

Report of Three Children with Leptospirosis in Rural Area of the East of Turkey

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Department of Microbiology, ¹Department of Pediatrics, Yuzuncu Yil University School of Medicine, Van, Turkey, ²Van Health Services Vocational College, Yuzuncu Yil University, Van, Turkey

KURTOĞLU, M.G., TUNCER, O., BOZKURT, H., ÇAKSEN, H., BERKTAŞ, M., CEYLAN, E. and KIRIMI, E. *Report of Three Children with Leptospirosis in Rural Area of the East of Turkey.* Tohoku J. Exp. Med., 2003, **201** (1), 55–60 — Leptospirosis is a systemic infection usually producing fever with hepatorenal involvement, meningoencephalitis, and hemorrhage. In this article, we present three children between 10 and 13 years of age with leptospirosis. The purpose of this paper is to emphasize that leptospirosis is a problem in our country with farmers/cattle and that leptospirosis should be considered in certain ill children. The main symptoms were headache, fever, fatigue, abdominal pain and unconsciousness. Two patients had hepatic and renal involvement. The other had hepatic, pulmonary and probably pericardial involvement. In all children spirochetes were demonstrated in blood and urine smears by dark-field microscopy and they were also isolated from urine and blood cultures by using Flecher medium. All patients were treated with penicillin; however, one subsequently required additional antibiotics due to *Klebsiella pneumoniae* septicemia. While one patient was discharged in a good health, the others were taken to their home by parents without completing treatment. In conclusion, we would like to emphasize that leptospirosis is still a public health problem in our region (Eastern Turkey) in where the majority of population are farmers and raise domestic animals such as cattle in rural areas. Additionally, leptospirosis should be considered in children admitted with headache, unconsciousness, fever and abdominal pain. ——— leptospirosis; child; spleen; abscess; brain; Turkey

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Leptospirosis, an ubiquitous zoonotic disease, is a systemic infection usually producing fever with hepatorenal involvement, meningoencephalitis, and hemorrhage (Courtin et al. 1998). According to a 1997 epidemiological review, the incidence of leptospirosis was 90/100 000 person-years with a mortality rate of 4% patients. Those affected (100 males, 44 females) were mainly aged 20 to 40 years. Incidence in rural areas (112 per 100 000 person-years) was seven times higher than in urban settlements (Perrocheau and Perolat 1997). There is not any information about its incidence and mortality rate in Turkey. However, local studies carried out in Turkey shown that the disease is most common in male farmers from rural areas, and it is present in cattle and human beings (Leblebicioğlu et al. 1996; Özdemir and Erol 2002). In this article we report three children with leptospirosis due to unusual presentation. There was a positive history of exposure to livestock in all children. Our purpose of this paper is also to emphasize that leptospirosis is a problem in our country with farmers/cattle and that leptospirosis should be considered in certain ill children.

MATERIALS AND METHODS

Case reports

Case 1. A 13-year-old girl was admitted with a seven-day history of headache and irritability, and three-day history of unconsciousness. The personal and family history was unremarkable.

Physical examination revealed fever was 36.9°C, pulse rate 80/minutes, respiratory rate 24/min and arterial tension 90/60 mmHg. The weight and height were within normal ranges. Her general condition was bad. She was stuporous and could response only pain stimuli. Skin turgour was decreased. Examination of cranial nerves was normal. Thorax and abdominal examination were also normal.

On admission urinary analysis revealed pH was 8; density 1025; 3+ protein, glucose

trace; nitrogen positive; ketone negative; bilirubin positive; and five leukocytes and abundant erythrocytes were recorded on urinary sediment examination. Urinary protein level was 4.9 g/m²/day. Urine and serum osmolality were 750 mOsm/kg and 405 mOsm/kg. Routine blood analysis revealed: hemoglobin of 11.5 g/100 ml, leukocyte count of 24 700/mm³, platelet count of 55 000/mm³, and erythrocyte sedimentation rate of 25 mm/hours. On peripheral blood smear polymorphonuclear leukocytes were predominant, the morphological characteristics of red blood cells were normochromia and normocytosis. Serum electrolytes, renal and liver function tests were as follows; blood glucose level was 223 mg/100 ml; serum sodium level 189 mEq/liter; potassium 5.6 mEq/liter; chloride 121 mEq/liter; blood urea nitrogen (BUN) 127 mg/100 ml; creatinine 6.7 mg/100 ml; calcium 7.9 mg/100 ml; phosphorus 7.4 mg/100 ml; uric acid 19.5 mg/100 ml; total bilirubin 1.2 mg/100 ml; aspartate aminotransferase (AST) 366 U/liter; alanine aminotransferase (ALT) 126 U/liter; lactate dehydrogenase (LDH) 4020 U/liter; and creatine kinase (CK) 9560 U/liter. Prothrombin (PT) and partial thromboplastin time (PTT) were 18.7 and 28.9 seconds, respectively. Hepatitis markers were unremarkable. Cerebrospinal fluid examination was normal. Spi-

