Interdepartmental Conference

Leptospirosis 2001

Kajee Pilakasiri, Ph.D.*
Yupin Suputtamongkol, M.D.**
Winai Ratanasuwan, M.D.***

Abstract : **A 20-year-old man was admitted to Siriraj Hospital because of high fever and jaundice. He also had acute renal failure. According to the other clinical manifestations and laboratory investigations, the differential diagnosis included severe systemic infections, especially leptospirosis and scrub typhus. A definitive diagnosis was obtained by a positive microscopic agglutination test for *Leptospira interrogans*, serovar bratislava. Serological tests for scrub typhus and dengue infection were negative. The number of patients with leptospirosis has been increasing in many hospitals and outbreaks of the disease have been reported in northeastern Thailand since 1997. In October 1999, *Leptospira interrogans*, serovar pyrogenes was isolated from the blood of a febrile patient with clinical leptospirosis in Burirum province. This pathogen was used to study the progressive microanatomical changes within organs including the kidney, lungs, liver, gastrocnemius and hamstring muscles of infected hamsters. The kidney showed degenerative changes of the renal tubular cells and many pathological appearances of the glomerular tuft. Interstitial nephritis and pyelonephritis were also found. In the lungs, the alveolar and interalveolar capillaries were engorged with red blood cells. Both bronchopneumonitis and interstitial pneumonitis were observed. The liver showed cloudy swelling of hepatocytes which lead to dissociation of the hepatic cords. Vascular and sinusoidal congestion, prominent Kupffer cells and inflammatory cell infiltration in the parenchyma, and sinusoids as well as the portal area were demonstrated. Hepatocellular necrosis was found scattered throughout the hepatic lobules. Some hamsters showed blood vessel congestion in the gastrocnemius and hamstring muscles. Inflammatory cell infiltration was shown in the perimysium of the gastrocnemius muscle of one hamster. Another showed necrosis of some muscle fibers together with inflammatory cell infiltration which are signs of muscular inflammation. The prevention and control of Leptospirosis is also discussed.**

เรื่องย่อ : เลปโตสไปโรซิส 2001

ขจี ปิลกศิริ ปร.ด.*, ยุพิน ศุพุทธมงคล พ.บ.**, วินัย รัตนสุวรรณ พ.บ.***
*ภาควิชากายวิภาคศาสตร์, **ภาควิชาอายุรศาสตร์, ***ภาควิชาเวชศาสตร์ป้องกันและสังคม, คณะแพทยศาสตร์ศิริราชพยาบาล, มหาวิทยาลัยมหิดล, กรุงเทพมหานคร 10700.*

สารศิริราช 2544; 53: 811-815.

**Department of Anatomy, **Division of Infectious Diseases and Tropical Medicine, Department of Medicine, ***Department of Preventive and Social Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700.*
From Interdepartmental Conference, June 22, 2001.

ชายอายุ 20 ปี เข้ารักษาที่โรงพยาบาลศิริราชเนื่องจากมีอาการไข้สูง ดีซ่าน และมีอาการไตวายเฉียบพลัน จากลักษณะอาการแสดงทางคลินิกและการตรวจทางห้องปฏิบัติการ ได้รับการวินิจฉัยว่าเป็นโรคติดเชื้อที่รุนแรง ซึ่งน่าจะเป็น เลปโตสไปโรซิสและสครับไทฟัส จากการวินิจฉัยที่น่าเชื่อถือด้วยวิธี microcopic agglutination test ให้ผลเป็นบวกสำหรับ *Leptospira interrogans* ซีโรวาร์ bratislava ส่วนการตรวจทางซีโรโลยีของสครับไทฟัสและไข้เลือดออกให้ผลลบ จำนวนของผู้ป่วยที่ติดเชื้อเลปโตสไปโรซิสมีจำนวนเพิ่มขึ้นในหลาย ๆ โรงพยาบาล และพบรายงานการระบาดของโรคนี้ในภาคตะวันออกเฉียงเหนือของประเทศไทยตั้งแต่ปี 2540 ในเดือนตุลาคม 2542 ได้มีการแยกเชื้อ *Leptospira interrogans* ซีโรวาร์ pyrogenes จากเลือดของผู้ป่วยที่เป็นไข้ร่วมกับอาการทางคลินิกของเลปโตสไปโรซิสในจังหวัดบุรีรัมย์ นำเชื้อดังกล่าวมาใช้เพื่อศึกษาความก้าวหน้าของการเปลี่ยนแปลงทางจุลกายวิภาคศาสตร์ในอวัยวะต่าง ๆ ประกอบด้วย ไต ปอด ตับ กล้ามเนื้อน่อง และกล้ามเนื้อ hamstring ของแฮมสเตอร์ที่ติดเชื้อ ไตแสดงการเปลี่ยนแปลงของการเสื่อมของ renal tubular cell และ glomerular tuft พร้อมกันนี้ได้พบลักษณะของ interstitial nephritis และ pyelonephritis ร่วมด้วย สำหรับปอด ถุงลม และ interalveolar capillaries คั่งด้วยเซลล์เม็ดเลือดแดง พบลักษณะของ bronchopneumonitis และ interstitial pneumonitis ตับแสดงการบวมของเซลล์ตับซึ่งทำให้เกิดการแตกกระจายของ hepatic cord มีการแสดงลักษณะ congestion ของหลอดเลือดและ sinusoid พบ Kupffer cell เด่น และมี inflammatory cell infiltration ทั้งใน parenchyma sinusoid และ portal area พบ hepatocellular necrosis กระจายทั่ว hepatic lobules แฮมสเตอร์บางตัวแสดงลักษณะ congestion ของหลอดเลือดในกล้ามเนื้อน่องและ hamstring พบ inflammatory cell infiltration ใน perimysium ของกล้ามเนื้อน่องของแฮมสเตอร์ 1 ตัว แฮมสเตอร์อีกตัวแสดง necrosis ของเส้นใยกล้ามเนื้อร่วมกับมีการซึมแทรกของ inflammatory cell infiltration ซึ่งเป็นสิ่งบ่งชี้ว่าเกิด muscular inflammation ขณะเดียวกันมีการอภิปรายเกี่ยวกับการป้องกันและควบคุมโรคเลปโตสไปโรซิสร่วมไปด้วย

