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# Leptospirosis: twelve Turkish patients with the Weil syndrome\*

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## Abstract

Twelve cases of leptospirosis followed by the Infectious Diseases Clinic of the Cukurova University Medical School, Adana, Turkey, between January 1994 and November 1995 are reported. Included are their clinical manifestation, laboratory findings and serotype. Nine men and three women with an average age of 40.4 years were studied. Symptoms, clinical manifestations, laboratory findings and treatment of the disease are evaluated. All of the patients had fever and chills and the following symptoms: nausea and vomiting (91.6%), lower back pain and myalgia (58.3%), headache (50%), epistaxis (16.6%) and confusion (25%). The predominant clinical findings were jaundice (91.6%), hepatomegaly (41.6%), dyspnea (25%), conjunctival suffusion (33%), and nuchal rigidity (33%). Diagnosis was based on dark-field examination of the blood, cerebrospinal fluid and urine specimens. Also, microscopic agglutination tests (MAT) were carried out for serodiagnosis. MAT showed *L. interrogans* serovar icterohaemorrhagiae in 11 cases and *L. interrogans* serovar gripposocova in one case. There was cross reaction with *L. biflexa* patoc in all cases. Agglutinations were tested in the same specimens twice and confirmed in the Microbiology Laboratory of the Etlik Veterinary Research Institute in Ankara. All cases were treated with penicillin and doxycycline. In the end; 83.3% of the patients were cured and 16.6% died due to hepatorenal failure.

**KEYWORDS:** leptospirosis, Weil syndrome

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## Brief Note

### Leptospirosis: Twelve Turkish Patients with the Weil Syndrome

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Twelve cases of leptospirosis followed by the Infectious Diseases Clinic of the Çukurova University Medical School, Adana, Turkey, between January 1994 and November 1995 are reported. Included are their clinical manifestation, laboratory findings and serotype. Nine men and three women with an average age of 40.4 years were studied. Symptoms, clinical manifestations, laboratory findings and treatment of the disease are evaluated. All of the patients had fever and chills and the following symptoms: nausea and vomiting (91.6%), lower back pain and myalgia (58.3%), headache (50%), epistaxis (16.6%) and confusion (25%). The predominant clinical findings were jaundice (91.6%), hepatomegaly (41.6%), dyspnea (25%), conjunctival suffusion (33%), and nuchal rigidity (33%). Diagnosis was based on dark-field examination of the blood, cerebrospinal fluid and urine specimens. Also, microscopic agglutination tests (MAT) were carried out for serodiagnosis. MAT showed *L. interrogans* serovar *icterohaemorrhagiae* in 11 cases and *L. interrogans* serovar *gripposocova* in one case. There was cross reaction with *L. biflexa patoc* in all cases. Agglutinations were tested in the same specimens twice and confirmed in the Microbiology Laboratory of the Etlik Veterinary Research Institute in Ankara. All cases were treated with penicillin and doxycycline. In the end; 83.3% of the patients were cured and 16.6% died due to hepatorenal failure.

**Key words:** leptospirosis, Weil syndrome

**L**eptospirosis is an infectious disease caused by one of the spirochetes of the genus *leptospira* and characterized by generalized vasculitis. It is primarily an enzootic disease but human infections can occur by direct contact with an infected animal's urine or stool or indirectly by contact with contaminated water or soil (1-5).

Today, more than 240 serovars or serotypes have been established and the most widely recognized serotypes are *L. canicola*, *L. icterohaemorrhagiae*, *L. pomona*, *L. autumnalis* and *L. grippityphosa* (6, 7). The disease occurs with two distinct clinical manifestations that are icteric and anicteric in nature (1, 8). The icteric form is also known as Weil syndrome and accounts for up to 5-10% of the cases with a serious clinical course (2). It is mainly characterized by impairment of renal and hepatic function, hemorrhage and vascular collapse (9). Leptospirosis should be considered in cases of fever, icterus, chills, serious headache, myalgia and animal contact history. Aseptic meningitidis should also be investigated as part of a differential diagnosis of leptospirosis (1, 6, 8).

Twelve patients with leptospirosis are evaluated in this study. We present their clinical manifestations, diagnostic parameters and serotypes.