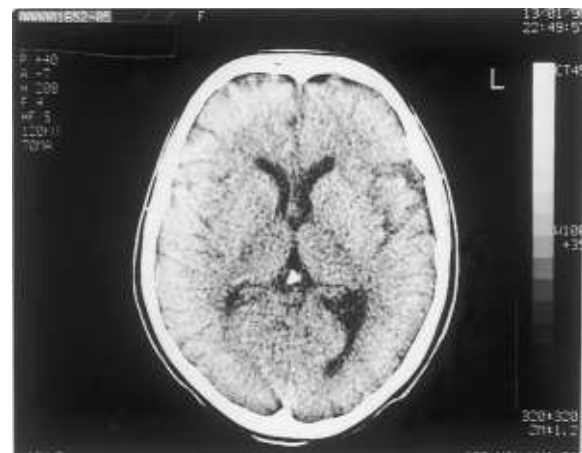


Fig. 1. Cranial CT appears an ischemic area on the left parietal lobe, which is 3×4 cm a diameter.

rochetes were demonstrated in blood and urine smears by dark-field microscopy. By using Flecher medium spirochetes were isolated from urine and blood cultures. Thorax radiography was normal. Abdominal ultrasonography was normal. Cranial computed tomography (CT) revealed an ischemic area on the left parietal lobe, which is 3×4 cm a diameter (Fig. 1).

The patient was hospitalized in order to investigate the etiology of unconsciousness. On the basis of clinical and laboratory findings leptospirosis was diagnosed during her follow-up and penicillin G (6 million U/m²/day six times a day) was given for 10 days. Peritoneal dialysis was also performed for three days because of acute renal failure. On the 3rd day of admission, liver function tests were markedly impaired. On the 6th day of admission severe melena was noted and a packed of blood transfusion was given. On the 11th day of admission, she was taken to home by parents without improvement. During discharge, the liver and renal function tests were markedly abnormal (AST 1750 U/liter; ALT 609 U/liter; BUN 247 mg/100 ml; creatinine 16 mg/100 ml; CK 9560 U/liter; LDH 436 U/liter). Unfortunately, she was not admitted to control examination. And we did not receive any information about her prognosis.

Case 2. A previously healthy 10-year-old boy was admitted with a 10-day history of headache, fever, abdominal pain and fatigue, and six-day history of speech disorder and confusion. The personal and family history was unremarkable.

Physical examination revealed fever was 37°C, pulse rate 140/minutes, respiratory rate 36/min and arterial tension 80/40 mmHg. The weight and height were 17 kg (<3rd percentile) and 120 cm (<3rd percentile) respectively. His general condition was bad. He was stuporous and could response only pain stimuli. Examination of cranial nerves was normal. Thorax examination revealed bilateral inspiratory rales. He had 5 cm hepatomegaly and 3 cm

splenomegaly. The remainder of the physical findings was normal.

On admission urinary analysis revealed pH was 5.5; density 1010; four erythrocytes, abundant leukocytes and bacteria were recorded on urinary sediment examination. Routine blood analysis disclosed; hemoglobin was 10.8 g/100 ml, leukocyte count 2200/mm³, platelet count 75 000/mm³, erythrocyte sedimentation rate 4 mm/hours. Bone marrow examination was normal. Serum electrolytes, renal and liver function tests were as follows; blood glucose level was 83 mg/100 ml; serum sodium level 120 mEq/liter; potassium 2.9 mEq/liter; chloride 88 mEq/liter; BUN 25 mg/100 ml; creatinine 0.7 mg/100ml; calcium 10.9 mg/100 ml; phosphorus 2.3 mg/100 ml; uric acid 4.3 mg/100 ml; total protein 5.5 g/100 ml; albumin 2.7 g/100 ml; total bilirubin 1.3 mg/100 ml; direct bilirubin 0.6 mg/100 ml; AST 344 U/liter; ALT 313 U/liter; LDH 3440 U/liter; and CK 1180 U/liter. Serum amylase level was normal. PT and PTT were 17 and 38 seconds respectively. Hepatitis markers, salmonella and brucella agglutination tests were unremarkable. Cerebrospinal fluid examination was normal. Spirochetes were demonstrated in blood and urine smears revealed by dark-field microscopy. Additionally, spirochetes were isolated from urine and blood cultures by using Flecher medium. Thorax radiography showed perihiler pneumonic infiltration. Echocardiographic examination revealed mild pericardial effusion. Cranial CT was normal.

