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Early Hemidiaphragmatic Paralysis Followed by Polyradiculomyelitis as a Complication of Leptospirosis – Case Study Report

Rana paraliza hemidijafragme uz kasniji razvoj poliradikulomijelitisa kao komplikacije leptospiroze – izvješće o studiji slučaja

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Case report / Prikaz bolesnika

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Abstract

We describe a patient with acute encephalomyeloradiculitis during leptospirosis. Unilateral diaphragmatic paralysis, noted on the 7th day of illness, appeared as the first neurological deficit. The patient was treated with amoxicillin/clavulanic acid for seven days, from the 7th day of illness. The symptoms of polyradiculitis appeared in the second phase of the illness, and progressed during high dose dexamethasone therapy. The patient recovered completely.

Sažetak

Opisujemo bolesnika s akutnim encefalomijeloradikulitisom tijekom leptospiroze. Kao prvi neurološki deficit je 7. dana bolesti zabilježena unilateralna paraliza ošita. Bolesnik je od 7. dana bolesti liječen amoksicilin/klavulonskom kiselinom kroz 7 dana. Simptomi poliradikulitisa su se pojavili u drugoj fazi bolesti te su progredirali unatoč započetom liječenju visokim dozama deksametazona. Bolesnik se u konačnici potpuno oporavio.

Introduction

Leptospirosis is a spirochetal zoonosis of ubiquitous distribution, recently recognized as an important emerging infectious disease. The spectrum and severity of clinical symptoms in humans is ranging from subclinical infection to Weil's syndrome and severe pulmonary haemorrhage syndrome, with mortality rates >10% and >50%, respectively [1]. Nervous system involvement associated with *Leptospira* species infections is usually observed in the second phase of the illness and is considered immune-mediated [2].

Case report

A 44-year-old, previously healthy man was admitted to the University Hospital with a seven-day history of fever to 39.2ºC, chills, diffuse myalgias, headache, conjunctival injection, vomiting, mild dyspnea and a non-productive cough. On admission, positive physical findings included a temperature of 39.2°C, bilateral conjunctival injection, absent breath sounds over the left lung base and a 4cm palpable liver. Laboratory findings revealed a leukocyte count of 10.4 x 10^9/L (neutrophils 77%), an erythrocyte sedimentation rate of 86mm/h (Westergreen), C-reactive

protein of 187 mg/L, and moderately increased total bilirubin and liver enzymes. Other routine hematologic, biochemical and microbiologic analyses of blood and urine were normal. Chest X-ray on admission revealed an elevated left diaphragmatic cupola with loss of air space superiorly (Figure 1).

Leptospirosis was suspected on admission and amoxicillin/clavulanic acid, 1.2 grams intravenously every eight hours, was started. After 24 hours the dose was switched to 1 gram every 12 hours orally for the following six days. On the second day of therapy, fever resolved and a transient maculopapular rash appeared. A dull pain in both axilla and shoulders was noted on the 11th day of illness. After seven days of antimicrobial therapy the patient was discharged with normal auscultatory and neurologic examination but continued to complain of a headache and pain in both axillary areas and shoulders.

Seven days following his discharge (21st day of illness), he was readmitted complaining of a continuous headache and progressive pain in both shoulders and upper extremities accompanied by paresthesias and muscle weakness. A neurologic examination revealed decreased tendon reflexes in both arms with 3/5 muscle weakness and diminished sensation, and mild tremor in both hands. The patient was also anxious and depressed. Electromyoneurographic (EMNG) examination of the upper extremities showed signs of axonal nerve damage. Examination of the cerebrospinal fluid revealed 8 mononuclear cells/mm^3 and an elevated protein range of 0.478 g/L (upper normal range 0.45 g/L). Electroencephalographic examination showed diffuse slow waves. An X-ray of the neck was normal. A repeated chest X-ray on the 21st day of illness showed a normal position of both diaphragmatic cupolas. Intravenous dexamethasone, 48 mg/day devided in 4 daily doses was introduced on the 3rd hospital day and gradually tapered over the following 20 days, being administered orally from the 14th day of the therapy. On the 20th day of dexamethasone therapy, the patient complained of increased weakness, pain and paresthesias in the upper and lower extremities and the dexamethasone dose was increased. During gradual tapering of the corticosteroids dose over the following 40 days, physical therapy was also performed, and clinical symptoms gradually started to decrease. EMNG parameters in both upper and lower extremities were normal on the 40th day after the appearance of peripheral neurological symptoms.

Acute-phase serum from the 7th day of illness was positive for *Leptospira saxkoebing* 1:2000 and negative for the other 11 tested serovariants by the serologic microscopic agglutination test. Convalescent serum taken 14 days later was positive for *L. saxkoebing* 1:4000, *L. hardjo* 1:2000, *L. ballum* 1:500, and *L. poi* 1:500. Enzyme-linked immunoabsorbent assays for *Borrelia burgdorferi,* tick borne encephalitis virus, and *Mycoplasma pneumoniae* were negative in the paired sera.

Discussion

Although being the disease with broad spectrum of clinical manifestations [3], other than aseptic meningitis, which is clinically present in ≤25% of all leptospirosis cases, other neurological manifestations (meningoencephalitis, polyneuritis, subarachnoid hemorrhage, myelopathy, myeloradiculophaty, Guillain-Barré syndrome, transverse myelitis, cerebellar dysfunction, and tremor/rigidity) are uncommon [2,4]. Prognosis is generally good and sequels are rare.

