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Successful Management of Leptospira with Icterus Manifestation and Acute Kidney Injury at District Hospital

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Abstract

Leptospirosis is an infectious disorder of animals and humans and the diseases produce high morbidity and substantial mortality in in tropical and subtropical regions. It is characterized by a broad spectrum of clinical manifestations, varying from asymptomatic infection to fulminant, fatal disease. In cases involving both icterus and acute kidney injury (AKI), timely diagnosis and appropriate management are crucial, especially in resource-limited settings like district hospitals. A 19-years-old man was referred to dr. H. Koesnadi District Hospital emergency department with fever, nausea, and jaundice six days prior to admission. On Physical examination, he was found to be febrile (38,5^{o}C), icteric with conjunctival injection but no suffusion, hepatomegaly, and jaundiced skin. Laboratory tests demonstrated leukocytosis, thrombocytopen, elevated trasminase levels, hyperbilirubinemia, hyponatremia, as well as elevated renal function. IgM *Leptospira* was positive. He was successfully treated with antibiotics and supportive therapy. Leptospirosis in human infection occurs after exposure to environmental sources, mainly animal urine, contaminated water or soil, or infected animal tissue. In its mild form, leptospirosis may present as nonspecific symptoms such as fever, headache, and myalgia. Severe leptospirosis, are characterized by jaundice, hepatorenal failure, encephalopathy, and pulmonary hemorrhage. Leptospires are highly susceptible to a broad range of antibiotics. Penicillin IV is the main treatment for sever leptospirosis but ceftriaxone, cefotaxime, or doxycycline is a satisfactory alternative. With timely intervention, even severe cases involving icterus and AKI can be managed effectively, reducing morbidity and mortality in district hospital.

Keywords: Leptospirosis, Leptospira, Icterus, Acute Kidney Injury.

Introduction

Leptospirosis is an infectious disorder of animals and humans and is the most common zoonotic infection in the world. This infection is easily transmitted from infected animals through their urine, either directly or through infected soil or water.[1] The disease is caused by pathogenic *Leptospira* species and is characterized by a broad spectrum of clinical manifestations, varying from asymptomatic infection to fulminant, fatal disease. In its mild form, leptospirosis may present as nonspecific symptoms such as fever, headache, and myalgia. Severe leptospirosis, are characterized by jaundice, hepatorenal failure, encephalopathy, and pulmonary hemorrhage, is often referred to as Weil's syndrome.[2,3]

These diseases produce high morbidity and substantial mortality in in tropical and subtropical regions where environmental conditions favor the bacteria's survival. Based on the 2022 Indonesian Health Profile, there were 1,419 cases of leptospirosis in Indonesia reported in ten provinces (Banten, DKI Jakarta, West Java, Central Java, DI Yogyakarta, East Java, South Sulawesi, Southeast Sulawesi, East Kalimantan, and North Kalimantan). Of the reported cases, there were 139 deaths with a case fatality rate (CFR) of 9.8%. East

Java Province is the second largest contributor after Central Java to all cases in Indonesia with 28.3% cases.[4]

In cases involving both icterus and acute kidney injury (AKI), timely diagnosis and appropriate management are crucial, especially in resource-limited settings like district hospitals.[1] This case report presents a patient diagnosed with severe leptospirosis, manifesting as icterus and AKI, successfully managed at a district hospital. The case highlights the challenges and strategies in managing complicated leptospirosis in a non-tertiary care setting, with a focus on early recognition, supportive care, and appropriate antimicrobial therapy.

Case Report

A 19-years-old man was referred to dr. H. Koesnadi District Hospital emergency department with fever, nausea, and jaundice six days prior to admission. He did not complain cough, vomiting, abdominal pain, petechiae, diarrhea neither change in urination. The patient worked as farmer in rice fields. He reported swimming in lake one week prior to symptoms. He denied history of recent travel, sick contacts, eating uncooked foods, and animal bites. On Physical examination, he was found to be febrile (38,5^{o}C), icteric with conjunctival injection but no suffusion, hepatomegaly, and jaundiced skin (Figure 1). There was no finding hepatomegaly, and Murphy signs negative. Laboratory tests demonstrated leukocytosis (26.610/μL), thrombocytopenia (132.000/μL), increased trasminase (SGOT 63 U/L, SGOT 71 U/L), significant hyperbilirubinemia (total bilirubin 33,48 mg/dl, direct bilirubin 26.83 mg/dl), hyponatremia (Na 130 mEq/L), as well as elevated renal function (creatinine 6,73 mg/dL and ureum 419 mg/dL). Blood gas analysis data suggests a mild metabolic acidosis with some respiratory compensation. He was tested negative for WIDAL test, anti HAV, and HbsAg test, but was found positive for IgM *Leptospira*. Abdominal ultrasound showed bilateral parenchymal kidney disease and did not demonstrate gallbladder inflammation, common bile duct dilatation, or evidence of gallstones. The patient was treated with Ceftriaxone 2x2 gr IV, Omeprazole 2x40 mg IV, Ondansetron 3x8 mg IV, Santagesik 3x1 gr IV, UDCA 3x1 tablet oral, and Lesipar 2x1 tablet oral. After four days treated, the fever, nausea, and icteric resolved (Figure 2). Laboratory follow up showed improvement in leukocyte (WBC 22.160/μL), thrombocyte (272.000/μL), total bilirubin 29,25 mg/dL, direct bilirubin 22,87 mg/dL, creatinine 1.81 mg/dL, and ureum 132 mg/dL.

