Suspected Weil's Disease Case in Rural Hospital Area: A Case Report

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Abstract

Background: Leptospirosis is a zoonotic disease of worldwide distribution caused by Leptospira genus bacteria. Weil's disease is a form of severe leptospirosis with conjunctival suffocation, jaundice, and acute kidney injury. **Methods:** We present a case of suspected Weil's disease patient in our health care unit in rural hospital area. Complimentary databases were collected from PubMed and Scholar Google. **Case Illustration:** A 43 years old male, came to the ER complaining of fatigue followed by calf aches. He is a farmer who always goes barefoot. Icterus was found in the whole body, especially the sclera. Gastrocnemius muscle pain was also present. Laboratory examination shows leukocytosis and thrombocytopenia with elevated liver and renal function tests. There is no specific laboratory test for leptospirosis available in our health care unit. The patient was suspected of Weil's Disease based on history taking, physical examination, and general laboratory test. Injection of antibiotics and oral drugs were given to the patient. **Discussion:** Leptospirosis is one of the most highly prevalent in tropical countries with 73% of cases, particularly in South-East Asia. An increase in urea and creatinine in patients is a sign that strongly suggests Weil's disease. The diagnosis, in this case, did not use direct or indirect tests of leptospira due to limited equipment in hospitals located in rural areas. **Conclusion:** The diagnosis of leptospirosis in this case was based on a history of high-risk patient occupation, accompanied by clinical symptoms and general laboratory results.
Keywords: Weil's disease, leptospirosis, icterus, gastrocnemius

1. Introduction

Leptospirosis is a zoonotic disease of worldwide distribution with a highly variable clinical course caused by infection with Leptospira genus bacteria, a pathogenic spirochaete. (Evangelista, V., 2013; Haake, DA, Levett, 2015; Kokudo et al., 2009; Mcbride et al., 2005; Moreira Marques et al., 2020; Thayaparan et al., 2013) Leptospira is a gram negative flagellated and motile spirochaete. (Moreira Marques et al., 2020) It most commonly affects resource-poor populations, resulting in significant morbidity and deaths. (Rajapakse, 2022; Thayaparan et al., 2013)

The infection is estimated to cause one million cases and around 58,900 deaths annually. (Rajapakse, 2022) Incidence rate is estimated to be more than 10 cases per 100.000 of population in tropical climates and significantly less (0.1 – 1 per 100.000) in temperate climates. (Rajapakse et al., 2015) Water, soil, livestock, small mammals are the main reservoirs that can affect humans directly or indirectly through animal faeces and urine. (Moreira Marques et al., 2020) Occupation was recognized as an important risk factor before animal host species were identified. Rodents were first identified as a potential source of human infection, followed by dogs. (Guerra, 2009)

Leptospira infects humans through mucosal surfaces or through disrupted skin epithelia, escaping innate immune defenses and proliferates in the blood-stream, disseminating to all organs. (Moreira Marques et al., 2020) Sign and symptoms of leptospirosis are generally mild, and only 5% of cases develop Weil's disease, the most severe form of leptospirosis. (Kokudo et al., 2009) Infection of humans leads to a variety of adverse effects, including chronic interstitial nephritis, mastitis, myocarditis, and hemolytic crisis, resulting in multiorgan failure. (Palaniappan et al., 2007)

The incubation period for leptospirosis is two to twenty days, mostly seven to twelve days. There are two major phases in Leptospirosis. The first phase, designated as anicteric is usually mild, non-fatal, febrile, and self-limited, ranging from eight to ten days, where leptospires can be found in the blood (leptospiremia). (Moreira Marques et al., 2020) It is followed by an immune response where IgM antibodies appear in the blood. (Rajapakse, 2022) Some of the first phase followed by the second phase, the icteric phase, also known as Weil's disease, is usually more severe and potentially fatal if not treated. In this phase, leptospires can be isolated in urine (leptospiuric phase), because of its special adherence to tubule epithelial cells. (Moreira Marques et al., 2020) Presumably, the organisms settle in higher concentrations in the proximal tubules of the kidney (and other organs) during this phase. It may last several weeks if the patient survives. The pathogenesis of severe leptospirosis is poorly understood; however, it is thought to be due to a form of vasculitis, which deranged tissue microcirculation and endothelial disfunction. Although jaundice is prominent feature, death often results from complications of acute kidney injury, myocardial involvement, or pulmonary hemorrhage. (Rajapakse, 2022)

