

## Alveolar haemorrhage in a patient with Leptospirosis

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**Abstract:** *Alveolar haemorrhage due to pulmonary vasculitis in the course of leptospirosis, although not uncommon, is rarely included in the differential diagnosis of pulmonary haemorrhagic syndromes. We present a case of a patient, treated in the ICU for leptospira infection, with a late onset of diffuse alveolar haemorrhage. A 68-year-old man was transferred in the ICU after a progressive CNS impairment. His lab tests were indicative for a severe hepatic dysfunction and renal impairment in need of intermittent haemodialysis. A presumptive diagnosis of leptospirosis was done, confirmed later by positive serologies. At the end of the icteric phase and while weaning from mechanical ventilation, multiple episodes of haemoptysis started, resulting in severe deterioration of oxygenation. Chest X-ray showed new bilateral patchy infiltrates and a High Resolution Computed Tomography scan revealed diffuse airspace disease with bilateral ground-glass opacities. Methylprednisolone 1g daily for 3 days, followed by prednisolone, 20 mg every 6 hours, was given. The patient responded with bleeding cessation and successful weaning. Twelve days later he was discharged to the ward improved. Haemorrhagic alveolitis usually occurs at the after the "leptospiemic" period of the disease. The case presented is suggestive of a delayed, post-"immune" onset of symptoms responding well to high dose steroid therapy. Hippokratia 2006; 10(2): 92-93*

**Key words:** *leptospirosis, alveolar haemorrhage, vasculitis, steroids*

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### Introduction

Differential diagnosis of pulmonary haemorrhagic syndromes rarely includes leptospirosis, although according to literature, this is not uncommon.<sup>1</sup> Human patients suffering from leptospirosis present with a diverse array of clinical manifestations, including the more severe and often fatal pulmonary form of the disease. Most human fatalities in leptospirosis are due to haemorrhage, but aetiology of haemorrhage has not been established. Although pulmonary haemorrhage in leptospirosis was first reported more than a half century ago, only recently has emerged as a potentially prominent feature of the infection.<sup>2,3</sup> We present a case of a patient with diffuse alveolar damage presenting as severe haemoptysis, after leptospira infection.

### Case report

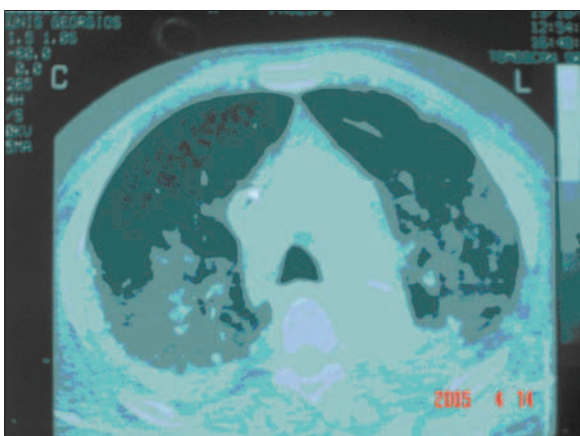
A 68-year-old man, with free previous history, complaining for fatigue, muscle weakness and fever, was admitted to the hospital. Two days later, he developed an icteric laboratory profile along with abdominal distention, renal impairment and thrombocytopenia. Three days later he was transferred to the ICU, after a progressive CNS impairment with delirium and partial loss of consciousness in need of intubation. Brain, lung and abdomen CT imaging did not show any specific findings, apart from pleural effusion accompanied by atelectasis of the basal pulmonary segments and renal inflammatory enlargement. His lab tests showed severe hepatic dysfunction with a max total bilirubin 10.1 mg/dl (direct component 6.8 mg/dl), low albumin (2 g/dl) and slight liver enzymes

elevation, thrombocytopenia of  $15 \times 10^3/\mu\text{L}$ , renal impairment with a serum creatinine of 5 mg/dl and urea of 195 mg/dl (normal values 30-55 mg/dl) and oligoanuria in need of intermittent haemodialysis. His empirical antibiotic treatment included ceftriaxone and clarithromycin for a probable pneumonia and ampicillin/sulbactam after a presumptive diagnosis of leptospirosis, confirmed later by positive serologies. Beside medical, his treatment comprised intermittent haemodialysis, mechanical ventilation and nutritional support.