#### Patients and Methods

In this study, 12 leptospirosis cases are reported. The patients were admitted to the Infectious Diseases Clinic of the Çukurova University Medical School in Adana, Turkey between January 1994 and November 1995. The following methods were used in addition to

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clinical and laboratory evaluation as a means of diagnosis. The first method was dark-field examination; leptospiras were found in the blood, urine and cerebrospinal fluid of patients. The second method was a microagglutination test (MAT). MAT was performed in the Microbiology Department. The serotypes which were used as antigens in MAT were kindly supplied by the Etlik Veterinary Research Institute in Ankara. Results of MAT were confirmed in the Microbiology Laboratory of the Etlik Veterinary Research Institute. Serum specimens were tested for antibody reactions against *L. icterohaemorrhagiae*, *L. gripposocova*, *L. hardjo*, *L. icterobianchi*, *L. copenhageni*, *L. heptosejroetopa* and *L. biflexa patoc*. MAT titers of > 1:100 were accepted as a positive result.

## Results and Discussion

Patients included 9 men and 3 women aged between 17 and 65 years (average 40.4 years). Five of the patients were farmers, one was a construction laborer, one was a motorcycle mechanic and these patients might be contaminated with water or soil (1-5, 9, 10). All of the patients had fever and chills, eleven had nausea and vomiting, seven complained of back pain and myalgia, six suffered from headache, one had diarrhea and two had epistaxis. In physical examinations, eleven patients had jaundice, five had hepatomegaly, four had splenomegaly, nuchal rigidity and conjunctival suffusion and three had rash and lymphadenopathy, confusion and dyspnea (Table 1). In laboratory results, all cases had leucocytosis and elevation of ESR, bilirubin, blood urea nitrogen (BUN), aspartate aminotransferase (AST) and alanin aminotransferase (ALT) and lactic dehydrogenase (LDH). Trombocytopenia and elevated serum creatinin phosphokinase (CPK) levels were found in six patients. Six patients had hematuria and seven patients had proteinuria (Table 2). In dark-field examinations, leptospira was seen in all cases in the blood and in the cerebrospinal fluid in four cases. Leptospira was also seen in the urine in 8 cases (Table 3).

Leptospirosis is a spirocetal antropozoonosis which produces a wide spectrum of clinical manifestations in humans. Methods of diagnosing of leptospirosis are not accurate and practical in clinical situations (1, 4, 8). Diagnosis should be done by either isolation of the microorganism from the clinical material or by an antibody titer following the determination that telltale clinical manifestations are present (8, 11). An MAT using live

**Table 1** Symptoms and clinical findings in 12 patients with leptospirosis

Symptoms	Frequency No (%)	Clinical findings	Frequency No (%)
Fever	12 (100)	Jaundice	11 (91.6)
Chills	12 (100)	Hepatomegaly	5 (41.6)
Headache	6 (50)	Splenomegaly	4 (33.3)
Myalgia	7 (58.3)	Rash	3 (25)
Nausea/ Vomiting	11 (91.6)	Conjunctival Suffusion	4 (33.3)
Epistaxis	2 (16.6)	Nuchal rigidity	4 (33.3)
Confusion	3 (25)	Dyspnea	3 (25)
Diarrhea	1 (8.3)	Lymphadenopathy	3 (25)

**Table 2** Laboratory findings in 12 patients with leptospirosis

Parameters	Frequency No (%)
WBC > 10,000/mm <sup>3</sup>	12 (100)
ESR > 10h	12 (100)
ALT > 40 u/L	12 (100)
AST > 40 u/L	12 (100)
Creatinin > 1.6 mg/dL	10 (83)
BUN > 25 mg/dl	12 (100)
Platelets < 50000/mm <sup>3</sup>	6 (50)
Bilirubin > 1.4 mg/dl	12 (100)
LDH > 450 u/L	12 (100)
CPK > 195 u/L	6 (50)
Hematuria	6 (50)
Proteinuria > 30 mg/dl	7 (58.3)

ALT: Alanin aminotransferase.

AST: Aspartate aminotransferase.

BUN: Blood urea nitrogen.

LDH: Lactate dehydrogenase.

CPK: Creatinin phosphokinase.

leptospira organisms should be considered positive when it is greater than 1:100 (6). *L. interrogans serovar icterohaemorrhagiae* was found to be dominant in 11 cases, and in one case *L. interrogans serovar gripposocova* was found to be dominant by MAT. There was cross reaction with *L. biflexa patoc* assays in all cases (Table 3).