Figure 1. Clinical Manifestation on admission

Figure 2. Clinical Manifestation After 4 Days of Treatment

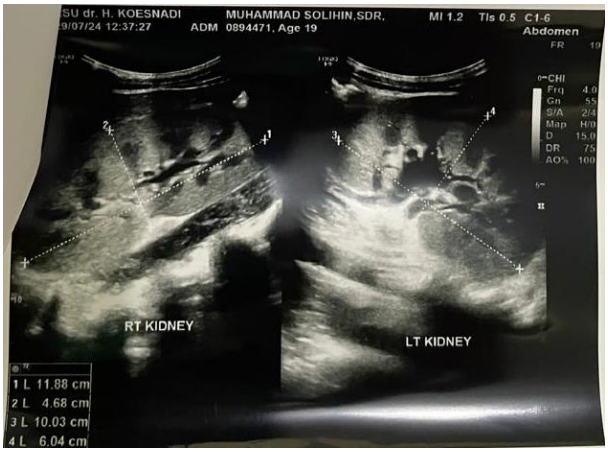

Figure 3. Abdominal Ultrasound Showed Bilateral Parenchymal Kidney Disease

Discussion

Leptospirosis is a zoonosis with a 10 times higher incidence in the tropics than in temperate regions. It is caused by Leptospira, a pathogenic spirochete, and human infection occurs after exposure to environmental sources, mainly animal urine, contaminated water or soil, or infected animal tissue. Portals of entry include abrasions or cuts in the mucous membrane.[5] These diseases produce high morbidity and substantial mortality in in tropical and subtropical regions where environmental conditions favor the bacteria's survival, peak incidence during rainy seasons.[6] Most cases occur in men. Certain occupational groups are at especially high risk, including veterinarians, agricultural workers, sewage workers, slaughterhouse employees, and workers in the fishing industry. Recreational exposure and domestic-animal contact are prominent sources of leptospirosis. Leptospira can be found in various domestic mammals including rodents, cattle, sheep, dogs, cats, and other livestock. Recreational freshwater activities, such as canoeing, windsurfing, swimming, and waterskiing, place persons at risk for infection.[2,7] Our patient is male, worked as farmers. Large rice field area is also a potential breeding site or breeding habitat that is conducive to the Leptospirosis reservoir.[8] He also had history of swimming in lake which increased the risk factor for developing leptospirosis by ingestion contaminated water. The infection occurred during rainy season. This happens related to the character of the *Leptospira* bacteria that will survive in water, wet soil, vegetation, and mud with temperatures more than 22^{o}C.[9]

The disease is caused by pathogenic *Leptospira* species and is characterized by a broad spectrum of clinical manifestations, varying from asymptomatic infection to fulminant, fatal disease. In its mild form, leptospirosis may present as nonspecific symptoms such as fever, headache, and myalgia. Severe leptospirosis, are characterized by jaundice, hepatorenal failure, encephalopathy, and pulmonary hemorrhage, is often referred to as Weil's syndrome.[2,3] Transmission occurs through cuts, abraded skin, or mucous membranes, especially the conjunctival and oral mucosa. After entry, the organisms proliferate, cross tissue barriers, and disseminate hematogenously to all organs (leptospiremic phase). The incubation period is usually 1–2 weeks but ranges from 1 to 30 days. The acute leptospiremic phase is characterized by fever of 3–10 days's duration, during which time the organism can be cultured from blood and detected by polymerase chain reaction (PCR). During the immune phase, resolution of symptoms may coincide with the appearance of antibodies, and leptospires can be cultured from the urine. The distinction between the first and second phases is not always clear: milder cases do not always include the second phase, and severe disease may be monophasic and fulminant.[2]

Most patients are asymptomatic or only mildly ill (aniteric syndrome) and is self-limited. They presents with a nonspecific flu-like illness like fever, chills, headache, nausea, vomiting, abdominal pain, conjunctival suffusion (redness without exudate), and myalgia. Muscle pain is intense and especially affects the calves, back, and abdomen. The headache is intense, localized to the frontal or retroorbital region (resembling that occurring in dengue), and sometimes accompanied by photophobia. The illness may last a few days before the fever resolves. Aseptic meningitis may be present and is more common among children than among adults. The natural course of mild leptospirosis usually involves

spontaneous resolution within 7–10 days, but persistent symptoms have been documented. Although the onset of severe leptospirosis may be no different from that of mild leptospirosis, severe disease is often rapidly progressive and is associated with a case–fatality rate ranging from 1 to 50%.[1,2]