The clinical features of leptospirosis are similar to many diseases, especially in tropical countries, such as dengue, malaria, rickettsial infection, and bacterial sepsis. They all have the main symptom of fever. (Rajapakse, 2022; Rozalena et al., 2018) Even though it is a life-threatening infection and recognized as an important cause of Weil's disease, the classic presentation of leptospirosis with conjunctival suffocation, jaundice, and acute kidney injury, which is characterized by multiorgan failure and carries a high mortality, most patients present only with a mild febrile illness. (Moreira Marques et al., 2020) Fever, chills, myalgia, and headache are commonly complained by the patient developing on the 3rd to 4th day. Myalgia can be severe, and can usually involves the calf, abdomen (mimicking acute abdomen) and paraspinal muscles (resulting in meningism). Conjunctival suffusion is a characteristic finding. (Rajapakse, 2022) Untreated patients with the icteric form have a higher mortality rate than those with the anicteric form of leptospirosis. The most severe complication of Weil's disease is the development of oliguria; subsequently, anuria and renal failure develop, the latter being the most common cause of death. (Guerra, 2009)

Diagnosis of leptospirosis is made largely on the presence of suggestive clinical features such as headache, myalgia, prostration, jaundice, conjunctival suffusion, oliguria, meningeal irritation, hemorrhage, cardiac failure, arrhythmia, cough, breathlessness, skin rash, or any other evidence of organ involvement or dysfunction, with a history of risk exposure. (Rajapakse, 2022)

Many diagnostic tests are available for leptospirosis, but the availability of such tests in resource-poor settings is limited. Broadly, the diagnostic tests are divided into those which provide direct evidence of infection (demonstration of leptospires or its DNA, or culture) and tests providing indirect evidence of infection (demonstration of antibodies to leptospirosis). (Rajapakse, 2022) Blood cultures, polymerase chain reaction (PCR), and dark-field microscopy of body fluid can all be used in direct tests for leptospira isolation. On the 6th to 10th day, antibodies are detected, so the serological method in the form of a microscopic

agglutination test (MAT) can be done. The leprodipstick assay can also detect leptospira, which is specific to IgM antibodies. (Chacko et al., 2021; Evangelista, V., 2013; Rajapakse, 2022)

Most leptospirosis cases are mild and resolve spontaneously. Early initiation of microbial therapy may prevent some patients from progressing to more severe disease. Identification of leptospirosis in its early stages is largely a clinical diagnosis and relies on a high index of suspicion based on the patient's risk factors, exposure history, and presenting sign and symptoms. A negative result of rapid diagnostic test should not be relied on to rule out early infection. For these reasons, empirical therapy should be initiated as soon as the diagnosis of leptospirosis is suspected. (Haake, DA, Levett, 2015)

Therapy for patients with leptospirosis severe enough to merit hospitalization usually involves intravenous penicillin (1.5 million units IV every 6 hours), ampicillin (0.5 – 1 gram IV every 6 hours), ceftriaxone (1 gram IV every 24 hours), or cefotaxime (1 gram every 6 hours). Adult outpatients with early disease should receive either doxycycline 100 mg orally twice per day or azithromycin 500 mg orally once per day. Severe leptospirosis is a medical emergency requiring both antibiotics and proper supportive therapy to improve mortality rates. (Haake, DA, Levett, 2015)

2. Methods

In this study, the writer will present a case of a suspected Weil's disease patient who was hospitalized at Petrokimia Gresik Hospital, a rural hospital area located in East Java. This study will discuss the diagnosis and treatment given to the patient. The patient has agreed that his case will be used as learning material in the form of a case report. Complimentary databases were collected from PubMed and Scholar Google.

