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Leptospirosis presenting with acute renal failure, thrombocytopenia, and hyperbilirubinemia

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Abstract. Leptospirosis is a spirochaetal zoonotic disease associated with a broad spectrum of clinical manifestations from asymptomatic to multi-organ failure and death. Acute liver and renal involvement in severe forms of leptospirosis is known as Weil's disease. Gold-standard serology test results may delay treatment and can cause rapid clinical deterioration. We present a patient with severe leptospirosis that was treated with empiric treatment without confirming the gold-standard confirmatory serology tests.

Keyword**:** Leptospirosis, acute renal injury, thrombocytopenia, hyperbilirubinemia.

Abstrak. Leptospirosis merupakan penyakit zoonosis yang memiliki spektrum manifestasi klinis yang luas, mulai dari asimtomatik hingga kegagalan banyak organ. Pada kondisi leptospirosis yang berat, keterlibatan akut organ liver dan ginjal dapat dianggap sebagai penyakit Weil. Pemeriksaan tes serologi baku emas dapat memperlambat pengobatan dan menyebabkan perburukan kondisi klinis. Kami mempresentasikan pasien dengan leptospirosis berat yang dirawat dengan terapi empiris tanpa menunggu konfirmasi pemeriksaan serologi baku emas.

Kata kunci: Leptospirosis, gagal ginjal akut, trombositopenia, hiperbilirubinemia

Introduction

Leptospirosis is a type of zoonosis that is endemic to many tropical regions and is a major public health threat, with the annual morbidity in Indonesia estimated at 39.2 cases per 100.000[1,2]. Hosted by several animals, most famously the brown rat (Rattus norvegicus), the organism itself (Leptospira) is commonly spread by the animals' urine, infecting water reservoirs regularly used by humans[2]. Leptospirosis typically manifests as fever, nausea, vomiting, headache, myalgia, and anorexia[3–5]. This disease is a significant public health threat in both rural and urban areas[7].

Because of its similarity of symptoms to other tropical diseases like typhoid or dengue, leptospirosis has largely been overlooked. A diagnosis of leptospirosis is usually considered when the patient starts to develop symptoms of Weil's disease, such as jaundice, renal failure, and haemorrhagic manifestations[6]. Weil's disease could develop due to *Leptospira* targeting and residing mainly in renal tubules, releasing toxins damaging vascular endothelium and increasing their permeability[5,7].

Management of Leptospirosis and/or Weil's disease includes alleviating their symptoms, monitoring the liver and renal function levels, and administering antibiotics intravenously such as penicillin (1.500.000 unit/6 hours), ceftriaxone (1 g/daily), or cefotaxime (1 g/6 hour). There seems to be no clear difference in choosing which antibiotics to treat the patient[10,11].

Case Report

A 62-year-old male presented at the emergency department of a secondary health care facility with fever and myalgia for the last seven days. He explained that the rise in body temperature was mild during the first three days. In the upcoming days, the fever went up and made him shiver throughout the night. His temperature slightly decreases after taking over-the-counter paracetamol, but the fever persists several hours later. He also complained about having nausea, decreased urination, and diminishing appetite. The patient had a history of hypertension and admitted only wearing an open-toe slipper while walking on a flooded road last week. He has no significant history of blood transfusion, recent traveling, and contact with a sick person.

Vital signs during his initial encounter in the emergency department showed a temperature of 37.5° Celsius, pulse rate of 64 bpm, respiratory rate

20/min, and blood pressure 120/80 mmHg. Physical examination revealed scleral icterus and conjunctival redness without purulent exudates accompanied by mild conjunctival swelling along the palpebral fissures. He also experienced muscle pain, and there was apparent tenderness in both calves.

Initial laboratory tests showed thrombocytopenia, elevated renal function test, hyperbilirubinemia, and positive leptospirosis rapid serology. The impression on the patient's chest x-ray P/A view was left ventricular hypertrophy with cardiomegaly and aorta lengthening without any lung infiltrates. ECG displayed normal sinus rhythm, and abdominal ultrasound demonstrated structurally normal bilateral kidneys with an increased echogenicity and heterogeneous liver parenchyma.