The pathogenesis of central nervous system and peripheral nerve lesion in patients with leptospirosis remains unclear. Presumed pathogenic mechanisms include both direct effect of leptospires and immune-mediated injuries of the central nervous system. Diffuse vasculitis occurring during and after the initial phase seems to be responsible for most of the neurological syndromes, while circulating immune complexes could be associated with the other syndromes observed in the second (immune) stage of the disease. In one patient with severe form of the disease, who developed an immune-mediated meningomyeloencephalitis with overlapping acute motor axonal neuropathy and nephritic syndrome the presence of serum anti-ganglioside antibodies (GD1a positive, GM1 and asialo-GM1 weak positive) were described. Positive anti-ganglisoide antibodies and a compatible clinical picture strongly suggest that neurological impairment was due to diffuse, immune-mediated process [5].

In our patient, the diaphragmatic paralysis was noted on the 7th day of illness, when leptospiraemia ends, and specific antibodies are detected. The diaphragmatic paralysis was unilateral, clinically presented by mild dyspnea and a non-productive cough, and spontaneously resolved before clinical paresis of the upper and lower extremities appeared. Diaphragmatic paralysis has been described in patients with syphilis, primary tuberculosis, *Mycoplasma pneumoniae* infection and Lyme disease [6-9]. However, according to our knowledge this is the first description of this neurological manifestation in a patient during an early stage of leptospirosis.

Although randomized or placebo controlled trials have produced conflicting results regarding clinical effects, prompt antimicrobial treatment is strongly recommended for severe leptospirosis [1,10]. Antimicrobial therapy prevents or reduces the duration of leptospiuria [10]. The role of corticosteroid therapy for neurologic complications of leptospirosis is still an opened question. Some reports have suggested a reduced severity and duration of illness following their use [4]. In our patient, the symptoms of acute radiculomyelitis gradually progressed in a descending pattern during dexamethasone therapy, pointing to the need for further studies.

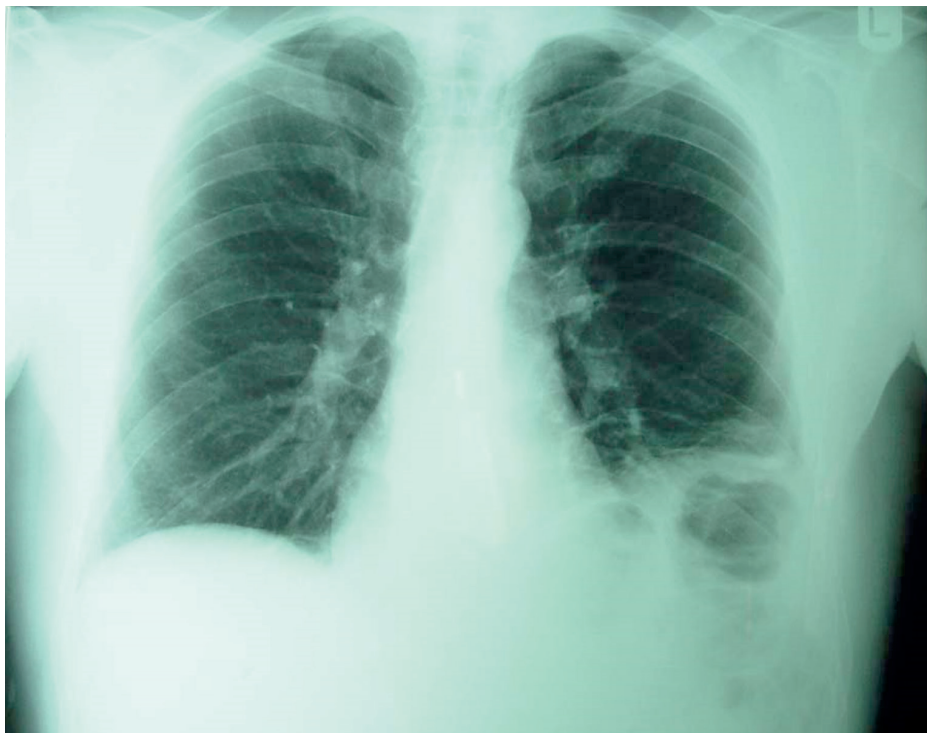
Although pulmonary manifestations in leptospirosis are common, only acute respiratory distress syndrome, se-

vere pulmonary hemorrhage syndrome, progressive weakness of the thoracic muscles due to intramuscular hemorrhage, paralysis due to severe hypokalemia resulting from proximal tubular dysfunction, and severe forms of rhabdomyolysis and/or polyradiculitis, have been described as indications for artificial ventilation [11,12].

In conclusion, it could be emphasized that diaphragmatic paralysis could appear as a neurological complication during an early stage of leptospirosis, what could be followed by other central and peripheral neurological manifestations. Its bilateral appearance could have significant impact on respiratory function in a patient even during the early stages of leptospirosis. The role of corticosteroid therapy for neurological complications of leptospirosis still remains controversial and based on the clinical course of disease in our patient, we can conclude that its use certainly could not have prevented the progression of the neurological symptoms.

Figure 1. Chest X-ray on the 7th day of the illness in a patient with leptospirosis; an elevated left diaphragmatic cupola with loss of air space superiorly

Slika 1. *Radiogram srca i pluća na 7. dan bolesti bolesnika s leptospirozom; elevirana lijeva kupola dijafragme s posljedičnim superiornim gubitkom zračnog prostora*



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