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Leptospirosis-Associated Severe Pulmonary Hemorrhagic Syndrome with Lower Back Pain as an Initial Symptom

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Conflict of interest: None declared

Patient: Female, 45
Final Diagnosis: Leptospirosis
Symptoms: Back pain • fever • headache • Hemoptysis • nausea • sepsis
Medication: —
Clinical Procedure: —
Specialty: Infectious Diseases

Objective: Rare disease

Background: Leptospirosis is a zoonosis transmitted through urine of infected animals. Symptoms range from mild influenza-like symptoms to severe pulmonary hemorrhagic syndrome (SPHS); the latter are often fatal. The serogroup distribution in Denmark has changed from 1988 to 2012, with Icterohaemorrhagiae and Sejroe now being predominant.

Case report: A 45-year-old Danish woman living in an area endemic for Hanta virus, without prior medical history, was admitted because of lower back pain radiating to the left hip, fever, headache, nausea, and malaise. Two weeks before admission she had been bitten by a mouse or a rat. Blood tests revealed raised white cells and CRP, electrolyte imbalances, raised creatinine, low thrombocytes, and a slightly decreased clotting factor (II, VII, and X). Treatment with broad-spectrum intravenous antibiotics and supporting therapy was initiated very quickly. Eight hours after admission she died from respiratory failure where severe hemoptysis was observed. Leptospiral DNA was later detected in a urine sample.

Conclusions: This case represents leptospirosis with severe pulmonary hemorrhagic syndrome. In spite of immediate treatment with broad-spectrum antibiotics, the patient died a few hours after hospital admission.

MeSH Keywords: Back Pain • Hemoptysis • Hemorrhagic Septicemia • Leptospirosis

Full-text PDF: <http://www.amjcaserep.com/abstract/index/idArt/900477>

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Background

Leptospirosis is a zoonosis caused by spirochetes maintained in the renal tubules of certain animals, such as cattle and rats. Transmission occurs primarily through direct or indirect contact with urine from infected animals. Symptoms range from mild influenza-like illness, Weil's syndrome (jaundice, renal failure, hemorrhage, and myocarditis with arrhythmias) to pulmonary hemorrhage with respiratory failure [1].

Pulmonary involvement in leptospirosis was first described in 1943 [2,3]. In recent years, severe pulmonary hemorrhagic syndrome (SPHS) caused by leptospirosis has gained increased attention due to the 1995 outbreak in Nicaragua and the emergence of leptospirosis-associated SPHS in Brazil from 2003 to 2005 [4,5].

In Denmark, a non-endemic area, leptospirosis had an average annual incidence rate of 0.34/100,000 inhabitants from 1980 to 2012, with 4 being fatal. In the same period, serogroup distribution changed, with Icterohaemorrhagiae and Sejroe becoming predominant [6]. Serovars of the Icterohaemorrhagiae serogroup are associated with more severe forms of leptospirosis [7,8].

SPHS has a mortality rate of over 50% and death may occur in less than 72 hours after onset of symptoms [2,8].

To the best of our knowledge, a case of leptospirosis debuting with severe back pain and terminating with severe pulmonary involvement has not been reported in Denmark. Herein, we describe a case of leptospirosis-associated SPHS.

Case Report

A 45-year-old Danish woman without prior medical history was admitted because of lower back pain radiating to the left hip, fever, headache, nausea, and malaise. The woman lived in an area endemic for Hanta virus.

Two weeks before admission, she was bitten by a mouse or a rat, and 2 days before admission she contacted the doctor on call, complaining of severe back pain. She was referred to the outpatient clinic, where the suspicion of a Hantavirus infection or sepsis without known focus was raised, and she was then hospitalized.

Initially, temperature was 39.7°C, blood pressure was 104/77 mmHg, peripheral saturation was 96%, and heart rate was 132 beats/min.

A healed, non-infected scratch mark was found on her left thigh. Physical examination was otherwise normal and jaundice was not found.

Blood tests revealed white blood cells $11.4 \times 10^9/L$, C-reactive protein 288 mg/L, thrombocytes $59 \times 10^9/L$, hemoglobin 7.2 mmol/L, creatinine 127 $\mu\text{mol/L}$, and erythrocyte sedimentation rate 51 mm. Liver function test results were normal. Kidney function tests revealed creatinine 127 mmol/L, urea 11.3 mmol/L, potassium 2.9 mmol/L, and sodium 126 mmol/L. Blood cultures, urine cultures, tests for specific Hanta IgG and IgM, and influenza throat swab were negative. Immunoglobulins and plasma protein were normal.

Liver function tests showed a slight increase in alanine transaminase (ALT) 48 U/L, gamma-glutamyl transpeptidase (GGT), while bilirubin and alkaline phosphatase were normal. Clotting factors II, VII, and X were 0.69 arbitrary units per liter. Other laboratory markers consistent with disseminated intravascular coagulation were not taken before she died (Table 1).

