Diagnostic Problems in Leptospirosis Patients : A Case Report

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Abstract

Leptospirosis is a zoonosis infection found in almost every part of the world but is mostly endemic in tropical and subtropical countries. In 2013 there were 640 new cases reported with 60 death cases (CFR 9.37%). An increase in new cases had caused an outbreak in Sampang, Madura due to a flood following a high rainfall. A male patient aged 45 years old with Leptospirosis. The diagnosis was made based on the epidemiology, clinical manifestations, and Microscopic Agglutination Test (MAT) examination data. In the early treatment, the examination of IgM and IgG Leptospira showed negative results a confirmation with MAT examination was done subsequently. Diagnosis using MAT also provides information about an outbreak in a region. Upon receiving antibiotic and symptomatic treatments and clinical recovery, the patient's condition continued to improve.

Keywords :*Leptospira, Leptospirosis, Microscopic Agglutination Test*

Introduction

Leptospirosis is an infectious disease affecting humans and animals. Precisely, this disease is a zoonosis disease that could affect humans, one of the most common zoonoses in the world. Leptospirosis is also known as flood fever, for it appears primarily because of a flood.The most common reservoir of this bacteria is rodents and mice(2).In Indonesia, this disease is considered a re-emerging disease, meaning a new case could appear sporadically with the potential to cause an outbreak.

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In 2013 there were 640 new cases with 60 death cases (CFR 9.37%) reported. The increased cases were due to an outbreak in Sampang, Madura. Whereas until October 2014, there were 411 new cases with 56 death cases (CFR 13.63%) reported. The increased cases were due to an outbreak in DKI Jakarta and Central Java due to a flood following a high rainfall(3).

The diagnosis was made based on the isolation of the bacteria from blood or urine. Dark-field microscope examination often gives false value, while rapid quantitative examination to detect IgM and IgG leptospira is commonly used as a screening tool, although it frequently shows negative results, especially in the early phase of leptospirosis. The gold standard of diagnosis is the Microscopic Agglutination Test (MAT) serology examination. The current development in molecular research has contributed to the characteristic correlation study amongst pathogen strains and outbreak investigation epidemiologically

in a region[2].

Case Description

Mr. A.S, 45 years old, resided in Sampang, Madura. The patient was referred from Sampang Hospital with calf muscle pain ten days before hospital admittance accompanied by fever, headache, dizziness, vomiting dark-colored blood, stomachache, and nausea. The patient also complained of reddened eyes since three days before hospital admittance that changed into yellowish, shortness of breath not affected by activity, with no cough and chest pain observed. The patient also complained of tea-colored urine with a reduced volume of approximately 500 mL/24 hrs since three days before hospital admittance, with no black stools observed. The patient had a history of contact with rodents and history of flood in his residence. The IgG and IgM Leptospira examinations from Sampang Hospital showed negative results.

From the physical examination, the patient showed a weak general condition with GCS of 4-5-6. The vital signs examinations showed blood pressure of 100/70 mmHg, heart rate of 80 x/min, respiratory rate of 20 x/min, and axillary temperature of 36.7^0C. Head and neck examinations showed icteric sclera and conjunctival suffusion. Thorax inspection showed petechiae in thethoracalregion. On heart auscultation we obtained single S1 and S2 heart sounds, no murmur, gallop, or friction. Lungs examination showed normal results. Upper extremities examination showeddry reddish warm hands, petechiae on the left shoulder, no edema, and no palmar erythema. Lower extremities examination showed dry reddish warm foot and no edema.

Laboratory examinations showed hemoglobin of 12.2 g/dl, leucocyte of 11,700/mm^3, thrombocyte level of 34,000/mm^3, HCT of 37.2%, neutrophil of 84.6%, aPTT of 31/22.8, PPT of 11.3/12.1, BUN of 104 mg/dl, SK of 7.52 mg/dl, albumin of 2.25 g/dl, blood sugar level 71 mg/dl, direct bilirubin 11.51 mg/dl, total bilirubin 12.96 mg/dl, SGOT 29 U/L, SGPT 27 U/L, Na 133 mmol, K 3.5 mmol, Cl 101 mmol, CRP 108.91 mg/dl, non-reactive HbsAg, IgM Leptospira (+), IgG Leptospira (-), alkaline phosphatase 108 U/L, and non-reactive HCV. MAT examination with icterohaemorrhagicserogroup result showed a titer of 1:640. From urinalysis it was obtained results as followed: Glucose (-), Bil (+3), Ket (-), SG 1.010, BLD +/- intact, pH 5.5, Prot (+), Uro 3.2, Nit (-), yellow in color, normal clarity, Eryt -2/HPF, Leuko -2/HPF, Low epithelial cells, Crystals (-), Cylinder (-). Chest X-ray and electrocardiogram showed normal results.

The patient was diagnosed with Leptospirosis. The patient was given soft diets high in carbohydrates and protein of 1.900 kcal, D5:NS(1:2) IV fluid 1.500 ml/24hrs, Ceftriaxone 1 gr I.V. BID, Omeprazole 40 mg I.V. BID, Sucralfate suspension 1 tablespoon QID. On the ninth days of hospitalization, the patient's condition continued to improve; no fever, no icteric on the sclera, no blood vomiting, no calf pain, and the urine production was 2.000 cc, clear yellow in color.

Discussion

Leptospirosis is a zoonosis infection found in almost every part of the world but is generally endemic in tropical and subtropical countries. There is more than 250 serovar of *Leptospira* genus known to have caused broad spectrum of various diseases, ranging from mild to life threatening conditions[4]. The incidence of Leptospirosis could be affected by several factors, including culture and social backgrounds, occupancy, behavior, and environment. Humans are at risk of contracting this disease in correlation to their occupancies; farmers, stock farmers, miners, gutter cleaners, soldiers, and other jobs exposed to *Leptospira* contaminated water are at high risk of contracting this disease[2,5].