Presentation of case

A 20- year-old man was admitted to Siriraj Hospital because of high fever, and jaundice. This patient had become febrile, chill, severe headache, nausea, vomiting and myalgia 10 days before admission. He developed a cough with blood streaked sputum the next day and mild watery diarrhea the day after. He was initially treated with oral amoxycillin 2 gram per day. He developed a subconjunctival hemorrhage, and jaundice 4 days prior to admission to hospital. He was a rice farmer, from Kanlasin Province. He had come to work in Bangkok 2 weeks ago. He did not drink alcohol and had stopped smoking 3 months ago.

On admission, his temperature was 38.9°C, his pulse was 116/ min, blood pressure was 130/ 50 mmHg, and respiratory rate was 18/ min. Examination revealed a young man, with no pallor, marked jaundice, a subconjunctival hemorrhage on the nasal side of the left eye, and mild hepatomegaly, which was not tender and no splenomegaly. He had mild tenderness in both calves. The results of laboratory studies performed on this patient are shown in Table 1. Chest radiograph was normal.

Differential disgnosis and discussion

This patient was previously healthy and just finished his rice farming in North- Eastern Thailand 2 weeks prior to this illness. He had had an acute febrile illness with nonspecific symptoms such as severe headache, nausea, vomiting, and watery diarrhea. Examination revealed a subconjunctival hemorrhage of left eye, marked jaundice, slight hepatomegaly and mild muscle tenderness. Laboratory investigations revealed mild leukocytosis, without left shift, marked hyperbilirubinemia with

slight elevation of AST/ ALT, and normal alkaline phosphatase. He also had acute renal failure. The differential diagnosis included severe systemic infections, especially leptospirosis and scrub typhus (thick blood film for malaria was negative). The definitive diagnosis was obtained by a positive microscopic agglutination test for *Leptospira interrogans*, serovar bratislava (at a titer of 1: 400). Serological tests for scrub typhus and dengue infection were negative. He gradually improved and was discharged from hospital 2 weeks later.

Leptospirosis is a zoonosis, caused by *Leptospira interrogans*. Human infection occurs through direct contact with infected animals or through exposure to fresh water or soil contaminated by infected animal urine[1]. Yunibandhu first reported 4 patients with leptospirosis in Thailand in 1943[2]. In subsequent years, recognition of leptospirosis was infrequent. Physicians annually reported between 50- 272 cases of leptospirosis to the Public Health Ministry of Thailand in the past decade[3]. The number of patients with leptospirosis has been increasing in many hospitals and recent outbreaks of the disease have been reported in northeastern Thailand since 1997[4]. Several new serotypes of *L. interrogans* have been recognized in these patients. Clinical manifestations of leptospirosis are nonspecific and laboratory confirmation is necessary for the definitive diagnosis of leptospirosis[1,5]. Although there are several serological tests available, their performance varies widely geographically. In Thailand none of these serological tests are sensitive tests when tested during the first week of illness. Therefore acute-phase serum collected 1 to 2 weeks after the onset of illness and convalescent serum collected again at 3 to 4 weeks after the onset should always be obtained to facilitate serological diagnosis. Specific treatment of leptospirosis is simple and most patients with leptospirosis recover[6]. However, the mortality of leptospirosis is high in Weil's syndrome and in patients who develop massive pulmonary hemorrhage. Close monitoring of vital signs, urine output and early peritoneal or hemo-dialysis or ventilatory support are important in these patients.

Prevention and control of Leptospirosis

Infectious agent : Leptospires, member of the order Spirochaetales. Pathogenic leptospires belong to the species *Leptospira interrogans*, which is subdivided into about 23 serogroups and more than 200 serovars.

