Case Report

Severe Leptospirosis with Unusual Manifestation

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Summary

We report a case of an 8-year-old aborigine boy referred to our hospital for respiratory insufficiency with skin eruptions over the trunk and limbs. The skin condition was diagnosed as acquired ichthyosis. He also had a non-bleeding form of disseminated intravascular coagulopathy. Radiograph of the lungs showed bilateral perihilar opacities with bilateral pleural effusion. The diagnosis of leptospirosis was confirmed by a 4-fold rise in microagglutinating titre and polymerase chain reaction assay.

Key words: leptospirosis, disseminated intravascular coagulopathy (DIC), pleural effusion, acquired ichthyosis

Introduction

Leptospirosis is a spirochetal zoonosis worldwide in distribution that causes clinical illness in humans as well as animals. It is a disease with protean manifestations ranging from inapparent infection to fulminant and fatal disease. Leptospirosis mainly affects the liver and kidney. We present a case of anicteric leptospirosis with multiple organ involvement, including skin, which is a rare presentation. The epidemiological evidence was a clue towards arriving the diagnosis.

Case Report

An 8-year-old boy of Malaysian aborigine origin, presented initially to a district hospital with a 2-week history of fever associated with progressive abdominal distension, diarrhoea and acute shortness of breath. The fever was preceded with a 1-week history of dry, itchy, thickened skin over the trunk and limbs, which was not present before. At the district hospital, he was treated for septicaemia, and a possibility of typhoid fever. He was covered with a course of penicillin/gentamycin and subsequently changed to ceftriaxone. Re-evaluation several days later revealed a more tense and tender abdomen with circulatory insufficiency and he was referred to our hospital for further management. The patient resided in a small village in the vicinity of a palm oil estate and gave a history of bathing frequently in the river.

Physical examination on arrival revealed a febrile, pale, tachypnoeic and toxic-looking child. His skin was not jaundiced. There was generalized xerosis, thickened, cracked skin with fine scales over the trunk and limbs; however, the mucous membrane, scalp, hair and nails were normal. Percussion of the chest wall was dull with reduced breath sounds at both lower zones. Further examination of the abdomen revealed tenderness and fullness over the epigastrium. In addition, there was hepatomegaly of 5 cm below the right costal margin, minimal ascites and presence of sluggish bowel sounds. He also had a non-tender scrotal swelling. The remainder of the examination was normal.

The full blood count on admission yielded anaemia (Hb 8.0 g/dl), leucocytosis (WBC 25.3 × 10^3/µl) with predominance of neutrophils (69.3%) and thrombocytopenia (PLT 29 × 103/µl). The prothrombin time (>150s) were prolonged, and screening for disseminated intravascular coagulopathy (DIC) yielded low fibrinogen (145 mg/dl; normal: 228–445 mg/dl) and increased D-dimer (2 mg/dl; normal: <0.5 mg/dl). Liver function test was compatible with a mild anicteric hepatitis picture; bilirubin was 22 µmol/l, alanine transaminase and aspartate transaminase (>150s) were prolonged, and screening for disseminated intravascular coagulopathy (DIC) yielded low fibrinogen (145 mg/dl; normal: 228–445 mg/dl) and increased D-dimer (2 mg/dl; normal: <0.5 mg/dl). Liver function test was compatible with a mild anicteric hepatitis picture; bilirubin was 22 µmol/l, alanine transaminase and aspartate transaminase were 95 U/l and 198 U/l, respectively. Serum lactate dehydrogenase was also elevated at 2132 U/l (normal: 200–480 U/l) while renal function test, creatine kinase, amylase and myocardial-bound...
creatine kinase were normal. Routine urine examination showed presence of granular casts with 10–15 white blood cells and occasional red blood cells.

Chest radiograph (Fig. 1) demonstrated bilateral perihilar opacities and pleural effusion. Abdominal radiograph showed centrally located bowel loops and ultrasonography of the abdomen revealed hepatosplenomegaly with fluid collection in the pelvis. The electrocardiography was reported as sinus rhythm with no chamber hypertrophy, and the echocardiography showed structurally normal heart with evidence of high pulmonary pressure most likely due to severe lung infection.

Penicillin (200 000 unit/kg/day) was restarted to cover for leptospirosis, and ceftazidime (50 mg/kg/dose) was added for melioidosis. He was also transfused with blood products. He was referred to the dermatologist; a diagnosis of acquired ichthyosis was made and treated with topical emollient therapy. There was no family history of skin disorders. The patient’s parents showed no signs of ichthyosis; no other family members were examined. He became afebrile over the next four days and his respiratory function improved within a week of admission.

Blood, stool and urine culture were negative for bacterial growth. Examination of peripheral blood smear for malarial parasites and serology test for melioidosis were negative. The tuberculosis work-up was also negative; this included a Mantoux test, serial gastric lavage for acid-fast bacilli stain and culture for mycobacterium. Dark field microscopic examination revealed spirochaetes on direct smear. The immune haemagglutination test done to detect IgM antileptospira was also positive with reciprocal titre of 3200. Definitive evidence of leptospirosis was indicated with a 4-fold rise in microagglutinating titre (MAT). Polymerase chain reaction (PCR) for leptospirosis was also positive on blood sample (Fig. 2).

