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Title: Clinical Outcome of Leptospirosis: A Fatal Case Report

Running Title: A case report of Leptospirosis

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Abstract

Background: Leptospirosis is a widespread zoonotic disease that commonly seen in temperate and tropical areas. In here, we have presented the case of fatal Leptospirosis with thrombocytopenia and renal failure.

Case: A 22 years old soldier was referred to the Infectious Diseases clinic with the complains of fever, headache, dizziness, sore throat and weakness. He had a staying history of in a village and tick removal from his head. An extended polymorphic rash on the whole body, congestion on the sclera, hyperemic pharynx and hepatomegaly was observed. Laboratory examination revealed leukocytosis and impaired liver and kidney function tests. Antibiotic therapy with Penicillin G and gentamicin were started with the pre-diagnosis of Leptospirosis. Main diagnosis was confirmed by passive hemagglutination test positivity. On the fifth day of treatment bleeding continued and hemodialysis was carried out. Patient died on 6th day of treatment.

Conclusion: The physicians should be aware about the clinical presentations of Leptospira infections in endemic areas.

Key words: Leptospirosis, Leptospira, Outcome

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Introduction

Leptospirosis is a widespread and prevalent zoonotic disease, caused by pathogenic spirochetes of the genus *Leptospira*. It is common in both temperate and tropical areas (1). Common cause of human infection is direct or indirect exposure to urine from infected reservoir host animals that carry the pathogen in their renal tubules and shed pathogenic *Leptospira* which contaminate soils, streams, surface waters, and rivers (2). Humans may be infected by mucous membranes, abrasions on the skin (1). The various fauna of the East Kazakhstan is the favorable environmental source infection agents of natural focal infections, including Leptospirosis. Incidence of these diseases among the population is caused by epizooty among rodents (3). According to the monitoring of Leptospirosis increasing of its incidence is often observed in the winter and in the spring due to rise of biological activity of rodents. On average in the East Kazakhstan region 12 - 20 people annually get sick (3). In the Semey region for the last 15 years *Leptospira* infection in humans has not been registered. However, one case was appeared in Semey in 2012. In here we have presented the case with complicated of organ failure and fatal outcome.

Case Report

A 22 years old soldier was admitted to the Infectious Diseases clinic with the complains of fever (39^oC), headache, dizziness, sore throat, weakness, eruption all over the body, and pain in calf muscles of legs for six days. The patient had been hospitalized 3 days ago in the military hospital and initiated a combination of antibiotic therapy (with Ceftriaxone 2x2 g intravenously in a day and oral Amoxicillin-clavulanate 3x1 g in a day) by the diagnosis of community-acquired pneumonia and cholecystitis. On the chest X-ray pulmonary picture was strengthened on all fields, roots of lungs were expanded, deformed, heavy mainly on the right and sinuses were free on the admission. The patient was referred to our clinic because of a decrease in urine output and inadequate response to antibiotic treatment. He had a history of

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viral hepatitis three years ago. Before the beginning of his complaints, he was stayed in a village 40 km from the city for 15 days. He gave a history of a tick removal from his head 3 days before the beginning of complaints.

On the admission, the patient's vital signs were normal. An extended polymorphic rash on all the body was observed. A congestion and redness were present in the sclera. In the field of pillar part of the head primary affect as infiltrate was seen. The muscles of body were morbid in palpation. The pharynx was hyperemic. Hepatomegaly was observed with the abdominal palpation. Laboratory examination revealed leukocytosis and impaired liver and kidney function tests (Table 1). The urinalysis revealed proteinuria and pyuria; no bilirubinuria, and hematuria. An acute onset of symptoms, toxemia, myalgia, polymorphic exanthema with hemorrhagic component, dysfunctions in liver, kidneys and central nervous system (CNS) were supported a clinical diagnosis of leptospirosis with icteric and severe form. Antibiotic therapy with Penicillin G 2-million-unit x 6 times a day intravenously and gentamicin 0,08 g x 3 times a day intramuscularly were started.