Table 1. *Hospital Course with Temperature and Laboratory Investigation*

	Temperature	Platelet count	Ureum	Creatinine
Day 0	37.5	49	214	9.46
Day 1	37.3	50	385.2	8.50
Day 2	37.4	50	342.2	7.82
Day 3	37.2	88	350.5	5.43
Day 4	37.3	116	250	4.21
Day 5	37.1	140	203.4	3.42
Day 6	36.9	203	149.8	1.11
Day 7	36.7	325	74.6	1.02

Note. The Temperature refers to maximum measured temperature is in degree Celcius. The platelet count is in $*10^3$ with normal range of 150-450. The ureum is in mg/dL with a normal range of less than 31. The creatinine is in mg/dL with a normal range of 0.5-1.2.

The patient was admitted to the internal medicine ward, and his renal function test was being monitored regularly. He was treated with intravenous fluid, intravenous 2 gram of ceftriaxone every 24 hours, an intravenous corticosteroid, intravenous antiemetic, in addition to antipyretic and antihypertensive perorally. The patient had an excellent response to antibiotics and resolution of symptoms on outpatient follow-up; therefore, the patient was subsequently discharged.

Discussion

Leptospirosis is usually spread by humans coming into contact with infected water, whether via fecal-oral or an entry wound[9]. From the history taking, we learned that the patient has been walking on a flooded road, in which the bacteria may reside and infect the patient. The disease progresses in two clinical phases, known as septicaemic and immune[4,6]. In the first phase, humans that come in contact with the bacteria may present flu-like symptoms after 7-14 days[4]. Patients may present with conjunctival suffusion during this period, a clinical manifestation that usually won't appear with other nonspecific febrile tropical diseases such as dengue, typhoid, or malaria[4,5]. This particular clinical manifestation should raise suspicion, and therefore a quick serology test is suggested to confirm the diagnosis.

The second phase of leptospirosis may persist after one month after coming into contact with the bacteria[4,10]. In this phase, the body responds immunologically to the bacteria infection by releasing and regulating cytokines[3,7]. In mild cases, the body successfully balances those responses, so the infection is resolved asymptomatically[3,4]. However, in severe cases, the immune system would respond in a more volatile fashion, resulting in a cytokine storm that affects multiple organs, such as the liver, kidney, and heart[3]. Due to this phenomenon, we can see abnormal laboratory findings, such as elevated bilirubin levels, elevated liver enzyme levels, elevated kidney function levels, and thrombocytopenia[4,5,10]. The patient had several laboratory findings above; therefore, a rapid serology test was performed, and the diagnosis was confirmed.

The progression of leptospirosis, if left untreated, could develop into a severe form of the infection, known as Weil's disease[10,11]. A diagnosis of Weil's disease is usually made if the patient has presented with jaundice, renal failure, and haemorrhagic manifestations[5,6,15]. In this case, the patient presents a mild form of jaundice, seen in the physical examination findings of the icteric sclera. The patient's complaint of decreased urination and findings of high levels of kidney function suggests a renal failure is already in process. Although there were no apparent haemorrhagic manifestations, findings of thrombocytopenia may suggest there was a haemodynamic event involved[6,9,16]. This finding, however, can be attributed as a result of kidney failure and dehydration[5].

Definitively, a diagnosis of leptospirosis is made with a PCR test, and is considered the gold standard[10,11]. In secondary health care facilities that

lack the ability to perform the test, a rapid serology test using MAT can be performed instead[6,11]. A positive serology test may not specifically define the diagnosis; however, the PCR test may require two weeks to confirm the infection[6]. Therefore, using only the rapid test as the basis of diagnosis, treatment and management must start immediately in order to avoid disease progression that could cause multi-organ failures and eventually, morbidity and mortality[6,8].

The patient came with a prolonged nonspecific febrile syndrome, a common case amongst people living in tropical regions[6,11]. A thorough physical examination, a conclusive history taking, and a rapid diagnostic test must be performed to confirm a diagnosis of leptospirosis. Starting empiric therapy immediately without waiting for the gold standard test result to come out is preferred to avoid multi-organ failure and mortality in these cases[8].

Conclusions

The patient came with a prolonged nonspecific febrile syndrome, a common case amongst people living in tropical regions. A thorough physical examination, a conclusive history taking, and a rapid diagnostic test must be performed to confirm a diagnosis of leptospirosis. Starting empiric therapy immediately without waiting for the gold standard test result to come out is preferred to avoid multi-organ failure and mortality in these cases.

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