# A rare cause of pulmonary haemorrhage


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## CLINICAL PRESENTATION

A 55 year-old cattle farmer presented to hospital with a one-week history of flu-like symptoms and a cough productive of yellow sputum. He also reported mild haemoptysis. He had no past medical history and was a never smoker. He was not on any medication and had no known allergies. In the emergency department he had a low-grade fever, was mildly hypotensive and had oxygen saturations of 80% on room air. Initial investigations are shown below (Table 1 and Figure 1). In light of his deranged liver function tests and hyponatraemia, he was further investigated for atypical causative organisms.

The initial clinical picture was suggestive of sepsis secondary to community-acquired pneumonia with pre-renal kidney injury, and he was therefore treated with oxygen therapy, IV antibiotics and IV fluids.

**Table 1**

| Test | Results | Units | Ref Range |
|---|---|---|---|
| HB | 93 | g/L | 120 to 160 |
| WBC | 9.2 | 10^9/L | 4.0 to 11.0 |
| PLATELET | 109 | 10^9/L | 150 to 450 |
| MCV | 87.8 | Fl | 78 to 97 |
| NEUTROPHIL | 8.2 | 10^9/L | 1.7 to 8.0 |
| LYMPHOCYTE | 0.2 | 10^9/L | 1.0 to 4.0 |
| EOSINOPHIL | 0.00 | 10^9/L | 0.1 to 0.8 |
| HCT | 27.9 | | 0.37 to 0.47 |
| INR | 1.1 | Ratio | 0.8 to 1.1 |
| SODIUM | 129 | mmol/L | 133 to 146 |
| POTASSIUM | 3.7 | mmol/L | 3.5 to 5.3 |
| CHLORIDE | 98 | mmol/L | 95 to 108 |
| UREA | 20.1 | mmol/L | 2.5 to 7.8 |
| CREATININE | 240 | umol/L | 60 to 110 |
| eGFR | 25 | mL/min | |
| BILIRUBIN | 18 | umol/L | 0 to 21 |
| ALT | 118 | U/L | 0 to 40 |
| ALP | 185 | U/L | 30 to 130 |
| GAMMA GT | 108 | U/L | 0 to 38 |
| CRP | 151 | mg/L | 0.0 to 10.0 |
| Urine casts | Granular +WBC casts | | |
| Urine WBC | ++ | | |
| Urine RBC | + | | |
| HIV negative/Hepatitis C Ab level negative/Hep BsAg negative/legionella and pneumococcal urinary antigen negative | | | |

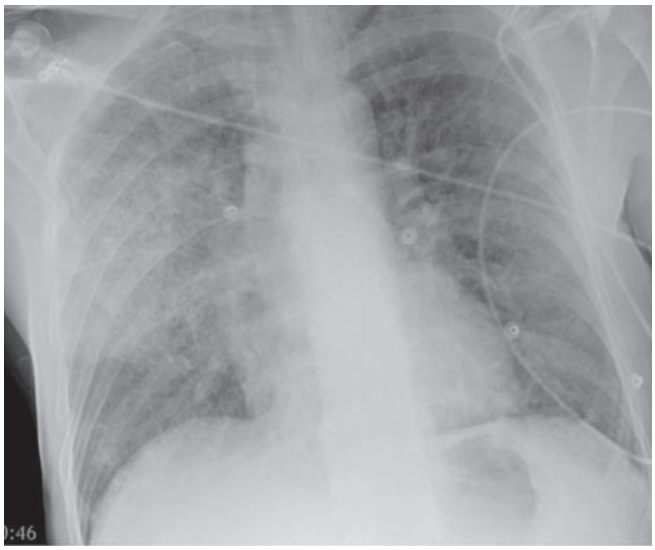

**Figure 1:** CXR shows marked airspace shadowing bilaterally

Later the same day, the patient deteriorated, and became profoundly hypoxic. He was transferred to the intensive care unit and intubated. A bronchoscopy performed post intubation revealed erythematous airways with contact bleeding and heavily bloodstained bronchial wash. AFB culture and MCS were performed and were subsequently negative. Repeat blood tests showed a drop in haemoglobin and worsening renal and liver function.

