

A Typical Presentation of Acute Meningitis in Icteric Leptospirosis: A Case Report

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Abstract: *Leptospirosis is an acute febrile zoonotic disease caused by pathogenic spirochetes of the genus Leptospira. It is an emerging disease in sub tropical and tropical countries. It transmitted to human via exposure of contaminated water or soil by infected animals. Clinical manifestations range from mild fever with flu-like symptoms to fulminant diseases such as Weil's disease. Diagnosis confirmation made by isolating the organisms and positive serologic testing. We report a case of atypical presentation of acute meningitis in a 28 years old patient with icteric leptospirosis. Patient came with fever and predominantly neurological symptoms 5 days prior to admission. Patient was experiencing headache, neck stiffness, altered consciousness and seizures. Diagnosis was concurred when serology tests positive for Leptospira antibody supporting the clinical signs and symptoms. Patient was then given 3rd generation cephalosporin antibiotic therapy and supportive symptomatic therapy. Leptospirosis is often under diagnosed, associated manifestations may overlap with dengue and typhoid fevers which are more common. It is further complicated with poor access to accurate diagnostic tests especially in remote healthcare facility with limited access and availability. It is important for physician to be aware of the diverse and uncommon manifestations of this disease to able to make timely diagnosis. Prompt and adequate treatment are critical to shorten the duration of illness, reduce shedding of the organism and avoid severe complications.*

Keywords: leptospirosis, aseptic meningitis, icteric, tropical disease, zoonosis

1. Introduction

Leptospirosis is an emerging zoonotic infection caused by pathogenic *Leptospira* species that can be found worldwide. Leptospirosis are widely found in tropical climate countries with heavy rainfall. It is estimated that there are 1.03 million cases of leptospirosis with approximately 59,000 deaths each year. ^[1] Majority of the cases are found in South East Asian countries, India and Latin America. ^[2] According to World Health Organization (WHO), in 2019 there are 920 cases of leptospirosis reported in Indonesia with 122 deaths, decreasing the Case Fatality Rate (CFR) to 13, 26% from the previous year which is 16, 5% in 2018. However, this number is predicted to be heavily underreported due to the annual morbidity data was recently estimated to be at 39.2 per 100,000 people. ^[3, 4] The occurrence of leptospirosis is related to risk factors of infections. The number of outbreak cases increased simultaneously with high rainfall and floods. Other risk factors of infections include low socioeconomic status, overcrowded areas with poor sanitation and drainage system, and recreational activities. Leptospirosis also occurs as occupational hazard for farmers, rice farmers, sewer worker, and ranchers. ^[1, 3, 4]

Naturally, infection occurs due interaction within agent and host in particular environment. Various mammals are natural hosts, and humans are infected after exposure to environmental sources such as animal urine, contaminated water and soil. Site of entry include skin cuts or mucosal abrasion. ^[5] In Indonesia, the most common host is rodent. Rodents shed the bacteria via their urine thus contaminating the environment. ^[3, 4] The spectrum of human disease caused by species is extremely broad, ranging from subclinical infection to severe syndrome which cause multiple organ failure with high mortality rate. Anicteric leptospirosis occurs in 80% of the cases, which presents mild fever and flu-like symptoms.

^[5] Severe form of the infection is called Weil's disease, where it is complicated with jaundice, acute renal failure, and bleeding diathesis with case fatality rate as high as 70%. ^[3, 6] Pulmonary hemorrhage is also an often observed severe complication. It leads to Acute Respiratory Distress Syndrome (ARDS) with mortality rates as high as 71% among the infected patients with pulmonary manifestations. ^[8, 9, 10] Neurological manifestations are uncommon, often overlooked and may be confused with other aseptic meningeal infections. ^[6, 8]

Leptospirosis often under diagnosed and may perplexing physicians particularly in the case where the neurological manifestations predominantly involved due to its rarity. Here we present the case of a 28 years old male with icteric leptospirosis, with neurological manifestations as the main highlight of the symptoms. We discuss the diagnostic possibility, therapeutic approach, and review the literatures for such cases particularly in health facility where resources are limited.