A chest X-ray showed diffuse alveolar infiltrates in the basal 2/3 of both lungs (Figure 1). Renal ultrasound was normal. Urine dipstick analysis showed traces of protein, blood, and leucocytes. ECG showed sinus tachycardia of 109 beats per minute.

Intravenous treatment with piperacillin-tazobactam 4+0.5 g 3 times daily and ciprofloxacin 400 mg 2 times daily was initiated because of sepsis. Intravenous isotonic sodium chloride and glucose with high flow was given to correct hypotension and electrolyte imbalances. Later, she was treated with 1 L of Ringer-acetate.

Eight hours after admission, peripheral oxygen saturation dropped to 80% despite oxygen flow 4 L per minute. Her respiratory rate increased to 44 per minute. Severe hemoptysis was observed and she was given 3 L of erythrocyte concentrate and 450 grams of fresh frozen plasma. Shortly thereafter, she went into cardiac arrest and died, although advanced life support was initiated.

Leptospiral DNA was later detected in a urine sample by PCR analysis. Microscopic agglutination test (MAT) performed on serum, however, was non-reactive for all 15 serovars tested.

Discussion

Due to the course of the disease, a medico-legal autopsy was performed. Therefore, the autopsy report is not available to us. We strongly believe, however, that this case represents an example of leptospirosis-associated SPHS.

The patient history with a rat bite, clinical manifestations with respiratory failure and hemoptysis, and paraclinical investigations with diffuse alveolar infiltrations, renal failure, and

Table 1. Biochemical results upon hospital admission.

Analysis	Units	Normal range	Patient result
Hemoglobin, B	mmol/L	7.3–9.5	7.2
Leucocytes, B	10E9/L	3.50–8.80	11.4
Sedimentation rate	mm	2–30	51
Thrombocytes, B	10E9/L	165–400	59
Neutrophils, B	10E9/L	1.50–7.50	10.8
Lymphocytes, B	10E9/L	1.00–4.00	0.25
Monocytes, B	10E9/L	0.20–0.80	0.34
Basophils, B	10E9/L	<0.20	0.02
Eosinophils, B	10E9/L	<0.50	0.02
Albumin, P	g/L	36–48	36
Calcium ion	mmol/L	1.18–1.32	1.03
Potassium, P	mmol/L	3.5–4.4	2.9
Urea, P	mmol/L	2.6–6.4	11.3
Creatinine, P	μmol/L	45–90	127
eGFR	mL/min	>59	44
Sodium, P	mmol/L	137–145	126
Clotting factor (II, VII, X)	arbitrary units per liter	0.70–1.30	0.69
ALAT	U/L	10–45	48
ALP	U/L	35–105	70
Bilirubin	μmol/L	5–25	12
GGT	U/L	10–75	38
CRP	mg/L	<6	288
Immunoglobulin A	g/L	0.70–4.30	1.17
Immunoglobulin G	g/L	6.1–15.7	7.7
Immunoglobulin M	g/L	0.4–2.30	0.69
Protein, P	g/L	64–79	66

positive urine leptospiral DNA strongly suggest leptospirosis-associated SPHS as the cause of this fatal course of the disease.

Only 4 deaths due to leptospirosis were reported in Denmark from 1980 to 2012 [6].

In Denmark, it is mandatory to report cases of leptospirosis to the State Serum Institute of Denmark to map the incidence of the disease. This will help map the serogroup distribution over time, which will help determine if the Icterohaemorrhagiae serogroup is still becoming more predominant.



Figure 1. X-ray of thorax shows diffuse alveolar infiltrates in basal 2/3 of both lungs.

Conclusions

Leptospirosis is a very rare disease in Denmark, and SPHS is a differential diagnosis not often considered. With back pain and fever as initial symptoms in a patient living in an area endemic for Hanta virus, leptospirosis is not the first diagnosis that comes to mind.

Studies have indicated that high-dose intravenous steroids such as methylprednisolone and dexamethasone improve the outcome of pulmonary leptospirosis, and in some cases, it might be life-saving [2,9,10].

In conclusion, leptospirosis is a disease that needs to be recognized by doctors, as it is a potentially severe or fatal infection. The diagnosis has to be suspected when a patient has been in contact with rodents or been where rats might live. Intravenous steroids should be considered for patients with confirmed leptospirosis. Furthermore, the use of gloves and other forms of protection is important when working in a potentially contaminated environment.

Although rare in Denmark, leptospirosis has to be suspected when anamnestic or clinical signs of the disease are present in a patient. This will probably result in faster initiation of treatment of the disease and its potential complications.

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