The patient was hospitalized with the diagnosis of pneumonia and probably leptospirosis. Aside from supportive therapy, penicillin G (300 000 U/kg/day) and chloramphenicol (100 mg/kg/day) were initiated. On the 3rd day of admission, liver function tests were markedly impaired (AST 1250 U/liter; ALT 241 U/liter) and his consciousness was completely decreased and became unresponsive to pain stimuli. On the 3rd day of admission, based on clinical and laboratory findings he was diagnosed with he-

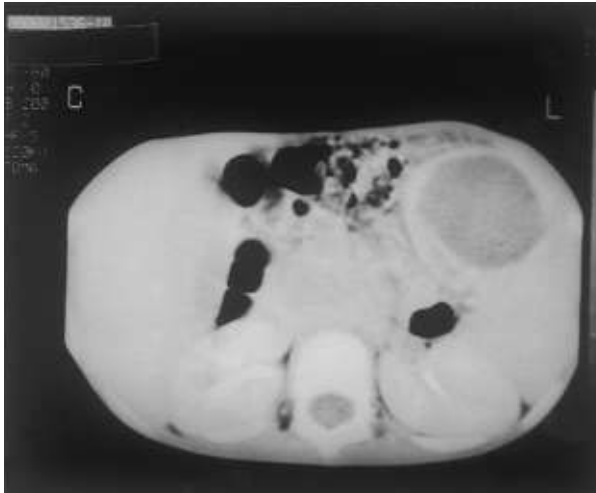


Fig. 2. Abdominal CT showing splenic abscess, which is 6×4 cm a diameter.

patic coma and L-dopa, lactulose, and metronidazole were initiated. On the 6th day of admission his comatous condition was improved. On the 16th day of admission, *Klebsiella pneumoniae* was isolated from urine culture and antibiotics were changed according to the antibiogram results. *Klebsiella pneumoniae* was also isolated from bone marrow culture. On the 18th day of admission, liver function tests were completely improved. On the 19th day of admission, simple partial convulsions on the left upper and lower extremities were noted; therefore, phenobarbital was given. On the 24th day of admission multiple cutaneous abscesses were detected on dorsal face of the right hand and left foot.

Later, they were improved with antibiotherapy. On the 46th day of admission abdominal ultrasonography was performed because of persistent high fever and splenic abscess, which is 6×4 cm a diameter, was diagnosed. An abdominal CT was also confirmed it (Fig. 2). He was referred to the Department of Pediatric Surgery to splenectomy on the 53rd day of admission, but the parents did not permit to surgical intervention and he was taken to home. Later, we could not obtain any information about the patient's condition.

Case 3. A previously healthy 11-year-old boy was admitted with a seven-day history of fever, diarrhea, vomiting, fatigue, headache and two-day history of confusion and lethargy. The personal and family history was unremarkable.

Physical examination revealed; fever was 37°C, pulse rate 88/minutes, respiratory rate 22/minutes and systolic arterial tension 60 mmHg. The weight and height were 32 kg (10–25th percentile) and 138 cm (25–50th percentile), respectively. He was lethargic. Generalized maculopapular rash was noted on the face, neck and thorax region. Generalized abdominal pain and joint pain, particularly during movement were diagnosed, but he had no organomegaly. Meningeal irritation signs were positive. The remainder of the physical findings was normal.