Fig. 1. Chest radiograph demonstrated bilateral perihilar opacities and pleural effusion.

Fig. 2. PCR was performed using the G1 and G2 primer pair targeting the secY gene of pathogenic leptospire. The expected size of the amplified product using the G1 and G2 primers is 285 basepairs. Lanes 1 and 12 are the 100Bp markers. Lane 2 is the reagent control, lane 3 is the positive control, and lanes 4 and 5 are the negative controls. This patient’s sample is on lane 6.
Paired serum was obtained at 3 and 5 weeks after onset of the illness. The MAT rose from an initial titre of 1:100 to 1:400 in the paired samples performed at the Regional Reference Laboratory for Leptospirosis in Institute of Medical Research. He was discharged after completing 14 days of penicillin therapy. Serial chest radiographs showed a return to baseline prior to discharge. Except for some mild scaly lesions at the back of the neck, the remaining skin was normal.

Discussion

Leptospirosis is a zoonosis of worldwide distribution with many wild and domestic animal reservoirs. Human infection typically results from exposure to infected animal urine, by direct contact or indirect exposure through water or soil. Leptospirosis is highly endemic in Malaysia, especially in the rural areas. A 10-year serological survey conducted throughout West Malaysia showed an incidence rate of 12.7% among febrile persons of various occupational groups [1]. In the survey, oil palm and rubber estate workers were most highly infected. There are 30 leptospiral serotypes so far isolated in this country.

Our patient had epidemiological evidence to suggest leptospirosis, he lived in a rural area near to an oil palm estate and frequently went swimming in the river. He had an anicteric form of leptospirosis with laboratory evidence of a positive serology and PCR. He also required blood products for severe thrombocytopenia and moderate DIC. Thrombocytopenia is usually associated with multiple organ involvement or acute renal failure in leptospirosis [2, 3]. However, thrombocytopenia has not been associated with DIC in previous reports [4, 5].

His other major problem was pulmonary disease, specifically severe pneumonia with bilateral pleural effusion and pulmonary hypertension. Pneumonia is not a prominent clinical manifestation of the leptospirosis. On occasion, however, pulmonary involvement can be the dramatic feature of the illness [6, 7]. The severity of respiratory disease is often associated with a more severe form of infection with multiple organ involvement as illustrated in our case [8]. Radiographic abnormalities are most commonly noted in the first week of disease, and the usual appearance is alveolar infiltrates appearing like snowflakes [9]. Bilateral pleural effusion is rarely described in leptospirosis [7]. In general, resolution of the abnormalities seen on radiographs occurs faster than other form of bacterial pneumonia with an average of 6–10 days of illness, although the more severe form may take a longer period as observed in our patient.

This case is also of interest as he presented with ichthyosis, acquired during the course of the illness. The condition was diagnosed on clinical grounds without a histological biopsy. The sudden appearance of ichthyosis, especially in adults has been considered a marker of systemic disease and should prompt further investigation. Acquired ichthyosis may develop in patients of any age with certain forms of malignant disease, autoimmune disorders, leprosy, tuberculosis, malnutrition, and other systemic disorders, as a side effect of cholesterol-lowering drugs or without apparent cause [10]. To our knowledge, association of ichthyosis and leptospirosis has not been reported before. We postulate that the spirochetes could have entered through the break in the skin as the skin manifestation preceded the other symptoms in the patient.

Leptospires are slender (0.1 × 6–12 μm) tightly coiled, flexible, gram-negative bacteria that can be best visualized by dark-field microscopy. However, this technique has low sensitivity and specificity, and is not recommended [11, 12]. Criteria for definitive diagnosis are either culture isolation of the organism from any clinical specimen or 4-fold or greater rise in antibody titre in the presence of a compatible clinical illness. Culture is insensitive and slow; it may take as long as 4–6 weeks for the organism to be detected. On the other hand, serology is the most frequently used diagnostic approach for leptospirosis [12]. The MAT, using live antigen, is ‘gold standard’ for serological diagnosis of leptospires. It is highly sensitive and specific, although time consuming and requires significant expertise from its users. Simpler and faster serological tests include indirect haemagglutination, IgM and IgG ELISAs, and various rapid IgM assays. The results of serodiagnostic studies typically are negative at the time of clinical presentation, and testing should be repeated to document seroconversion. The most recent diagnostic approach is based on PCR. PCR assay has important implication for patient care as the diagnosis can be made early [12].

Our case highlights several unusual features of leptospirosis; these include ichthyosis, bilateral pleural effusion and chemical evidence of DIC. The multi-system organ involvement of the disease may also be confused with other infectious diseases in the tropics like influenza, dengue haemorrhagic fever, malaria, enteric fever and melioidosis. A high index of suspicion and adequate laboratory support is essential in order to institute timely intervention that could minimize mortality.

References