On the 16<sup>th</sup> day of his ICU stay, at the end of the icteric phase, with an INR of 1.5 and while on weaning from mechanical ventilation, multiple episodes of haemoptysis started, resulting in mild blood loss but severe deterioration



**Figure 1.** *CXR on first haemoptysis day.*



**Figure 2.** High resolution lung CT scan during haemoptysis.

of oxygenation ( $\text{PaO}_2/\text{FIO}_2=149$ ). Chest X-ray showed new bilateral patchy infiltrates (Figure 1). Hydrostatic cardiogenic pulmonary oedema was excluded after a pulmonary artery catheterization with normal capillary wedge pressure. Sepsis was excluded after negative cultures including protected specimen brush. Bronchoscopy was avoided because of poor oxygenation but a high-resolution lung CT scan revealed diffuse airspace disease with bilateral ground-glass opacities (Figure 2). An immune origin, leptospirosis-related, diffuse alveolar haemorrhage was diagnosed and a steroid regimen of methylprednisolone 1g for three subsequent days was given, followed by prednisolone 20 mg every 6 hours. The patient responded very well, haemoptysis ceased and soon he was weaned from the ventilator. Twenty-seven days after ICU admission and twelve days after the onset of alveolar haemorrhage, he was discharged to the ward in improved general state but still in need of haemodialysis. He fully resumed his renal function four days later and was discharged from the hospital 15 days later.

## Discussion

Leptospirosis, a zoonosis caused by spirochetes from the species *Leptospira interrogans*, occurs worldwide, but is commoner in tropical regions. Wild or domestic animals are its reservoir. Humans become infected from direct contact with the urine of infected animals or from exposure to soil, water or other contaminated material.<sup>1</sup> Patient's past history investigation revealed a probable contamination by rat.

Leptospirosis produces two general patterns. In the less severe and generally nonfatal form, often called anicteric leptospirosis and accounting for 90% of cases,

the illness begins abruptly and includes headache, myalgias, fever, nausea, vomiting. The more severe form of leptospirosis, called icteric leptospirosis or Weil disease, in addition to the above features causes jaundice, renal impairment, and major haemorrhagic complications.<sup>4</sup> Both mild and severe cases often have an initial "leptospiremic" period and a subsequent "immune" phase marked by antibody production and urinary excretion of leptospira.

Pulmonary symptoms occur in both the nonicteric and icteric forms. Many case reports and clinical series document the frequent occurrence of diffuse pulmonary hemorrhage and haemoptysis usually on the 5<sup>th</sup>-9<sup>th</sup> day of the disease. The case presented here is suggestive of a delayed, post-immune onset of symptoms, on the 16<sup>th</sup> day of the disease. Radiographic findings appear as early as 24h after symptoms begin, although more commonly 3 to 9 days later. Three patterns are observed: i) small snowflake-like nodular densities corresponding to areas of alveolar haemorrhage, ii) large confluent consolidations, iii) a diffuse ill-defined ground-glass pattern that may represent resolving haemorrhage.<sup>1</sup>

*Leptospira* causes disease through a toxin-mediated process by inducing small-vessel vasculitis. The specific toxin responsible remains unknown. Diffuse petechiae involve the lung parenchyma, pleural surfaces and tracheobronchial tree. Microscopic examination usually demonstrates areas of intra-alveolar and interstitial hemorrhage, but other findings, including pulmonary oedema, fibrin deposition, hyaline membrane formation and proliferative fibroblastic reactions are frequent.