On admission urinary analysis revealed pH was 5; density 1018; protein (+), ketone trace; abundant erythrocytes and leukocytes were recorded on urinary sediment examination. Urinary protein level was 4.9 g/m²/day. Routine blood analysis disclosed; hemoglobin 10.9 g/100 ml, leukocyte counts 24 200/mm³, platelet counts 208 000/mm³, erythrocyte sedimentation rate 17 mm/hours. On peripheral blood smear polymorphonuclear leukocytes were predominant. Serum electrolytes, renal and liver function tests were as follows; blood glucose level was 90 mg/100 ml; serum sodium level 136 mEq/liter; potassium 3.4 mEq/liter; chloride 108 mEq/liter; BUN 57 mg/100 ml; creatinine 3.6 mg/100 ml; calcium 8.1 mg/100 ml; phosphorus 5.5 mg/100 ml; uric acid 15.3 mg/100 ml; total protein 4.3 g/100 ml; albumin 2.2 g/100 ml; total bilirubin 0.13 mg/100 ml; direct bilirubin 0.03 mg/100 ml; AST 74 U/liter; ALT 52 U/liter; alkaline phosphatase 86 U/liter; LDH 302 U/liter; and CK 180 U/liter. Serum amylase level was normal. PT and PTT were 29 and 45 seconds respectively. Hepatitis markers, salmonella and brucella agglutination tests were unremarkable. Cerebrospinal fluid examina-

tion was normal. Spirochetes were demonstrated in blood and urine smears by dark-field microscopy. By using Flecher medium spirochetes were isolated from urine and blood cultures. Thorax radiography was normal. Abdominal ultrasonography revealed Grade-I renal parenchymal disorder and mild intraabdominal free fluid. Electroencephalography and cranial computed tomography were normal.

The patient was hospitalized with the diagnosis of leptospirosis. Aside from supportive therapy penicillin G (8 million U/m²/day six times a day) was given for 10 days. On the 5th hospital day her general condition became good and his consciousness became normal. Liver and renal function tests became to normal ranges on the 7th day of admission. He was discharged from hospital in a good health on the 10th day of admission. On the 2nd week of follow-up he was symptom-free, and physical examination was completely normal.

DISCUSSION

The clinical expression of leptospirosis is polymorphic with a previous study indicating that 60% of the patients present with mild symptoms and 40% present with acute forms such as Weil's disease (icteric leptospirosis) (Perrocheau and Perlot 1997). Singh et al. (1999) reported that the disease presented as two separate clinical dysfunctions-the hepatorenal form and the pulmonary form though some degree of overlap was present. Hepatorenal form occurred late in the course of the disease and the mortality rate was relatively low. In contrast pulmonary complication occurred quite early and the case fatality rate in those patients was very high (6.7% vs. 42.9%) (Singh et al. 1999). Additionally, they noted refractory hypotension probably due to myocarditis, neck stiffness and altered sensorium due to central nervous system involvement in some patients in their series (Singh et al. 1999).

In clinical practice visceral organ involvement has been reported in various frequencies in

different series. In the study of Perrocheau and Perlot (1997) main clinical dysfunctions were icterus and/or renal dysfunction in 50% of patients, cardiac dysfunction in 65%, acute myalgias in 58% and pulmonary dysfunction in 50%. Although hemorrhages were uncommon (17%), 40% of the cases demonstrated thrombocytopenia ($<50\,000/\text{mm}^3$). Pancreatic involvement with hyperamylasemia was evidenced in 50% of cases (Perrocheau and Perlot 1997). In the series of Saltöu et al. (1997), which includes 12 patients, 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%) (Ragnaud et al. 1994). Leblebiciöu et al. (1996) reported that myalgia and jaundice were recorded in all 12 patients. Signs included vomiting in 9 patients, hemorrhages in 6, and renal function was impaired in 6 (Leblebiciöu et al. 1996). In a series of 79 cases hepatonephritic forms were the most common (29.1%), followed by febrile or flu-like symptoms (25.3%), hepatitis (20.2%), nephritis (17.8%), and meningitis (7.6%) (Suter et al. 1983). Courtin et al. (1998) noted that of 154 cases of leptospirosis, 91 (59.1%) cases had pulmonary involvement and mortality due to leptospirosis was two-fold higher in cases with pulmonary involvement. (Courtin et al. 1998). In 30 cases of leptospirosis, jaundice (70%), acute renal failure (67%), meningitis (50%) and hemorrhagic signs (50%) were among the major visceral manifestations (Ragnaud et al. 1994).