3. Case illustration

A 43-year-old male presented to the emergency room with complaints of fatigue for a week and calf aches that made him difficult to walk. Yellowish-pigmented eyes and the whole body with reduced urine volume were also complained. Nausea, vomiting, fever, and dyspnea were denied. A day before admission, there was a nosebleed of limited volume. The patient stated that four days before, he had been treated in the clinic but did not see any improvement in his complaints, especially of calf aches. He works as a farmer who always goes barefoot and did not have any previous medical history.

On physical examination, the vital signs were normal with a blood pressure of 104/67 mmHg, a pulse of 87 beats per minute (bpm), and 36.8^{o}C for body temperature. The skin of the body presented jaundice (yellowish). Scleral icteric (figure 1) and bilateral conjunctival suffusion were notable in the ocular examination. The heart and lungs examination revealed no abnormalities, while the abdomen was soft but tender in the epigastrium area. Hepatomegaly and Murphy's sign were not found. Gastrocnemius muscle pain was very notable in the examination.

The result of a complete blood count (CBC) shows thrombocytopenia (platelets of 50.000 cells/mm3) and leukocytosis (white blood cell count (WBC) of 22.57 x103 cells/mm3) with hemoglobin of 11,2 g/dL and the other samples showed elevated renal function tests (urea 336 mg/dL and creatinine 4.65 mg/dL) and liver function tests (AST 94 U/L and ALT 96 U/L) as seen in table 1. There was no abnormality on chest radiography and electrocardiography showed normal sinus rhythm at 74 beats per minute. The other

investigations, such as the leptospiral strip test for IgM antibodies and the MAT, were not done because they were not available at our hospital

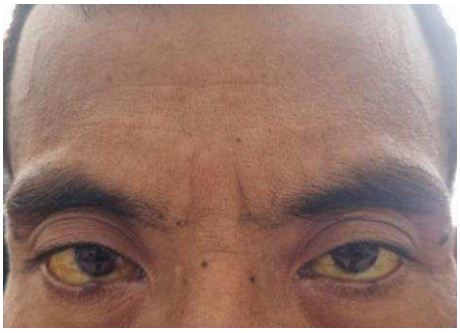

Figure 1. Scleral icteric

From history taking, physical examinations, and laboratory results, the patient was diagnosed with suspected Weil's disease. The antibiotic ceftriaxone 1 gram was used intravenously, along with conservative therapies such as prorenal and lesikol. On the following day, the symptoms gradually improved, followed by elevated platelets of 79.000 cells/mm3 and decreased WBC of 20.87 x 103 cells/mm3. He was discharged in good clinical condition with instructions to return in three days and to continue taking antibiotics orally for five days. On further follow-up, there were no symptoms and the skin was still jaundiced but getting better.

Table 1. laboratory result

Complete Blood Count		
Haemoglobin (g/dL)	11.2	13.0-18.0
WBC (cell/mm3)	22.57 x103	4.1-10.9
HCT (%)	29.4	40-50
Platelet (cells/mm3)	50 x103	150 -450
Erythrocyte (cells/mm3)	3.90	4.5-5.5
Renal Function Test		
Urea (mg/dL	336	<50
Creatinine (mg/dL)	4.65	0.7-1.2
Liver Function Test		
AST (U/L)	94	<40
ALT (U/L)	96	<41

