

CASE REPORT

Leptospirosis in pregnancy: A lesson in subtlety

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Abstract

Introduction: Leptospirosis is a zoonotic disease caused by spirochaete of the genus *Leptospira*. Human infection occurs after exposure to water or soil contaminated by urine from an infected animal. Most patients manifest as self-limited systemic illness. However 10% of patients manifest as severe disease associated with high fatality. The disease affects mostly men, cases involving pregnant women are uncommon. We presented a case of leptospirosis in a pregnant woman leading to mortality of both mother and foetus. **Case Report:** A 28-year-old woman at 18 weeks of gestation, had shortness of breath and collapsed. She was brought unconscious to the emergency department and died shortly after arrival. A week prior to this, she had presented to the same hospital with pain on both thighs. Examination of the patient and ultrasound of the foetus revealed normal findings. Post mortem examination revealed hepatosplenomegaly and congested lungs; no jaundice, meningeal inflammation or cardiac abnormalities was evident. Histopathology examination of the lungs revealed pulmonary haemorrhages and oedema. Multiple infarcts were seen in the spleen and the kidneys showed foci of acute tubular necrosis. Laboratory investigations revealed *Leptospira* IgM antibody and PCR for leptospira were positive. This case illustrates the subtleness of clinical presentation of leptospirosis. The diagnosis was obscure even at post-mortem and was only suspected following histopathological examination, leading to further investigations. **Conclusion:** Leptospirosis may have a subtle presentation and a high index of suspicion for this infection is required for early identification of the disease.

Keywords: Leptospirosis, pregnancy, maternal death, autopsy

INTRODUCTION

Leptospirosis is a zoonotic disease caused by pathogenic spirochaetes of the genus *Leptospira*.¹ Infection occurs through direct contact with urine or tissues of infected animals such as during handling of animals by veterinarians, workers at dairy farms or abattoirs, butchers and hunters; even children could be exposed to the disease via contact with their pets. Infection could also be the result of indirect contact, for example exposure to infected wet soil or water occurring during water recreational activity, rice farming and flooding after heavy rains.^{2,3,4}

Leptospire may enter the body through injured skin such as via cuts or abrasions, mucous membrane and conjunctivae exposure or inhalation of microscopic droplets.⁵ Upon

entering the body, widespread haematogenous dissemination and penetration of tissue barriers will occur. Transendothelial migration of spirochaetes is facilitated by a systemic vasculitis, accounting for a broad spectrum of clinical illness. Severe vascular injury may lead to pulmonary haemorrhage, ischaemia of the renal cortex and tubular-epithelial necrosis. Destruction of hepatic microarchitecture may result in jaundice and liver cell injury, with or without necrosis.⁶

Leptospirosis is associated with a very broad spectrum of severity, ranging from subclinical illness followed by seroconversion to two clinically recognisable syndromes; a self-limited systemic illness seen in approximately 90% of infections, and a severe, potentially fatal illness accompanied by any combination of renal failure,

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liver failure and pneumonitis with haemorrhagic diathesis.^{6,7}

The disease affects men more than women.⁸⁻¹⁰ The global incidence is 0.1 to 975 cases per 100,000 population, with fatality of 6.85%. Factors influencing fatalities include prevalent serovars, health care services and socioeconomic status of the population¹¹. Data on leptospirosis in pregnancy is scant¹²⁻¹⁹. Most of the reported cases resulted in death of the foetus and is rarely associated with maternal mortality.¹²⁻¹⁹ We report a case of a pregnant woman with subclinical leptospirosis who developed pulmonary haemorrhage resulted in a fatal outcome. The aim of this case report is to create awareness of the possible subtle clinical features of this disease that pose a challenge to its diagnosis which may result in fatality.

CASE REPORT

A 28-year-old lady was brought unconscious to the emergency department (ED) and died shortly after arrival. She was pregnant at 18 weeks of gestation, complained of difficulty in breathing prior to collapse at home. Blood investigations showed low haemoglobin (10.2 g/dL), high total white cell count ($20.68 \times 10^9/L$) and low platelets ($26 \times 10^9/L$). Cardiac enzymes: creatine kinase, aspartate aminotransferase and lactate dehydrogenase were all raised, at 6302 U/L, 252 U/L and 514 U/L respectively. The liver function test showed increased globulin (35 g/L) and increased alanine aminotransferase (129 U/L).