2. Case Report

A 28 years old male presented with high grade fever for 6 days prior to admission. Fever accompanied by severe headache before admission and alteration of patient's mental status. Patient progressively became more drowsy and unresponsive. On the day of admission, patient developed multiple episode of tonic seizures, each lasted about 10-15 seconds. Patient also experienced muscle pain, dry cough, nausea, anorexia, and fatigue throughout the period. Patient works as water sport staff at beach side. On admission, his level of consciousness according to GCS (Glasgow Coma Score) was 10 (E2V3M5), his blood pressure was 100/60 mm/Hg, heart rate 74 beats/min, respiratory rate 24 times/min, and temperature 39, 3°C. Physical examination

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findings are icteric sclera, neck rigidity, positive Kernig's sign, hepatomegaly and abdominal tenderness. Other physical examinations were unremarkable. His blood tests showed: Hemoglobin (11, 3 g/dl), leukocytosis (19,500/mm³), thrombocytopenia (24,000/mm³), elevated bilirubin levels (Total Bilirubin 16, 64 mg/dl, Direct Bilirubin 9, 76 mg/dl, Indirect Bilirubin 7, 08 mg/dl), elevated ureum levels (106 mg/dl), elevated serum creatinine levels (6, 4 mg/dl), eGFR = 11 ml/min/1.73 m², elevated liver enzymes (ALT 84 mg/dl, AST 144 mg/dl). Urinalysis was within normal range. Chest x-ray was normal and ECG showed normal sinus rhythm. Patient was admitted, and was given Ceftriaxone 1 gram every 12 hours, along with adequate intravenous fluid therapy and symptomatic therapies. Intravenous diazepam was administered for the seizures. CSF was not obtained for examination due to limited access of molecular and microbiological tests in the hospital. Patient was tested for Dengue serology IgG and IgM, blood smear tests, HIV serology, hepatotropic viruses, Widal test and Anti *Leptospira* IgM. Chest xray showed normal results. Cranial imaging was normal. After 2 days, the Immunoserology test of Anti *Leptospira* IgM turned out to be positive. Other serologies tests were negative and so did the blood smears for malarial parasite. His diagnosis was reviewed and based on epidemiological data, further confirmed with positive serum IgM ELISA, patient was diagnosed with icteric leptospirosis. Antibiotic therapy was continued along with diazepam and other symptomatic therapies. Vital signs were examined every hour and fluid balance was monitored every 12 hours. Patient condition eventually improved by the third day of admission, his consciousness level increase to GCS 15 with absence of seizures. Antibiotics were continued for 5 days. He was discharged on the sixth day of admission, recovered and alert with normal vital signs. Icterus were slowly disappeared. Platelet levels were increased, renal functions were return back to normal, and bilirubin levels were down significantly.

3. Discussion

Leptospirosis incidence is significantly higher in warm climate or tropical regions. There were about 39.2 cases per 100,000 population reported in Indonesia. Risk factors for infection including poor sanitation, low socioeconomic urban areas, and occupational hazard for several professions.^[2, 4] Large proportion of cases and deaths were estimated to occur in adult males with age of 20-49 years old.^[1] Clinical manifestations are vast ranging from mild flu-like symptoms to severe symptoms, called Weil's syndrome consisting of jaundice, acute renal failure, and bleeding. Neurological manifestations of leptospirosis (neuroleptospirosis) are uncommonly found as primary manifestations nor initial manifestations.^[5, 6] It is reportedly only in 5-10% of the cases. The most common form of neuroleptospirosis is aseptic meningitis. Other severe neurological complications are encephalitis, intracranial bleed, cerebellitis, and acute disseminated encephalomyelitis.^[5, 8] Aseptic meningitis is the presence of clinical and laboratory evidence of meningeal inflammation in the absence of bacterial cultures in the cerebral spinal fluid (CSF). Leptospirosis is responsible for 5-13% of all cases of aseptic meningitis.^[5, 6, 9]