4. Discussion

In this case, we know that the patient's main complaints are fatigue and calf muscle aches. Both symptoms are commonly found in a patient with leptospirosis, specifically for calf muscle aches. Yellowish-pigmented eyes and the whole body with reduced urine volume were also complained by the patient were some signs that

usually happened when the patient reached the icteric phase. Reduced urine volume is a warning sign of severe leptospirosis which is also known as Weil's disease. It happens when the organisms settle in higher concentrations in the kidney. Four days before admission, the patient said that he was having mild fever with fatigue and he went to see a doctor nearby. As we know before, patients with leptospirosis mostly come with mild fever although the disease is severe enough to cause mortality. Those complaints were very synchronized with the leptospirosis disease timeline, in which the incubation periods were usually within seven to twelve days. And in the 3rd or 4th day, the patient usually begins to complain of fever and fatigue. (Rajapakse, 2022)

Leptospirosis is one of the most highly prevalent in tropical countries with 73% of cases, particularly in South-East Asia. It can be affected by a human in a rural or urban population. The riskiest population are farmers, those in live contact with the workplace that is exposed to rodents, and people living in an area where sanitation is poor. Human infection occurs from direct contact with carrier animals or with environmental contamination of leptospira. (Mcbride et al., 2005) From the case above, the patient is one of the riskiest populations, he works as a farmer and never uses footwear while working. Thus, increasing the exposure to environmental contamination in the rice field.

Some signs can be seen in the results from the general laboratory examination. A CBC will show a normal to moderately elevated score above the average range. Liver function tests show an elevation of aminotransferases, and hyperbilirubinemia occurs in patients who show jaundice. Besides that, there is an increase in creatinine, which indicates renal function impairment. (Rozalena et al., 2018) In patients, there are hematologic abnormalities in the form of a very high increase in leukocytes, which indicates a severe infection, followed by a decrease in platelets and anemia. The anemia frequently observed in Weil's syndrome is caused by blood loss, renal failure, or an ill-defined hemolytic process. An increase in urea and creatinine in patients is a sign that strongly suggests Weil's disease, accompanied by an increase in liver function tests and the presence of clinical jaundice. In jaundice patients, transaminase and alkaline phosphatase concentrations are not always elevated and may be normal. Jaundice is not associated with hepatocellular disease or hepatic necrosis. (Chacko et al., 2021) The diagnosis, in this case, did not use direct tests (culture and/or PCR) or indirect tests (MAT, ELISA, or leptodipstick) to detect leptospires due to limited equipment in hospitals located in rural areas.

The clinical clue that may differentiate suspected Weil's disease from other diseases, in this case, is due to a history of risk exposure where the patient frequently goes barefoot while working in the fields. The patient also has typical symptoms such as jaundice, calf aches, conjunctival suffusions, and any other evidence of an organ disorder (liver, kidney, and hematological involvement). According to the literature, a detailed history of exposure and symptoms is important for confirming leptospirosis. (Chacko et al., 2021) Any patient with a history of high risk and the following symptoms: jaundice, hemorrhage, fever, headache, myalgia, and involvement of organ dysfunction should be suspected of having leptospirosis. In several studies, it was explained that the serological test results from the first week showed a negative value. So, if the serological test results are negative, it does not rule out the possibility of a diagnosis of leptospirosis. The established diagnosis of leptospirosis does not only depend on tests, the history is also very important, especially in finding risk factors and carrying out an appropriate physical examination.

In most cases, leptospirosis can resolve spontaneously. (Pothukuchi et al., 2018; Rajapakse, 2022) In severe cases, intravenous antibiotics should be given immediately to patients suspected of leptospirosis or Weil's disease. Administration of intravenous ceftriaxone at 1 gram per day for 7 days is non-inferior to penicillin G to manage severe cases of leptospirosis. In mild cases, oral antibiotics may be given in the form

of doxycycline 100 mg twice per day, amoxicillin 500 mg 4 times per day, or azithromycin 500 mg once per day for 3 days. Supportive therapy like fluid administration can be given to prevent oliguric renal failure. In severe cases of leptospirosis where kidney function has been damaged, dialysis can be performed. (Chacko et al., 2021; Haake, DA, Levett, 2015; Rajapakse, 2022) The patient was immediately given 1 gram of ceftriaxone intravenously twice a day. In severe cases of leptospirosis or when organ failure is present, intravenous antibiotics are administered. The patient also received supportive therapy, namely lesikol and prorenal, to treat liver and kidney dysfunction. Hemodialysis was not performed on the patient because the patient's clinical condition was still good.