Her medical record revealed that the patient had presented to the ED with bilateral thigh pain one week earlier. Documented vital signs showed her blood pressure was 126/79 mmHg, pulse rate

was 65/minute and her temperature was 36.8°C. She was afebrile and physical examination indicated normal findings. An ultrasound scan showed good foetal development. Full blood count was normal with haemoglobin; 11.6 g/dL, total white cell count; $9 \times 10^9/L$ and platelet count was $264 \times 10^9/L$. As her vital signs and blood investigations were within normal limits, the attending physician noted that there was no indication for further ancillary procedures such as chest X-ray or ECG tracing to be performed. She was discharged home. According to her husband, the pain persisted and two days later, she developed fever and was generally unwell. Four days later, she succumbed to the unknown illness. There was no significant past medical history. There was no history of water recreational activity or contact with animals.

Autopsy findings

Post mortem examination was performed and a list of differential diagnoses was considered with particular attention given to infectious disease in view of leucocytosis. Hepatosplenomegaly and mildly congested lungs were observed (Fig. 1). The uterus and foetus were consistent with 16-18 weeks gestational period. There was no immediate cause of death concluded after the post mortem. Blood samples were taken for infectious disease screening which included dengue, *leptospira*, *Mycoplasma pneumoniae*, Chlamydia and Rickettsia antibodies. Tissue samples were taken for histology examination.

Microscopic examination of the lung showed pulmonary haemorrhage and oedema (Fig. 2). Multiple areas of infarcts were seen in the spleen, while the kidneys showed acute tubular

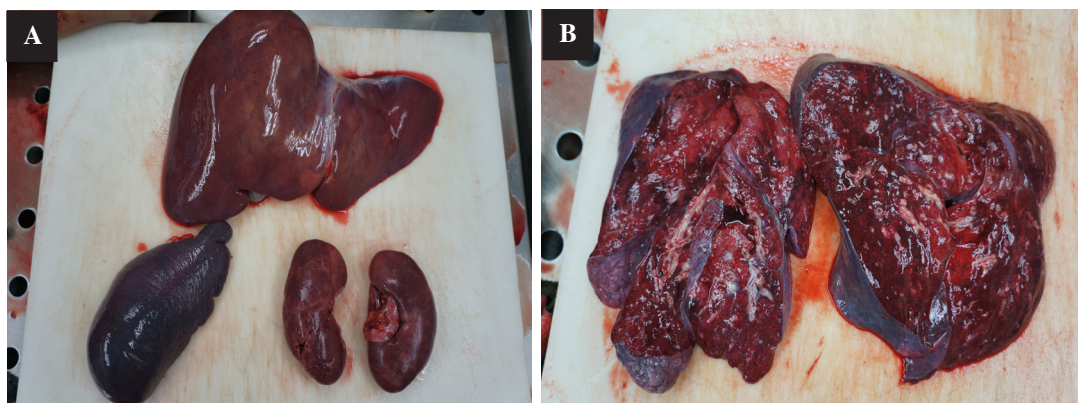


FIG. 1: (A) Enlarged liver (1695 grams) and spleen (405 grams) with normal sized kidneys. (B) Cut section of the lungs showed patchy lung congestion. No apparent pulmonary haemorrhage was noted on gross examination.

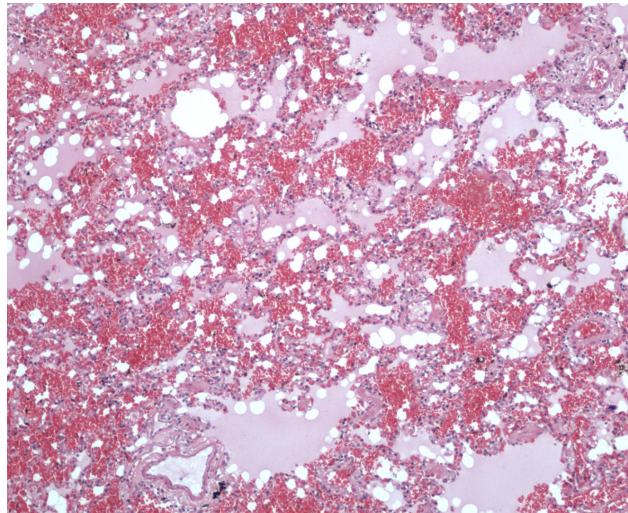


FIG. 2: Section from the lung showed intra-alveolar haemorrhage and oedema.

necrosis. Based on the previous history of muscle pain, presence of hepatosplenomegaly, raised liver enzymes and pulmonary haemorrhage on histology, a diagnosis of leptospirosis was suspected and further laboratory tests were requested. Serological analysis revealed a positive *Leptospira* IgM antibody. Subsequently, a polymerase chain reaction (PCR) test was performed on paraffin-embedded liver and kidney tissues at a reference laboratory. *Leptospira* deoxyribonucleic acid (DNA) was positive from the liver sample. Thus the cause of death was concluded as multiple organ failure with septicaemia secondary to leptospirosis.