The clinical manifestations of this disease are varied, ranging from mild fever to the icterohaemoragic form with complications in several organs, including the brain, kidney, and liver[1]. The incubation period ranging from 2-20 days with 7-10 days on average. The onset of the disease is sudden. It began with high fever, and one third of patients reported prodromal signs, such as fatigue and headache[7]. The clinical manifestations of Leptospirosis is biphasic, the acute phase last for approximately one week, followed by the immune phase accompanied by antibody production and expression of *Leptospira* in urine. Most complications of Leptospirosis are associated with the location of *Leptospira* in the tissues during the immune phase on the second week of the disease progression[6,7].

Most Leptospirosis infections are subclinical or mild. Few cases display unspecific manifestations, such as sudden fever, headache, myalgia, stomachache, red-eye, photophobia, nausea, and vomiting[7]. The ocular manifestations are usually seen in severe Leptospirosis while conjunctival suffusion could be seen in most cases. Conjunctival suffusion and icteric sclera are thought to be pathognomonic of Weil's disease. Anterior uveitis, whether unilateral or bilateral could develop after the resolution of the acute phase in few cases[6]. It could be followed by manifestations of organ damage, including liver, kidney, muscle tissues, and other organs. In severe cases, they could be accompanied by anemia, loss of consciousness, continued fever, icteric, and bleeding. Hemolysis could also contributed to the severity of icteric[2].

Kidney involvement is a crucial manifestation of severe Leptospirosis. Two mechanisms have been suggested in the development of kidney failure in Leptospirosis: (1) direct nephrotoxic due to several endotoxins or endotoxin-like substances, and (2) the anoxic effect due to kidney circulation disturbances[8]. In mild cases, several urine sediments are found, including albuminuria, microscopic hematuria, pyuria, and granular cast. Oliguria and anuria could develop in severe cases. Renal insufficiency usually developed simultaneously with icteric on days 3 to 4, followed by increased urea and creatinine levels that often need renal replacement therapy[6]. Polyuria could develop on days 10-18, and creatinine levels usually begin to decrease at the end of the second week and reached a normal level on weeks 3 to 5 after the onset of the disease, where kidney injury due to Leptospirosis is mostly not permanent[2]. Complications of severe Leptospirosis could affect several organs. Acute Kidney Injury (AKI) is reported in 16% - 40% cases, and it is crucial to distinguish between pre-renal azotemia (non-AKI) and AKI. Patients with pre-renal azotemia respond well with rehydration therapy, hence dialysis could be postponed until 72 hours. While in patients with AKI, oliguria is a predictor of mortality[9].

On direct bacteriology examination of blood and urine using a dark-field microscope, the rate of false-positive results is high since protein filaments are frequently found in the samples and highly resemble *Leptospira*.*Leptospira* could be isolated directly from the blood, urine, tissues, and culture. Culture results could be used for diagnosis[10]. Laboratory diagnosis of Leptospirosis is primarily based on serology examinations. Microscopic Agglutination Test (MAT), Enzyme-Linked Immunosorbent Assay (ELISA), and Immuno-fluorescent Antibody (IFA) test are the most frequently used serology examinations[10].

MAT is the main referenced test and is commonly used as the gold standard of serology test in evaluating new potential Leptospirosis diagnostic tests due to its high sensitivity. MAT could detect antibody in theserovar level so that it could detect different strains of *Leptospira*[2]. Using MAT, we could determine

the agglutination of antibodies found in the patient's serum by mixing it with *Leptospira*. Anti-*Leptospira* antibodies found in the serum will cause the *Leptospira* to adhere to each other and form clumps. This process is called agglutination and could be observed under a dark-field microscope. MAT could not differentiate antibodies agglutination of current, recent, or past infection. Ideally, like other serology tests, two samples must be examined subsequently to determine seroconversion or increased titer four-fold or more[5].

General treatment of Leptospirosis includes symptomatic and supportive therapies based on the severity of the signs and symptoms. Bed rest is recommended for 1 to 2 weeks for the mild disease and 2 to 4 weeks for the severe disease[11]. *Leptospira* are sensitive to several antibiotics, including Penicillin, Cefepim, Aminoglycosides, Tetracycline, and Macrolides. A study suggested that Penicillin and Cefepim have the lowest Minimal Inhibitory Concentrations (MIC) against *Leptospira.* Penicillin could eliminate *Leptospira* on the logarithmic growth phase but not on the stationary phase. Streptomycin demonstrates its ability to eliminate *Leptospira* both on the logarithmic growth and stationary phases. Tetracycline shows leptospirocidal effect only on a high concentration. Gentamycin, Tobramycin, and Isepamicinexhibit significant bactericidal effect on both the logarithmic growth and stationary phases[4]. Due to the biphasic nature of Leptospirosis, the effect of antibiotic agents given on the immune phase is doubtful[2].

The prognosis of Leptospirosis depends on the severity and complications of the disease. Anicteric Leptospirosis generally has a good prognosis, without jaundice, this disease is never fatal, although Pulmonary hemorrhage and myocarditis are reported in anicteric cases occasionally. The mortality rate of Weil's disease ranged between 15% - 40% and higher in elderly patients aged more than 60 years old[12].

Conclusion

It has been reported a male patient, aged 45 years old, with Leptospirosis. The diagnosis was made based on the epidemiology, clinical manifestations, and Microscopic Agglutination Test data. During early hospitalization, the IgM and IgG examinations showed negative results. MAT examination was done subsequently to confirm the diagnosis. MAT examination could also give information regarding an outbreak in a specific region. Symptomatic treatment and antibiotic agents were given to the patient, the patient's condition continued to improve.

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