Distribution : Worldwide, both in developed and developing areas, except for polar regions. Leptospirosis is a zoonotic bacterial infection and an occupational hazard for rice and sugarcane fieldworkers, farmers, sewer workers, veterinarians, dairymen, abattoir workers, and military troops.

Mode of transmission : Skin contact, (especially if abraded) or of mucous membranes with water contaminated with the urine of infected animals. Leptospires can survive in the environment for up to 6 months if the temperature and humidity are suitable. The optimal conditions for leptospires are a temperature between 28°-32°C, pH 7.2-8.0. An environment with temperature of 42°C can kill leptospires and temperature of 57°C can kill leptospires in 2-3 minutes.

Susceptibility and resistance : Susceptibility in humans is general. There is no difference in susceptibility between age group or sex.

Methods of control :[7]

1. Educate the public on the modes of transmission, to avoid swimming or wading in potentially contaminated waters and to use proper protection when work requires such exposure.
2. Protect workers in hazardous occupations by providing boots and gloves.
3. Recognize potentially contaminated water and soil and drain such waters when possible.
4. Control rodents in human dwellings, especially rural and recreational.
5. Segregate infected domestic animals; prevent contamination of living quarters, working and recreational areas by the urine of infected animals.
6. Chemoprophylaxis with doxycycline 200 mg once weekly (efficacy = 95% $p < 0.001$)[8] during a period of high exposure without appropriate barriers (boots, gloves).

Reservoirs: Wild and domestic animals such as rats, cattle, dogs, swine, cat, and raccoons. Serovars that have been identified in Thailand include :-

Serovars	Human	Rat	Dog	Cattle	Pig	Cat
L.australis	+	+	++	+		
L.bangkok BD92			+			
L.ballico	+					
L.lora		+				
L.bataviae	++	++	++	+		
L.autumnalis	++	++	+	++		
L.akiyami A		+				
L.rachamati	+					
L.forbragg		+				
L.canicola	++	++			++	
L.grippotyphosa	+	++	+			
L.hebdomadis	+	++	+	+		
L.hyos		++	+	+		
L.icterohaemorrhagiae	++	++	+			
L.javanica	++	++	++	+	++	+
L.pomona	+	+	+	++	++	
L.pyrogenes	++	++	+			

Table 1. Results of laboratory investigations.

Complete blood count:	
Hematocrit (%)	40
White- cell count (per mm.^{3})	12,300
Differential count (%)	
Neutrophils	53
Lymphocytes	30
Others	17
Platelet count (per mm.^{3})	243,000
Urine examination:	
Specific gravity	1.015
Albumin	1+
Sediments	rbc 1-2/ HD, wbc 2-3/ HD
Blood chemistries :	
Total/ direct bilirubin (mg/dl)	29.6/ 21.1
AST (U/L)	59
ALT (U/L)	94
Alkaline phosphatase (U/L)	130
Albumin/ globulin (G/L)	3.7/ 4.0
BUN (mg/dl)	89
Creatinine (mg/ dl)	4.0
Sodium (mmol/ L)	134
Potassium (mmol/ L)	3.7
Bicarbonate (mmol/ L)	23

Comment

Assistant Professor Kesorn Sripaoraya
Chairman, Department of Anatomy.

This is the first time in the history of the Anatomy Department that we have participated in an "Interdepartmental conference". I would like to thank the Faculty of Medicine, Siriraj Hospital who have given us this opportunity and would like to thank the Department of Medicine as well as the Department of Preventive and Social Medicine for their tremendous cooperation in this event. The "Leptospirosis 2001" presentation gives us the latest evidence to confirm the changes in organs after infection with the pathogen at different time intervals. The facts presented can not be obtained by any means from patients as we can only study the pathology at autopsy. Therefore, participants at this meeting can fill the gaps in their knowledge and use it for enable them to understand the pathogenesis and clinical manifestations of this disease much better.

REFERENCES

1. Farr RW. Leptospirosis. Clin Infect Dis 1995; **21:** 1-8.
2. Yunibandhu J. First report of Weil's disease in Thailand. J Med Assoc Thai 1943; **26:** 83 - 139.
3. Sundharagiati B, Harinasuta C. Studies on leptospirosis in Thailand (a review). J Med Assoc Thai 1964; **47:** 662- 679.
4. Tangkanakul W, Kingnate D. Leptospirosis epidemic in north-eastern Provinces, 1997. J Health Science 1998; **3:** 386- 395.
5. Faine S, Adler B, Bolin C, Perolat P. Leptospira and leptospirosis. Second edition. Med Sci Melbourne, Australia,1999.
6. Watt G, Padre LP, Tuazon ML, Calubaquib C, et al. Placebo-controlled trial of intravenous penicillin for severe and late leptospirosis. Lancet1988; **27:** 433-435.
7. Chin J, ed. Control of communicable diseases Manual. 17th ed. An official report of the American Public Health Association. 2000: 293-296.
8. Takafuji ET, Kirkpatrick JW, Miller RN, et al. An efficacy trial of doxycycline chemoprophylaxis against leptospirosis. N Engl J Med 1984; **310:** 497-500.