented, highlighting the clinical course, diagnostic challenges, and management strategies.

CASE REPORT

Patient Information

A 54-year-old male patient from East Jakarta, an area recently affected by flooding, presented to the hospital with a chief complaint of a fluctuating fever that had persisted for one week. Additional symptoms included non-radiating shortness of breath, epigastric discomfort, nausea without vomiting, and tea-colored bowel movements with normal frequency. The patient's medical history was significant for hypertension, which was managed with amlodipine 10 mg daily. There was no relevant family history of chronic illnesses or genetic disorders. Psychosocially, the patient lived in a flood-prone area, which may have contributed to his current condition. Prior to hospital admission, the patient sought treatment at a Community Health Center, where he was prescribed fever-reducing medications, but his symptoms did not improve. Upon hospital admission, he underwent further diagnostic evaluations and received a comprehensive treatment plan, including intravenous antibiotics and supportive care, leading to significant clinical improvement and eventual discharge in a stable condition.

Clinical Findings

On physical examination, the patient appeared moderately ill. His vital signs included a blood pressure of 144/66 mmHg, a heart rate of 105 beats per minute, a respiratory rate of 20 breaths per minute, a body temperature of 37.7°C, and an oxygen saturation of 95% on room air. His body weight was 55 kg, and his height was 160 cm, indicating a normal nutritional status. Notable physical findings included icteric sclera and tinea pedis between the toes of both feet, with no calf tenderness observed.

Table 1. Timeline

Event	Details	Date
Onset of symptoms	Fever, shortness of breath, epigastric discomfort	One week before admission
Initial treatment	Community Health Center, prescribed fever reducers	One week before admission
Hospital admission	Comprehensive evaluation and treatment initiation	Admission day
Ongoing treatment	Cefotaxime, omeprazole, paracetamol, ursodeoxycholic acid, lansoprazole, methylprednisolone	Hospitalization period
Follow-up assessments	Periodic ureum-creatinine tests, urine output monitoring	Hospitalization period
Discharge	Significant improvement and stable condition	After 5 days of treatment

Diagnostic Assessment

Diagnostic methods included a thorough physical examination revealing icteric sclera and tinea pedis. Laboratory testing showed a hemoglobin level of 8.7 g/dL, a hematocrit of 25.9%, a leukocyte count of 25,000/uL, blood urea nitrogen of 67 mg/dL, and serum creatinine of 0.9 mg/dL. A chest X-ray showed normal findings. The primary diagnostic challenge was the initial ineffective treatment at the Community Health Center, which necessitated further investigation and comprehensive evaluation upon hospital admission. The working diagnosis was icteric leptospirosis, with differential diagnoses not explicitly mentioned in the initial case report. The prognosis was positive with appropriate treatment, as evidenced by the patient's improvement and stable condition upon discharge.

Therapeutic Intervention

Therapeutic interventions included pharmacologic treatments such as antibiotics, antipyretics, gastroprotective agents, and steroids. The administration of therapeutic interventions involved cefotaxime 1 g intravenously three times a day, omeprazole 40 mg intravenously once a day, paracetamol 500 mg orally as needed for fever, ursodeoxycholic acid 250 mg three times a day, lansoprazole 30 mg three times a day, and methylprednisolone 125 mg once a day. Changes in therapeutic interventions were based on the patient's response to initial treatments and ongoing assessments of renal function and urine output.

Follow-Up and Outcomes

Clinician- and patient-assessed outcomes indicated significant clinical improvement, leading to the patient's discharge in a stable condition. Important follow-up diagnostic results included periodic monitoring of blood urea nitrogen and creatinine levels, which remained stable after initial assessments. Urine output was consistently maintained at 1 ml/kg/hour. The patient adhered to the therapeutic regimen, as monitored through hospital records, with no significant adverse effects reported during the treatment and follow-up period.

DISCUSSION

Leptospirosis is a zoonotic disease caused by the spirochaeta bacterium Leptospira transmitted through urine, either directly or through infected soil or water, to humans. The definition of a zoonotic disease is a disease that can be naturally transmitted from vertebrate animals to humans or vice versa.(Direktorat Jenderal Pengendalian Penyakit Dan Penyehatan Lingkungan, 2014) Leptospirosis causes a self-limiting *influenza-like illness*, but can also cause much more serious illness. Leptospirosis can progress to multiorgan failure with potential death.(Jiménez et al., 2018; Russell et al., 2018)

Leptospirosis is a widespread disease worldwide, particularly in the tropics. The global burden of disease is unknown due to lack of data, but estimates of incidence range from 0.1 to 1/100,000/year in temperate regions, to more than 100/100,000 per year during epidemics in the tropics.(Zenebe et al., 2013) Indonesia is the third highest country in the world with a *case fatality rate* (CFR) of 2.5%-16.45% or an average of 7.1%.(Nuraini et al., 2017) In 2010, 410 cases of leptospirosis were reported in Indonesia with 46 deaths (11.2%). The cases were found in 8 provinces namely DKI Jakarta, West Java, Central Java, Yogyakarta, East Java, Bengkulu, Riau Islands, and South Sulawesi.(Widjajanti, 2020; Zenebe et al., 2013)