5. Conclusion

This is a case report of a 43 years old male with suspected Weil's disease. The diagnosis was based on a history of high-risk patient occupation, accompanied by clinical symptoms of leptospirosis, as well as general laboratory results. The examinations to determine the presence of leptospira were not carried out due to limited equipment in hospitals located in rural areas. The patient immediately received intravenous antibiotics and symptomatic therapy. Despite having severe symptoms, complete and total recovery was achieved after proper treatment.

Conflict of interest

The authors declare no conflict interest financial or otherwise.

Acknowledgements

Declared done

References

Chacko, C. S., Lakshmi S, S., Jayakumar, A., Binu, S. L., Pant, R. D., Giri, A., Chand, S., & UP, N. (2021). A short review on leptospirosis: Clinical manifestations, diagnosis and treatment. Clinical Epidemiology and Global Health, 11(March), 100741. https://doi.org/10.1016/j.cegh.2021.100741

Evangelista, V., et al. (2013). Weil's disease - a case report. Department of Medicine, Hospital Beatriz Ângelo, Loures, Portugal, 757.

Guerra, M. A. (2009). Zoonosis update leptospirosis. Journal of the American Veterinary Medical Association, 234(4), 472–478. https://doi.org/10.2460/javma.234.4.472

Haake, DA, Levett, P. (2015). Leptospirosis in Humans. Curr Top Microbiol Immunol., 387, 65–97.

Kokudo, T., Nakamura, I., Nakamura-Uchiyama, F., Komiya, N., & Ohnishi, K. (2009). Weil's disease in a patient living in Tokyo. Internal Medicine, 48(18), 1707–1710. https://doi.org/10.2169/internalmedicine.48.2476

Mcbride, A. J. A., Athanazio, D. A., Reis, M. G., & Ko, A. I. (2005). Leptospirosis: current opinion in infectious diseases. Pmid, 18, 376–386.

Moreira Marques, T., Nascimento, P. O., Almeida, A., & Tosatto, V. (2020). Weil's disease in a young homeless man living in Lisbon. BMJ Case Reports, 13(6), 2019–2021. https://doi.org/10.1136/bcr-2019-233543

Palaniappan, R. U. M., Ramanujam, S., & Chang, Y. F. (2007). Leptospirosis: Pathogenesis, immunity, and diagnosis. Current Opinion in Infectious Diseases, 20(3), 284–292. https://doi.org/10.1097/QCO.0b013e32814a5729

Pothukuchi, V., Ahmed, S., & Reddy, K. N. (2018). A case report of Weil's disease. Journal of Dr. NTR University of Health Sciences, 7(3), 233. https://doi.org/10.4103/2277-8632.241282

Rajapakse, S. (2022). Leptospirosis: Clinical aspects. Clinical Medicine, Journal of the Royal College of Physicians of London, 22(1), 14–17. https://doi.org/10.7861/clinmed.2021-0784

Rajapakse, S., Rodrigo, C., Balaji, K., & Fernando, S. D. (2015). Atypical manifestations of leptospirosis. Transactions of the Royal Society of Tropical Medicine and Hygiene, 109(5), 294–302. https://doi.org/10.1093/trstmh/trv026

Rozalena, S., Handayani, L., Arman, A., Permata, M., & Hudari, H. (2018). Weil's disease in a 36 years old female: A case report. IOP Conference Series: Earth and Environmental Science, 125(1), 5–8. https://doi.org/10.1088/1755-1315/125/1/012066

Thayaparan, T., Abdullah, M., Robertson, I., Fairuz, A., & Suut, L. (2013). Leptospirosis, an emerging zoonotic disease in Malaysia. 2013 | , PhD, FASc - Academia.edu. Malaysian J Pathol, 35(2), 123–132.