In our case series, two patients (case 1 and case 2) had icterus and they were accepted as Weil's disease. Case 1 and 3 had hepatic and renal involvement. Case 2 had hepatic, pulmonary and probably pericardial involvement. Serum amylase levels were studied in case 2 and 3 and they were within normal ranges. These findings were consistent with literature data.

Additionally case 1 had ischemic area on the brain, which was probably due to leptospiral arteritis. Because it is well known that leptospire may cause arteritis and then ischemic stroke (Cheng 1982).

Penicillin is the first choice in the treatment of leptospirosis and patients were treated with penicillin in the most studies. Nonetheless, doxycycline or ampicillin has also been used successfully (Suter et al. 1983; Ragnaud et al. 1994; Leblebiciöü et al. 1996; Saltöü et al. 1997). In our series, all patients were given penicillin. The patient in case 2 required additional antibiotics due to *Klebsiella pneumoniae* septicemia.

Mortality rate was noted between 7% and 24% in various series (Everard 1984; Ragnaud et al. 1994; Leblebiciöü et al. 1996; Saltöü et al. 1997; Singh et al. 1999). In our study, only case 3 was discharged from hospital in a good health. The other two patients were taken to their home by parents without completing treatment.

Prevention of human leptospirosis is possible by instituting rodent control measures and avoiding contaminated water and soil. Immunization of livestock, family pets and human has been recommended as a means of eliminating animal reservoirs (Behrman et al. 2000).

We would like to emphasize that leptospirosis is still a public health problem in our country, particularly in our region (Eastern Turkey) in where the majority of population are farmers and raise domestic animals such as cattle. Additionally, we think that leptospirosis should also be considered in children admitted with headache, unconsciousness, fever and abdominal pain.

References

- Cheng, M.K. (1982) A review of cerebrovascular surgery in the People's Republic of China. *Stroke*, **13**, 249-255.
- Courtin, J.P., Di Francia, M., Du Couedic, I., Poubeau, P., Mahe, C., Baptiste, J. & Arvin-Berod, C. (1998) Respiratory manifestations of leptospirosis. A retrospective study of 91 cases (1978-1984). *Rev. Pneumol. Clin.*, **54**, 382-392. (in French)
- Everard, C.O., Edwards, C.N., Webb, G.B., White, H.S. & Nicholson, G.D. (1984) The prevalence of severe leptospirosis among humans on Barbados. *Trans. R. Soc. Trop. Med. Hyg.*, **78**, 596-603.
- Leblebicioğlu, H., Şencan, I., Sünbül, M., Altıntop, L. & Günaydın, M. (1996) Weil's disease: report of 12 cases. *Scand. J. Infect. Dis.*, **28**, 637-639.
- Özdemir, V. & Erol, E. (2002) Leptospirosis in Turkey. *Vet. Rec.*, **150**, 248-249.
- Perrocheau, A. & Perolat, P. (1997) Epidemiology of leptospirosis in New Caledonia (South Pacific): a one-year survey. *Eur. J. Epidemiol.*, **13**, 161-167.
- Ragnaud, J.M., Morlat, P., Buisson, M., Longy-Boursier, M., Monlun, E., Wone, C., Lebras, M., Beylot, J. & Aubertin, J. (1994) Epidemiological, clinical, biological and developmental aspects of leptospirosis: apropos of 30 cases in Aquitaine. *Rev. Med. Intern.*, **15**, 452-459. (in French)
- Saltoğlu, N., Aksu, H.Z., Taova, Y., Arslan, A., Canataroğlu, A., Dödar, I.H. & Kösal, F. (1997) Leptospirosis: twelve Turkish patients with the Weil syndrome. *Acta Med. Okayama*, **51**, 339-342.
- Singh, S.S., Vijayachari, P., Sinha, A., Sugunan, A.P., Rasheed, M.A. & Sehgal, S.C. (1999) Clinico-epidemiological study of hospitalized cases of severe leptospirosis. *Ind. J. Med. Res.*, **109**, 94-99.
- Suter, F., Minoli, L., Parisi, A., Filice, C., Maserati, R. & Farina, C.F. (1983) Current clinical aspects of leptospirosis. *Minerva Med.*, **74**, 1179-1186. (in Italian).
- Behrman, R.E., Kliegman R.M. & Jenson, H.B. (2000) *Nelson Textbook of Pediatrics*, 16th ed. W.B. Saunders Co., Philadelphia, pp. 908-909.