The differential diagnosis was narrowed to causes of multi-system disorder with associated pulmonary haemorrhage (for discussion of differentials, see Table 3, Figures 3 and 4). Further investigations included a vasculitis screen (Table 2), CT chest (Figure 2) and

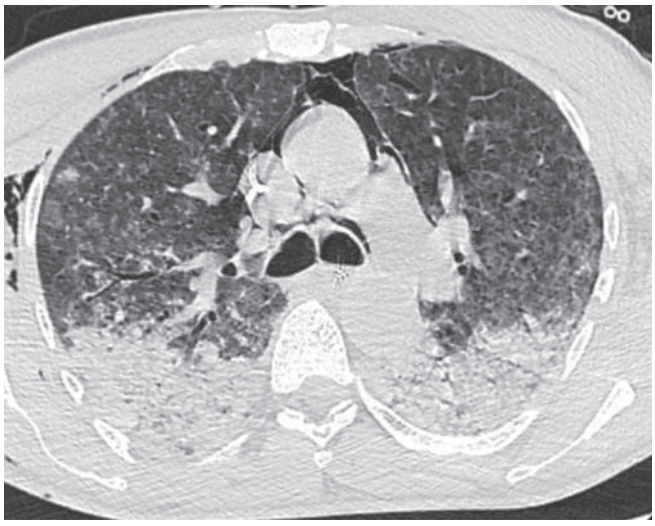

**Figure 2:** CT Chest with dense consolidation in both lower lobes. Also demonstrates pneumomediastinum with air tracking into the neck (managed conservatively)

leptospirosis serology. (The pneumomediastinum seen on imaging was thought to be related to his mode of ventilation and was managed conservatively without a chest drain.) With renal specialist input, a one-off dose of methylprednisolone was given pending results of the vasculitis screen. Treatment with broad-spectrum antibiotics was continued. He did not require inotropic support and stabilised from a ventilatory point of view on APRV and FiO2 80%.

**Table 2**

| **Antinuclear antibody** | **Weakly positive** | | |
|---|---|---|---|
| Complement C3 | 1.51 | g/l | 0.75 to 1.65 |
| Complement C4 | 0.29 | g/l | 0.14 to 0.54 |
| PR3 Antibody | 0.8 | U/ml | Positive >3.0 |
| MPO Antibody | 0.6 | U/ml | Positive >5.0 |
| Anti-GBM | 2.5 | U/ ml | 0 to 6.9 |
| CTD screen | Negative for Ro/La/Sm/RNP/Jo-1/Scl-70 and CENP-B | | |
| Anti dsDNA Abs | 6.2 | IU/Ml | 0 to 10 |

**Table 3**

| **Differential Diagnosis Pulmonary Haemorrhage** | |
|---|---|
| ANCA Associated Vasculitides | Anti-Coagulants/Bleeding Disorders |
| Goodpasture's Syndrome | Idiopathic Pulmonary Haemosiderosis |
| Drug Induced Vasculitis | Infections e.g. Leptospirosis |
| Connective Tissue Disorders | Illicit Drug Use e.g. cocaine |

## DIFFERENTIAL DIAGNOSIS OF PULMONARY HAEMORRHAGE

In any hypoxic patient, an acute drop in haemoglobin and diffuse alveolar air space shadowing on chest x-ray may suggest pulmonary haemorrhage. CT findings in pulmonary haemorrhage include ground-glass nodules and well-demarcated, typically lower zone, consolidation1. Typical appearances are shown in Figures 3 and 4.[2-3]

Table 3 lists some of the differentials to consider in pulmonary haemorrhage. Clotting parameters must always be checked, as pulmonary haemorrhage is a rare but important complication of anticoagulants.[4]