Leptospirosis risk factors include an individual's inherent conditions (such as history, age, gender, and family) and habits (such as daily activities). Infection can be acquired through work, off-duty activities, recreation, and hobbies of people who work or perform activities in an environment associated with rats or an environment contaminated with the urine of infected rats, such as agricultural or animal work, livestock workers, plantation workers, fish and poultry processors, ditch diggers, sewer workers, farmers, market workers, veterinarians, waste managers. Habits that increase the risk are activities in watery places with wounds on the body, the habit of not taking good care of wounds in areas of stagnant water, not wearing footwear, the habit of bathing in rivers, poor hygiene behavior such as the presence of garbage in the house and lack of knowledge about Leptospirosis.(Gautama, 2018; Srisawat et al., 2015; World Health Organization, 2020) In this patient, the risk factor found was a history of exposure to flooding 2 weeks before complaints appeared.

An important risk factor for Leptospirosis is the presence of rats in the house and the environment around the house. Rats are the main infectious animal of Leptospirosis (more than 50%).(Araujo et al., 2010) The presence of rats in the house has a 4 times higher risk of developing Leptospirosis. The types of rats that are often reservoirs of Leptospirosis are rats *(R. norvegicus)*, house mice *(R. diardii)*, garden rats *(R. exulans)* house mice *(Suncus murinus).* Besides the presence of animals around the house is also a risk factor such as dogs, cats, goats, cows etc.(Daher et al., 2010; Gautama, 2018; Srisawat et al., 2015; World Health Organization, 2020)

The clinical manifestations of leptospirosis are generally divided into two, namely *self-limited* anicteric disease and icteric disease (Weil's Disease) with more severe manifestations. The acute phase is characterized by sudden onset fever, chills, retroorbital headache, anorexia, abdominal pain, nausea and vomiting. Fever often exceeds ^{40}oC. Calf pain and conjunctival injection are characteristic of leptospirosis, but not always present. Other symptoms include anorexia, nausea, vomiting, abdominal pain, dizziness, lethargy, malaise, arthralgia, eye pain, and photophobia. Symptoms in the early phase are non-specific and are often difficult to distinguish from other causes of acute febrile illness.(Amin, 2016; Centers for Disease Control and Prevention, 2018; Rajapakse, 2022)

*Weil'*s disease refers to severe and life-threatening icteric leptospirosis, characterized by jaundice, renal dysfunction and bleeding. Jaundice first appears between the 5th to 9th day, maximum intensity 4 or 5 days later and persists for an average of 1 month. In the advanced phase, symptoms associated with complications may involve one or more organs or systems, namely *acute lung injury*, renal failure, liver involvement and bleeding manifestations (petechiae, bruising or hemorrhage, including epistaxis, conjunctival hemorrhage, hematemesis, melena, and rectal bleeding). Laboratory examination may find leukocytosis (15000-30000), neutrophilia, thrombocytopenia, and high *creatinine phosphokinase*. Bilirubin may be markedly elevated (predominantly rec fraction), but transaminases rarely exceed 3 times the upper limit. In impaired renal function ureum and creatinine will be elevated, hematuria, pyuria, proteinuria (usually less than 1 g/24 hours), and high urine specific gravity.(Amin, 2016; Rajapakse, 2022) In this patient, there is an increase in ureum which may be due to AKI but since there is no increase in serum creatinine, further monitoring of renal

function is needed. The diagnosis of leptospirosis is mostly made based on a suggestive clinical picture, in the presence of a history of risk exposure. Leptospirosis should be suspected in any patient with a history of risk exposure (walking in flood or contaminated water, contact with fluids from animals, swimming in flood water or ingesting contaminated water with or without wounds) with any of the following: headache, myalgia, prostration, jaundice, conjunctival suffusion, oliguria, signs of meningeal irritation, bleeding, signs of heart failure or arrhythmia, cough, shortness of breath, skin rash, or evidence of other organ involvement or dysfunction. Patients with these symptoms should be considered as suspected cases of leptospirosis.(Rajapakse, 2022)

Any suspected leptospirosis case with stable vital signs, an icteric sclera, good urine output, no meningismus/meningent irritation; sepsis/septic shock; difficulty breathing; or jaundice, and can take drugs orally is considered mild leptospirosis and can be managed on an outpatient basis. Suspected leptospirosis cases with unstable vital signs, jaundice or icteric sclera, abdominal pain, nausea, vomiting and diarrhea, oliguria/ anuria, meningismus/ meninges irritation, sepsis/ sepsis shock, altered mental status or difficulty breathing and hemoptysis are considered moderate - severe leptospirosis and need hospitalization.(Amin, 2016; Lei et al., 2021)