Leptospirosis is a biphasic illness, starting with leptospiraemic phase for 3-7 days, and followed by immune phase that can last up to 4-30 days.^[8] During the immune phase, immune complexes deposited and irritate the meningeal membrane. Inflammation process caused meningeal oedema and congestion. Microhemorrhage occurs due to infiltration of small and medium sized blood vessels by perivascular round cells. Microscopically, patchy demyelination can be found in the nervous system.^[6] Signs of the meningeal irritation will appear clinically as headache, vomiting, seizures, and alternate consciousness.^[8] During the early phase, *Leptospira* can be isolated from the blood and CSF, although cultures required 11-13 days for result, limiting its value in aiding diagnosis. Immunoserology tests such as MAT (microscopic agglutination test) and/or ELISA (enzyme-linked immunosorbent assay) are used frequently to detect antibodies during immune phase. Antibodies appear from day 5 to 7 of illness. Microbiological examination, such as Polymerase Chain Reaction (PCR) tests are used to detect DNA of the bacteria early in the disease. The PCR displayed advantage over serology tests due to the advantage of earlier positivity, hence faster diagnosis and prompt treatment. *Leptospira* DNA can be detected in initial phase in blood and in CSF and urine a few days after the onset of symptoms.^[4, 8, 12] CSF analysis performed in patient with leptospirosis may show a lymphocytic or neutrophilic pleocytosis with slightly elevated protein concentrations. Glucose concentrations are usually normal.^[8, 11]

Our patient was a 28 years old adult male, resides in Indonesia. He worked as water sport staff. He came with fever and loss of consciousness, preceded with severe headache and neck stiffness. He developed multiple episodes of tonic seizures in the emergency room and during his first day admission. These symptoms made the early diagnosis leaning heavily towards solely intracranial infections. Laboratory results showed thrombocytopenia, elevated bilirubin, kidney and liver functions. Serology tests were performed to exclude other infectious febrile disease such as dengue, malaria, typhoid, hepatitis, and HIV. Imaging examination showed clear result. Among all the tests, the serology IgM antibodies for *Leptospira* was tested positive. Our patient was diagnosed with icteric leptospirosis or Weil's disease, based on the epidemiological data, environmental exposure and clinical manifestations, aided further with the presence of IgM antibody for *Leptospira*. Pulmonary involvement was spared in this case.

Initial predominant neurological symptoms were a throwaway for physicians. Patient with such initial presentations are often treated empirically for cerebral malaria, dengue fever, viral encephalitis, hepatic encephalopathy and tuberculous meningitis.^[9] The presence of neuroleptospirosis was often diagnosed based on clinical data. There were several limitations in our case due to limited access and availability. CSF analysis and CSF serology tests were not performed to proof the presence of aseptic meningitis and antibody of the bacteria in CSF. PCR tests were also not available at our hospital, hence we were not able to detect the presence of *Leptospira* DNA in our patient. MAT was deemed as the gold standard of leptospirosis serology tests^[3, 4], but it was not available as well in our health facility, instead diagnosis was done with IgM ELISA

serology tests from patient's blood sample. Magnetic resonance imaging (MRI) is a good method for identifying acute disseminated encephalomyelitis. [5] But, we only have CT scan available as diagnostic cranial imaging, hence encephalitis could not be confirm nor rule out in this case. Since the diagnosis was made and confirmed via clinical and blood serology, CSF analysis does not have clinical consequences and affecting therapy given, unless other differential diagnosis need to be excluded. [11] Antibiotics therapy are supportive in shorten the duration of illness, reducing mortality and preventing complications. [6, 8, 11] Antibiotics of choice include penicillin, doxycycline, or 3rd generation cephalosporins. [11, 13] Our patient was given 1 gram ceftriaxone for twice a day following by supportive therapy for 5 days. Steroids were not given in this patient, due to its controversial role and lack of adequate supportive studies. [8] The patient showed positive response towards the therapy regimen. Prognosis of leptospirosis with neurological involvement is generally good, with meningitis resolves by 3-6 weeks. Neurological sequelae are unusual. [6, 9, 11] Although several studies shown that the presence of altered sensorium and seizures were known to lead to a worse prognosis [6], fortunately we did not found that in our patient. Liver and renal dysfunctions are usually reversible, with resolution within 4-6 weeks. [8] Patient was recovering well without further complications due to early diagnosis and prompt treatment.

4. Conclusion

Leptospirosis can appear with the form of acute meningitis aside from the classic symptoms. Although it is not commonly known as primary or initial manifestation of leptospirosis, it is important for physician practicing in endemic areas to be aware of such presentation of the disease and considering it as a differential diagnosis. Knowledge of patient's occupational history and environmental exposures are important. In cases where neurological manifestations were found along with acute febrile and hepatorenal dysfunction, a high index of suspicion for leptospirosis should be considered. Therapy should be initiated based on clinical judgement as laboratory confirmation can be delayed or limited due to poor resources.

5. Disclosure

All authors contributed equally. There is no conflict of interest in this case report.

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Author Profile



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