ANCA-associated pulmonary vasculitides are important to exclude. Early introduction of high dose corticosteroids and specialist nephrology input is of paramount importance. Goodpasture's often presents with pulmonary haemorrhage and is more common in young male smokers. Positive finding of anti-GBM antibodies should result in immediate supportive management with corticosteroids, cyclophosphamide, plasmapheresis and urgent renal review. [5]

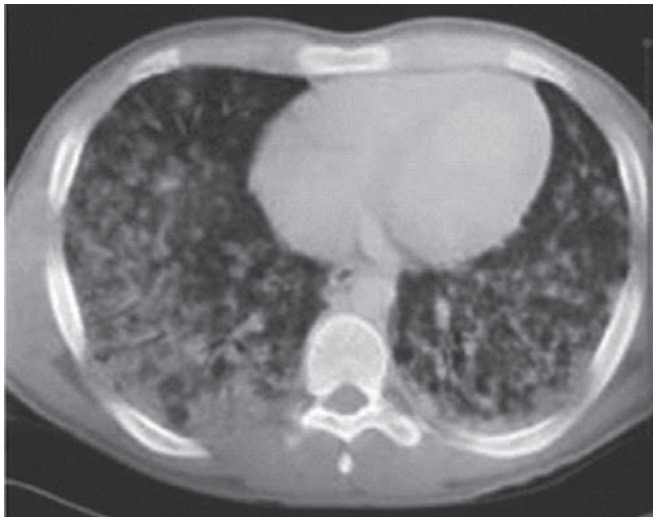

**Figure 3**

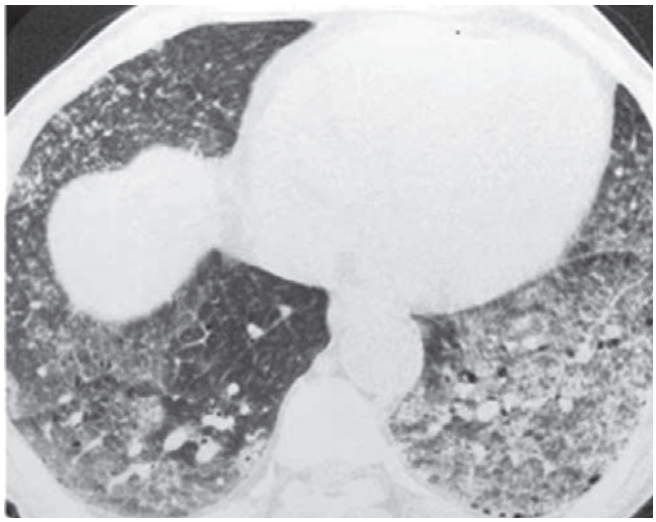

**Figure 4**

Less common causes include Idiopathic Pulmonary Haemosiderosis (IPH), a rare pulmonary condition, typically presenting in early childhood with haemoptysis, diffuse parenchymal infiltrates in CXR and iron-deficiency anaemia. Prognosis is variable and death following acute pulmonary haemorrhage is a recognised complication.[6]

## DIAGNOSIS, OUTCOME AND FOLLOW UP

On Day 6 of admission the microbiology laboratory reported a positive leptospirosis Nucleic Acid Amplification Test (NAAT) and negative leptospirosis IgM consistent with acute leptospirosis. The patient was treated with intravenous antibiotics followed by a one-month course of doxycycline, as recommended by the microbiology consultant.

The patient continued to make a good recovery and was extubated on Day 10 of admission. His renal and liver parameters improved and he was discharged twelve days after initial presentation to hospital. He was reviewed three months later in an intensive care follow up clinic. At this time he was back to work full-time as a farmer. He had occasional fatigue but otherwise no restrictions on his

usual daily activities. His bloods were completely normal and he was discharged back to community care.