Clinical manifestations and symptoms may not lead to a correct diagnosis of leptospirosis since there are variable and nonspecific findings. Fever, jaundice, myalgias and conjunctival suffusion are the most prominent findings in the clinical picture of leptospirosis. In this study, we observed the findings similar to those mentioned in other

**Table 3** Results of dark-field microscopy and microagglutination test (MAT)

Pt no/Sex	Age	Blood	Urine	CSF	Serotype	MAT (1 st)	MAT (2nd)
						Specimen	Specimen
1/M	17	+	- / +	+	<i>L. icterohaemorrhagiae</i>	400	800
2/M	39	+	+ / +		<i>L. gripposcovae</i>	200	400
3/M	51	+	- / +		<i>L. icterohaemorrhagiae</i>	400	800
4/M	46	+			<i>L. icterohaemorrhagiae</i>	3200	—
5/M	24	+	-	-	<i>L. icterohaemorrhagiae</i>	800	1600
6/F	66	+	- / +		<i>L. icterohaemorrhagiae</i>	100	400
7/M	26	+	- / +		<i>L. icterohaemorrhagiae</i>	100	200
8/M	26	+	+	+	<i>L. icterohaemorrhagiae</i>	100	200
9/F	45	+	+	+	<i>L. icterohaemorrhagiae</i>	100	200
10/M	66	+	-		<i>L. icterohaemorrhagiae</i>	100	400
11/F	63	+	-		<i>L. icterohaemorrhagiae</i>	400	800
12/M	17	+	+ / +		<i>L. icterohaemorrhagiae</i>	200	400

Pt: Patient; CSF: Cerebrospinal fluid.

studies (4, 9, 12). Diagnosis is usually accomplished by dark-field microscopic examination. Additionally, there are few cases of human leptospirosis reported in our country. Tuncel and Ögütman reported that leptospirosis is prevalent in people who have direct contact with meat and meat products in 1972 (13). Vardar isolated *L. interrogans serovar grippotyphosa* from the blood of domestic animals in the Çukurova region of Turkey (14). An antibody response to *L. grippotyphosa* in 11 % of the human population was detected in the same study. In a study of animals in the Çukurova region of Turkey, Walter E. *et al.* found that 61 % of them possessed antibodies against *L. hebdomadis* and 26 % of them possessed antibodies against *L. grippotyphosa* (15). Fazli SA collected 1,405 human serum specimens from the central and southeastern Anatolian region of Turkey in another study (16). In his study, he found antibody responses to *L. butembo* in 18 cases (42.9 %), to *L. icterohaemorrhagiae* in 16 cases (38 %) and to *L. grippotyphosa* in 8 cases (19 %) (16). He also reported that all of the positive cases (100 %) exhibited a cross reaction with *L. biflexa patoc* (17). MAT results showed that *L. interrogans serovar icterohaemorrhagiae* is the dominant strain as a pathogen in our study *versus L. interrogans serovar grippotyphosa* as described in the above studies.

Antibiotic therapy is the best way to treat leptospirosis. The antibiotics of choice are penicillin, ampicillin, amoxicillin and doxycycline (1, 12, 18). The antibiotic treatment should be started in the first four days after infection. Early therapy may prevent seroconversion and

may preclude serologic diagnosis (7). Doxycycline is most effective in patients with leptospirosis and it may prevent renal complications (8, 12, 19). A careful clinical observation and general supportive treatment in serious cases of leptospirosis are important for the prevention of fatal complications such as renal failure, hypotension and hemorrhage. Hemodialysis should be performed when necessary (7). For instance, one of our patients with serious renal failure and bilirubinemia had hemodialysis treatment.

Severe leptospirosis (Weil Syndrome) is a serious and life-threatening disease. People who live in subtropical area (like Çukurova, Turkey) and work in farming are particularly at risk. Patients who show fever, jaundice, myalgia, vomiting and conjunctivitis should be differentially diagnosed for leptospirosis. If untreated they are at risk of prolonged, serious renal failure which may lead to death. Differential diagnosis of leptospirosis has a prognostic value since the mortality rate of the disease is very high.

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