Many diagnostic tests are available for leptospirosis (Table 1). Diagnostic tests are divided into tests that provide direct evidence of infection (demonstration of leptospira or its DNA, or culture) and tests that provide indirect evidence of infection (antibodies to leptospirosis).(Mallhi et al., 2014; World Health Organization, 2001) Leptospira can be isolated from blood and cerebrospinal fluid samples on day 7 to day 10, and from urine during the second and third weeks. Culture and isolation is still the gold standard, can identify serovars, but requires special media with an incubation time of several weeks, and requires dark field microscopy, making it unsuitable for individualized treatment. Therefore, *polymerase chain reaction* (PCR) methods that detect leptospira DNA can be used. Diagnosis can also be made when there is a 4-fold or greater increase in antileptospira antibody titers or seroconversion in the microscopic agglutination test (MAT) in paired samples obtained at least 2 weeks apart.(World Health Organization, 2001) A strong IgM antibody response, appearing approximately 5-7 days after symptom onset, can be detected using several ELISA-based commercial assays, *latex* agglutination and immunochromatographic rapid test technologies. These serologic tests detect IgM antibodies specific to the Leptospira genus. However, it has low sensitivity (63-72%) in acute phase samples (less than 7 days of illness). If serum samples are taken after the seventh day, the sensitivity increases to >90%. Therefore, a second sample should be taken in cases of suspected leptospirosis with negative or questionable initial results.(Amin, 2016)

Given the difficulty in confirming the diagnosis of leptospirosis, the diagnosis of leptospirosis can be assisted using the modified Faine criteria which is a scoring system that includes clinical, epidemiological and laboratory parameters (Table 2.2). Based on the modified Faine criteria, a presumptive diagnosis of leptospirosis can be made if: (i) A score of part A or part A + part B = 26 or more; or (ii) A score of part A + part B + part C = 25 or more. A score between 20 and 25 indicates a possible but unconfirmed diagnosis of leptospirosis.(Amin, 2016; World Health Organization, 2001)

The clinical presentation of leptospirosis is often nonspecific and difficult to distinguish from other causes of acute febrile illness. Therefore, a high index of clinical suspicion is important. The differential diagnosis of leptospirosis includes dengue fever, typhoid, and sepsis (mostly caused by staphylococcal infection). Other differential diagnoses include influenza, pneumonia, arboviral infections (Chikungunya, Zika), rickettsial infections, acute viral hepatitis, pyelonephritis, and meningitis. In patients with bleeding manifestations, severe dengue and meningococcal infections should be considered. Malaria is an important

differential diagnosis in patients who have a history of travel to malaria endemic areas. Malaria should also be considered in visitors from malaria endemic areas.(Lei et al., 2021)

Early diagnosis and appropriate therapy are the most important points in the management of leptospirosis. Antibiotic treatment is considered efficient in all stages of the disease. Mild cases can be treated in an outpatient setting with oral amoxicillin (30-40 mg/kg/day) or ampicillin (50-100 mg/kg/day) 4 times a day for 7-10 days. Children > 8 years of age can receive doxycycline (2 mg/kg/dose) 2 times a day for 7-10 days. Patients with severe infection should be treated with intravenous penicillin 50,000-100,000 U/kg/day for 7-10 days, or with third-generation cephalosporins (ceftriaxone 1g once per day, cefotaxime 1 g every 6 hours) or erythromycin. In patients allergic to penicillin, erythromycin, 30-50 mg/kg/day, can be given in 3-4 doses for 7-10 days.(Chávez-Iñiguez et al., 2020; da Silva Junior et al., 2018; Shivakumar, 2013) In this patient, the therapy given was cefotaxime 1 g per 6 hours.

Mild, or aniconic, leptospirosis recovers spontaneously within a few days or a week.(da Silva Junior et al., 2018; Yaslianifard et al., 2018) Pulmonary complications, hyperbilirubinemia, AKI oliguria-anuria, diarrhea, hyperkalemia, advanced age, and having an underlying infection or disease worsen the prognosis, with mortality ranging from 12 - 36%.(Al Hariri et al., 2019) Other complications that can arise from leptospirosis infection are acute renal failure, neuroleptospirosis, myocarditis, hypokalemic paralysis, *acute rsespiratory distress syndrome* (ARDS) and pulmonary hemorrhage, and liver failure. Death from leptospirosis occurs in 10-15% of cases, usually from pulmonary hemorrhage, renal failure, or heart failure and arrhythmias due to myocarditis.(Rajapakse, 2022) In the patient in the case, the complication of AKI should be suspected due to the elevated ureum. Normalization of lab results indicates a milder course of the disease.

CONCLUSIONS

Leptospirosis occurs incidentally and is generally transmitted through rat urine during floods. Manifestations of leptospirosis range from self-limited, mild symptoms to severe symptoms and even death if treatment is delayed. The gold standard test for leptospirosis is the microscopic agglutination test. Early diagnosis and prompt management will prevent the severe course of the disease. Treatment is given medically with antibiotics and supportive care.

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