The classic presentation, often referred to as Weil's syndrome, encompasses the triad of hemorrhage, jaundice, and acute kidney injury. Jaundice occurs in 5–10% of all patients with leptospirosis; it can be profound and give an orange cast to the skin but usually is not associated with fulminant hepatic necrosis. Physical examination may reveal an enlarged and tender liver. Acute kidney injury is common in severe disease, presenting after several days of illness, and can be either nonoliguric or oliguric. The icteric phase may also involve the heart, CNS, and muscles. Petechiae and hemorrhages can be observed.[2]

Laboratory results usually show signs of a bacterial infection, including leukocytosis with a left shift and elevated markers of inflammation. Thrombocytopenia is common and is associated with bleeding and renal failure. Although the underlying mechanisms of thrombocytopenia have not been elucidated, it seems likely that platelet consumption plays an important role. A consumptive coagulopathy may occur, Typical electrolyte abnormalities include hypokalemia and hyponatremia. Hemodialysis can be lifesaving, with renal function typically returning to normal in survivors. Serum bilirubin levels may be high, whereas rises in aminotransferase and alkaline phosphatase levels are usually moderate.[2] A definitive diagnosis of leptospirosis is based on isolation of the organism from the patient, on a positive PCR result, or on seroconversion or a rise in antibody titer. Blood culture for leptospirosis remains the gold standard. PCR offers a great advantage: the capacity to confirm the diagnosis of leptospirosis with a high degree of accuracy during the first 5 days of illness, but is expensive. Dark-ground microscopy of body fluids (blood, urine, or CSF) can visualize *Leptospira* but this method is obsolete now due to low sensitivity Serologic test such as microscopic agglutination test (MAT) is most often used as a reference test. Standard tests are tedious, laborious and require well-equipped laboratories with experienced staff and are therefore restricted to a few centers. Traditional serological methods, such as the ELISA, are widely used to diagnose leptospirosis.[2,10,11] In this case, laboratory tests demonstrated leukocytosis, thrombocytopenia, increased trasminase, significant hyperbilirubinemia, hyponatremia, as well as elevated creatinine and ureum levels. Blood gas analysis data suggests a mild metabolic acidosis with some respiratory compensation. This blood gas analysis is consistent with compensated metabolic acidosis, likely due to a condition such as dehydration, sepsis, or renal dysfunction, which can be common in leptospirosis with acute kidney injury. He was also found positive for IgM *Leptospira.* ELISA can be performed with minimal training and typically provides results in 2–4 hours. Systematic review showed that IgM ELISA in all phases had a sensitivity of 86% and specificity of 84%, whereas the acute phase had a sensitivity of 90% and specificity of 91%. The results showed IgM ELISA could be useful as a screening and a confirmatory test, especially in regions with small laboratories that have difficulty performing other techniques such as MAT as in district hospital.[10] Although blood culture for leptospirosis remains the gold standard, but labour intensive and time consuming, requires high levels of biosafety levels.[11] In this case, abdominal ultrasound

showed parenchymal kidney disease bilateral and did not demonstrate gallbladder inflammation, common bile duct dilatation, or evidence of gallstones. This findings were compatible with previous studies that showed typically un-enlarged livers with normal parenchymal echogenicity, normal spleens, and non-dilated biliary tree.[12] *Leptospira* can infiltrate renal tubular cells, leads to direct nephrotoxic action and triggers an immune response that results in tubulointerstitial nephritis, acute tubular necrosis, and a risk of renal fibrosis.[13]

In mild cases, oral treatment with doxycycline, azithromycin, ampicillin, or amoxicillin is recommended. Severe leptospirosis should be treated with IV penicillin as soon as the diagnosis is considered. Leptospires are highly susceptible to a broad range of antibiotics, including the β-lactam antibiotics, cephalosporins, aminoglycosides, and macrolides, but are not susceptible to vancomycin, rifampin, metronidazole, and chloramphenicol. Ceftriaxone, cefotaxime, or doxycycline is a satisfactory alternative to penicillin for the treatment of severe leptospirosis.[14] Ceftriaxone is widely available and inexpensive in district hospital, making it the antibiotic of choice in this case. After four days follow up the patient showed clinical improvement with reduced icteric and jaundice. Laboratory results also showed decreased levels of leukocyte, thrombocyte, total bilirubin, direct bilirubin, creatinine, and urea. Higher mortality rates are associated with an age > 40, altered mental status, acute renal failure, respiratory insufficiency, hypotension, and arrhythmias.[1] However, in our patient, hemodialysis was not necessary, as a resolved of renal function with conservatives therapy.

Conclusion

In this case report, a 19-year-old male farmer presented with severe leptospirosis, manifesting as fever, jaundice, and AKI. His history of working in rice fields and recent swimming in a lake during the rainy season increased his risk of exposure to Leptospira bacteria. This case highlights the importance of early diagnosis and appropriate antimicrobial therapy in managing severe leptospirosis, especially in resource-limited settings like district hospitals. With timely intervention, even severe cases involving icterus and AKI can be managed effectively, reducing morbidity and mortality.

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