On the second day of treatment, agitation, visual hallucinations, jaundice and hepatomegaly increased, and urine output decreased. On the same day, the patient had sudden onset hematemesis. The patient was transported to the intensive care unit on the third day of treatment. The diagnosis of leptospirosis was confirmed by passive hemagglutination test (The titer was 1/160). *Leptospira* was also seen in peripheral blood smear. An analysis of cerebrospinal fluid (CSF) showed that: color - yellow, transparency - unclear, cytosis – 23, from them neutrophil - 4, lymphocytes - 19, protein - 0,33 g/l, glucose - 3,5 mmol/l. Microscopic examination and culture of CSF were negative. Daily fluid electrolyte and blood product follow-up was performed with the diagnosis of disseminated intravascular coagulation and hepatorenal insufficiency. On the fifth day of treatment bleeding continued and hemodialysis was carried out. Patient died on 6th day of treatment, despite of intensive therapy.

Discussion

Leptospirosis is a zoonoses diseases shows a wide variety of clinical manifestations. The incidence in the tropics is nearly 10 times higher than in temperate regions (4). Human

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infection occurs after the exposure to environmental sources, such as animal urine, contaminated water or soil, or infected animal tissue. Risk factors for infection include occupational exposure (farmers, rice farmers, veterinarians, abattoir workers, ranchers, trappers, loggers, sewer workers, pet traders, military personnel, and laboratory workers), household exposure, outdoor activities, and laboratory accidents (5). The patient had also a history of being in endemic area and tick attachment. He was also in military service training in the field.

Conjunctival erythema is an important and frequent sign of the infection. Hemorrhagic diathesis is also common finding due to the thrombocytopenia (6). In a six-year, case series of 182 patients, conjunctival suffusion had been observed in 55% of patients (7). The presented patient had the history of acalculous cholecystitis by abdominal ultrasonography in the military hospital. Acalculous cholecystitis is an under recognized presentation of acute Leptospirosis. In the literature, many cases had experienced cholecystectomy with antibiotic treatment in the therapy (8).

There was lymphocytic pleocytosis in the CSF examination of the patient Aseptic meningitis is observed in 50 to 85 percent of patients if CSF) is examined after seven days of illness. Generally, this finding has been associated to a host immune response to the organism rather than to direct infection (6); however, Romero *et al.* (9) have reported a 59% polymerase chain reaction positivity in the CSF examination of 39 leptospirosis patients with meningeal signs.

In hospitalized patients, mortality rates range from 4 to 52 percent (6). In one retrospective review of 282 cases reported the significant predictors of death in included central nervous system and pulmonary involvement (10). In another review of 35 studies, high case-fatality rates were associated with jaundice, renal failure, and age >60 years (11). This patient had a poor prognosis criterion included severe presentation of infection, jaundice, renal failure, and central involvement. The outcome of the patient was resulted in death despite adequate antibiotic treatment and intensive care support.

Conclusions

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The clinical presentation of *Leptospira* infection varies from asymptomatic through the severe and fatal form as seen in this case. The physicians should be aware about the clinical presentations of *Leptospira* infections in endemic areas.

Ethic Issue

A written consent was taken from the patient's mother.

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Table 1. A summary of the laboratory test results of the case according to hospital days.

Laboratory test	Hospital days						
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
WBC (X10 ⁹ /L)	4,2		11900	11900	16900		14200
Haemoglobin(g/dL)	15		12.2	11.9	8.1		7
Trombocytes(X10 ⁹ /L)	250			12	10		100
ESR (mm/h)	18		2	5	34		35
ALT (mmol/l)		1.64	1.08	0.61	0.168		
AST(mmol/l)		1,4		0.63			
Tbil(mcmol/l)		97.2	124	57	45		27
D bil(mcmol/l)		54	82	36			19
Protein (g/l)		64	55	54	67		61
BUN (mmol/l)		16.5	27.7	25	37.8		36
Creatinine (mcmol/l)		13.6	5.6	5.1	6.4		6,2
TT (30-40 sec)						54	300
APTT (30-40 sec)				55	39.3	43.9	62,8
INR (1.1)		2.2	1.26	1.12		1.59	
Fibrinojen (g/l)				1.93	2.66	2.18	

Abbreviations: WBC. White blood cell count, ESR. Erythrocyte sedimentation rate, Tbil: Total bilirubin, Dbil: Direct bilirubin, TT. Tromboplastin time, APTT. _Activated Partial Thromboplastin Time

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