Isolates of leptospira acquired from patients suffering from pulmonary haemorrhage have been used in animal studies to develop a similar pulmonary model. Although immunohistochemistry confirmed the presence of large numbers of leptospira in kidney, liver, intestinal tissues, and spleen, few inflammatory cells were seen. In marked contrast, few leptospira were detected in infected haemorrhagic lung tissue. On the other hand, immunofluorescence confirmed the presence of IgM, IgG, IgA and C3 along the alveolar basement membrane, suggesting an autoimmune process as the aetiology of this fatal complication.<sup>5</sup>

Leptospirosis is generally absent from differential diagnoses in reviews on diffuse alveolar hemorrhage. Clinicians should consider this infection, since the clinical features of leptospirosis are nonspecific and the histopathologic findings are similar to other causes of pulmonary capillaritis that produce diffuse alveolar haemorrhage.

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### Forthcoming Congresses

- 1) 3<sup>rd</sup> World Congress on "Quality in Clinical Practice"  
September 28 - October 1, 2006, Thessaloniki, Greece  
e-mail: geover@otenet.gr  
site: www.qcp-qolcongress.gr
- 2) 13<sup>th</sup> Annual International Meeting on Advanced Spine Techniques  
July 12 - 15, 2006, Athens, Greece  
e-mail: Lvarner@broad-water.com
- 3) 26<sup>th</sup> International Congress of Applied Psychology  
July 16 - 21, Athens, Greece  
e-mail: info@erasmus.gr
- 4) 31<sup>st</sup> Annual Meeting of the International Urogynecological Association  
September 6 - 9, Athens, Greece  
e-mail: iuga@cnc.gr
- 5) International Congress of Hormonal steroids / Hormones and Cancer  
September 13 - 17, Athens, Greece  
e-mail: info@erasmus.gr
- 6) 10<sup>th</sup> Panhellenic Congress on Pathology  
May 23 - 24, Ioannina, Greece  
e-mail: pennyh@triaenatours.gr
- 7) 2<sup>nd</sup> Inter - Congress of the European Society of Pathology  
June 24 - 25, Ioannina, Greece  
e-mail: pennyh@triaenatours.gr
- 8) 16<sup>th</sup> Congress of the Mediterranean League of Angiology and Vascular Surgery  
June 8 - 12, Crete Island, Greece  
e-mail: info@erasmus.gr
- 9) The Athens PCOS International Congress  
March 27 - 31, 2006  
Athens, Greece  
e-mail: info@erasmus.gr
- 10) XVIIth Annual Congress of the European Society of Paediatric Urology  
April 27 - 29, 2006  
Athens, Greece  
e-mail: info@eslu2006.com
- 11) EuroPREvent 2006,  
May 11 - 12, 2006  
Athens, Greece  
e-mail: georgiak@triaenatours.gr
- 12) Friendship & Unity, Psychology & Communication  
May 4 - 7, Athens, Greece  
e-mail: appachellas@yahoo.gr
- 13) International Congress on Cancer, Chemoprevention and Control with Tailored Molecular Targeting  
February 15, Ancient Epidavros, Greece  
e-mail: jng@otenet.gr
- 14) 4<sup>th</sup> Panhellenic - Conference of Pediatric Sub - Specialties  
March 18 - 19, 2006  
Athens, Greece
- 15) International Symposium on Urinary Tract Infection  
June 3 - 24, 2006  
Weimar, Germany
- 16) 43<sup>rd</sup> ERA - EDTA Congress  
July 15 - 18, 2006  
Glasgow, Scotland, UK
- 17) World Transplant Congress 2006  
July 22 - 26, 2006  
Boston, MA, USA  
e-mail: pballinger@ahint.com
- 18) World Congress on Nephrology 2007  
April 21 - 25, 2007  
Rio de Janeiro, Brazil  
e-mail: info@isn-online.org  
www.isn-online.org
- 19) 14<sup>o</sup> Πανελλήνιο Συνέδριο Νεφρολογίας  
Μάϊος 31 - Ιούνιος 3, 2006  
Χαλκιδική, Porto Carras