DISCUSSION

Leptospirosis has been identified as an emerging public health problem worldwide.¹⁰ It has been reported to be endemic especially in warm countries such as South America, the Caribbean and Oceania.² In Southeast Asia, major outbreaks of the disease had been reported in Jakarta (2003), Mumbai (2005) and Sri Lanka (2008).²⁰ In Malaysia, leptospirosis is a notifiable disease since 2010, with marked increase in cases seen in recent years. Between 2004 and 2012, a total of 12,325 cases of leptospirosis were reported.²¹ Overall age-standardised incidence rate of leptospirosis in Malaysia in 2012 and 2013 was 29.02 per 100,000 population, with the highest incidence seen in Malays followed by Indians.²¹ In 2004-2012, the state of Malacca has the highest incidence of the disease followed by Pahang,²¹ however more recent data shows that the disease is most prevalent in Kuala Lumpur, Selangor, Sarawak and Negeri Sembilan.²²

The factors significantly related to the increase incidence of leptospirosis are increased rainfall (or number of rainy days per month), flooding, monthly average temperature and recreational activities.^{21,22} Overall case fatality rate in Malaysia was 1.47% for 2012-2013 and overall age-standardised mortality rate was 0.45 per 100,000. Fatality was higher in males, with overall male to female ratio of 3.69:1.²¹

A few outbreaks of leptospirosis have been reported in Malaysia. In the year 2000, 304 athletes from 26 countries contracted the disease during a sports event (Borneo Eco-challenge).²³ 29 people were hospitalised, however, no deaths were reported. Another incident which occurred in 1999, 46 males were admitted to the hospital after swimming in a pond in an oil-palm plantation. One of the patients died due to pulmonary haemorrhage. Blood tests confirmed leptospirosis.²⁴ A drastic increase in cases was seen in 2014 associated with 92 fatalities.²² The increase in cases during this time period was thought to be attributed to the increase in rainfall and flooding that occurred during that year. Rats harbour the organism in their renal tubules and excrete them in their urine. It was postulated that the heavy rainfall and flooding had led to spread of *Leptospira*-contaminated water.²² This patient was also a victim to leptospirosis during this period.

There was only a few leptospirosis cases in pregnant women that has been reported. Leptospirosis during pregnancy may lead to a number of complications; infection during the first two trimesters may result in a spontaneous miscarriage. Infection contracted during the third

trimester may cause abortion or perinatal death.^{2,6} This patient contracted the disease during the early second trimester.

Leptospirosis manifests as a biphasic illness; the first phase is associated with presence of high fever, headache, myalgia, particularly in lumbar and calf muscles, arthralgia, pharyngitis, non-productive cough, abdominal pain, nausea and vomiting. The fever abates and returns at the start of the second phase. The second phase is characterised by jaundice, meningitis, renal failure, pulmonary haemorrhage, myocarditis and rhabdomyolysis.^{2,7} In this case, the patient had first presented to the ED due to bilateral thigh pain. There was no history of fever and the temperature taken confirmed that she was afebrile. The pain persisted and two days later, she developed fever and appeared generally unwell. Her final symptom was difficulty in breathing amid the high fever. Observing the sequence of events which took place, we postulated that at her first presentation to the ED, the patient most likely was at the end of the first phase of the illness. She went into the second phase of the illness at home which resulted in fatal complications. As thigh pain is an unusual presentation of leptospirosis, we hypothesised that in this patient, the thigh pain was an indication of skeletal muscle damage, corroborated by the raised CK.

Contact tracing revealed that she was most probably infected through ingestion of food bought from a shop known for rats' infestation, where use of contaminated cutlery and plates could lead to spread of the disease. This tragic incidence further highlighted the importance of hygiene practice at eateries. Indeed, the spread through contaminated items used in food related activities should also be a concern in addressing the issue of leptospirosis outbreaks in the country.

CONCLUSION

Leptospirosis may have an unusual and subtle presentation in a pregnant woman and an awareness of the atypical presentations together with high index of suspicion may lead to early identification of the disease.

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