## CONCLUSION

Leptospirosis is a zoonotic disease caused by spirochetes of the genus Leptospira. It was first described by Adolf Weil in 1886. There are over 250 serotypes of this microorganism, with Leptospira hardio and Leptospira icterohaemorrgiae being more frequently observed in the UK.[7] Despite this, it is an uncommon infectious disease in this country with 76 cases reported by Public Health England in 2014.[8]

Confirmation of Leptospirosis used to be through microscopic examination of centrifuged urine using dark-field illumination, as seen in Figure 5.[9] However, this method has been superseded by the Nucleic Acid Amplification Test (NAAT), a molecular technique which detects RNA or DNA of a pathogen as soon as it appears within a serum sample. This is thought to be a sensitive, but not specific diagnostic test in the setting of acute leptospirosis infection.[10-11]

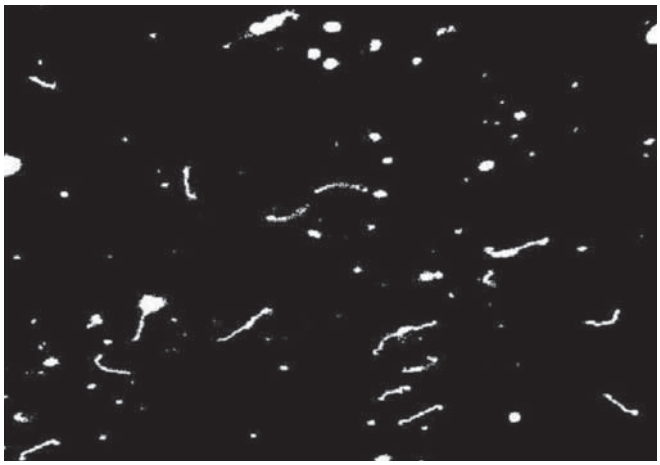

**Figure 5:** Confirmation of Leptospirosis using dark field illumination

The spectrum of leptospirosis varies greatly, ranging from a mild transient illness to multiple organ failure and can be fatal.[8] Typically, patients have mild influenza-like symptoms, sometimes accompanied by meningism. Multi-organ failure is seen in up to 10% of all Leptospirosis cases[12] and tends to affect the liver and kidneys (also known as Weil's Disease). These patients can also develop myocarditis and associated arrhythmias.[13] Renal involvement in Leptospirosis is uncommonly seen in Western countries and is more prevalent in South America, the Caribbean and parts of central Africa, where the disease is endemic. Clinical presentation can vary from subtle changes in renal function to profound acute kidney injury.[14] A report was published earlier this year in the UK of a patient who developed haemolytic uraemic syndrome secondary to leptospirosis; severe endotoxin injury to the renal interstitium from Leptospira was thought to be the ultimate culprit.[15] Most patients with renal involvement are treated with methylprednisolone and plasma exchange, if required, in the acute setting and the majority of cases do not require dialysis.[13, 14, 16]

Pulmonary haemorrhage is only rarely seen as the presenting feature of Leptospirosis and often only reported in countries where the disease is endemic.[17, 18] Profuse lung haemorrhage appears in severe forms of leptospirosis and mortality rates are high. Four patients were described to have severe pulmonary form of Leptospirosis in 2002 in Brazil and three died within 48 hours of onset of respiratory symptoms. Post-mortem histopathology concluded extensive pleuropulmonary haemorrhage with clear microscopic findings of haemorrhagic infiltrates within alveoli and septa. Detection of Leptospiral antigen in all three patients suggested invasive destruction of local lung tissue leading to progressive symptoms.[19] Other high-profile cases include the 1996 epidemic in the Seychelles in which 14 of 75 patients presented with pulmonary haemorrhage; six subsequently died[20] and the 1987 epidemic in Korea involved 37 cases of massive haemoptysis amongst 93 patients and 5 eventually died.[21]

This case highlights the importance of considering a wide differential diagnosis in patients presenting with pulmonary renal syndrome. Leptospirosis has a wide spectrum of clinical severity; so the diagnosis should be considered in at risk populations presenting with an unexplained multi-system disorder.

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