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Leptospirosis, An Unusual Differential of Diffuse Alveolar Haemorrhage (DAH) in a Non-Tropical ITU- A Case Report

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ABSTRACT

Severe leptospirosis has got very high mortality. Leptospirosis is overlooked in the UK and the confounders for low recognition, is partly due to low rate of incidence in this region, its protean manifestations, access to appropriate diagnostic tests, a broad differential for febrile illness or the lack of clinician's awareness. A delay in diagnosis and treatment may lead to increased disease severity and mortality. In this case report, we present a 25-year-old gentleman who had pulmonary hemorrhage as the earliest sign of severe leptospirosis without severe renal or hepatic involvement, which is a rare occurrence by itself.

Keywords: Pulmonary haemorrhage, Leptospirosis

INTRODUCTION

Leptospirosis is a zoonotic disease, even though common in the tropical countries; is a rare occurrence in the United Kingdom (UK) [1, 2].

Leptospirosis, due to its widespread occurrence is also called by many other colloquial names such as Weil's disease (the most severe disease) [3].

The causative organism for the disease is a spirochaete from the species *Leptospira*. These organisms are shed in the urine of animals to the environment from where humans are infected either directly or indirectly through infected soil or water. Humans are the incidental hosts for these organisms[4].

Leptospirosis can present with influenza like symptoms which is often self-limiting or can advance to a severe form which can affect the lung, liver or kidney[5]. Pulmonary involvement in Leptospirosis occur in 20-70% of individuals. The spectrum of pulmonary involvement can range from dry cough to pulmonary hemorrhage with fatality of around 50%[6]. The pulmonary hemorrhage in leptospirosis is attributed to the small vessel vasculitis, thrombocytopenia and consumption coagulopathy.

Leptospirosis is overlooked in the UK and the confounders for low recognition, is partly due to low rate of incidence in this region, its protean manifestations, access to appropriate diagnostic tests, a broad differential for febrile illness or the lack of clinician's awareness[7]. A delay in diagnosis and treatment may lead to increased disease severity and mortality[8].

In this case report, we present a 25-year-old gentleman who had pulmonary hemorrhage as the earliest sign of severe leptospirosis without severe renal or hepatic involvement, which is a rare occurrence by itself [10, 11].

CASE PRESENTATION

25-year-old presented to Emergency department with 4 days history of rigors, cough, feeling unwell, myalgia, headache, pleuritic chest pain and a day history of hemoptysis. A positive family history of lupus was also present. He had an occupational exposure to toilet/ sewage. Few hours down the course in the emergency department, he developed large bout of hemoptysis with desaturation and hypotension. At this point of time ITU was involved.

Upon assessment, airway was self-maintained and on assessment of breathing saturating was maintained at 96% on non-invasive ventilation with 65% FiO2 on PEEP of 5mmH_2O, tachypneic at 32 breaths per minute and crackles were present on bilateral lung fields. He was tachycardic at 140 beats per minute with blood pressure 88/56 mmHg with response to fluid, capillary refill was 2 seconds. He was conscious and GCS of 15 with no focal neurological deficit or neck stiffness. On exposure, patient was febrile but there was no rash, petechiae, or bite marks. Abdomen was soft to touch and did not show any hepatosplenomegaly, there was no stigmata of liver disease and no melena or no decreased urine output.

Patient was initiated on non-invasive ventilation and platelet transfusion for the thrombocytopenia. He was also administered broad spectrum antibiotics along with pulse methylprednisolone on the first day itself as infectious etiology and autoimmune etiology was considered as top in the list for this patient with diffuse alveolar hemorrhage. On day3 of the disease, we found that there was incidental subcutaneous emphysema without obvious pneumothorax or pneumomediastinum which is quite rare by itself. Respiratory consultation was taken, and the reason deemed to be prolonged high pressure NIV use with association of small sealed pneumothorax on the background of stiff lung for DAH. It was managed conservatively as there was no obvious deterioration of respiratory issues.

Workup on leptospirosis was particularly considered in this patient as he did have occupational exposure to toilet/sewage in role in building trade and as evidenced from the Chest X ray and CT chest images; diffuse alveolar hemorrhage being a classical finding in Weil's disease (Fig 1-7). Apart from the routine bloods (Table 1), HIV, atypical pneumonia blood and/or urine screens were negative. Urine analysis revealed proteinuria and microscopic hematuria.

Autoimmune etiology was also considered the tests such as Glomerular basement membrane antibodies – <1.9(0-6.9kU/L), ANCA myeloperoxidase – <0.3 (0-3.4kU/L), ANCA serine proteinase 3 – < 0.7 (0-1.9kU/L), Complement C3 – 0.99 (0.9-1.8g/L) and C4 – 0.11 (0.1-0.4g/L), Immunoglobulin A – 1.04 (0.7-4 g/L), G – 4.58 (7-16 g/L) and M – 0.82 (0.4-2.3 g/L), lupus anticoagulant – 1.02 (0-1.2), IgM beta-2 glycoprotein 1 antibodies – < 1.1 (0.5.9U/ml) were all negative.

Patient also underwent a transthoracic echocardiography which showed a normal ventricular function. The patient underwent a bronchoscopy with BAL; bacterial, mycobacterial, viral and fungal culture findings of the fluid were negative.

In the ITU, patient did have few further episodes of hemoptysis. At that point, even though invasive ventilation, plasma exchange and extracorporeal membrane oxygenation was considered, he gradually improved with the aggressive medical treatment. He was weaned off from the non-invasive ventilation. Patients' platelet count, mild renal and hepatic impairment gradually improved with the treatment. He was deemed clinically stable and stepped down to a ward after 4 days of intensive treatment in the ITU. Eventually, he did make a gradual recovery in the ward and was discharged home in a stable state.

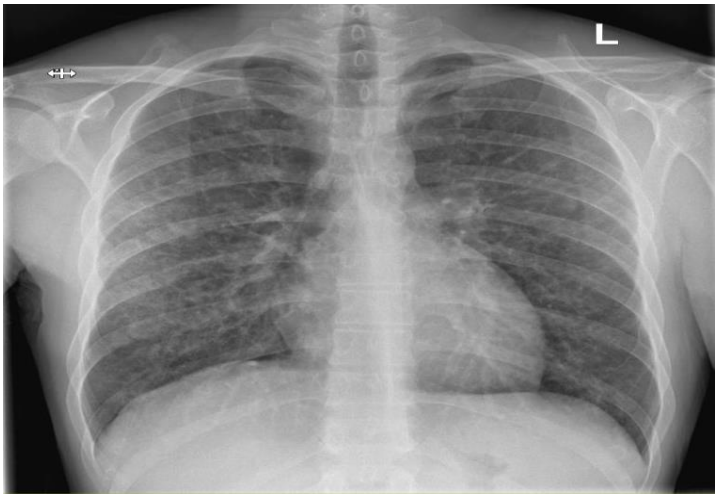

Fig1: Day 1 Chest X ray showing nodular and reticular opacifications bilaterally in the mid and lower zone

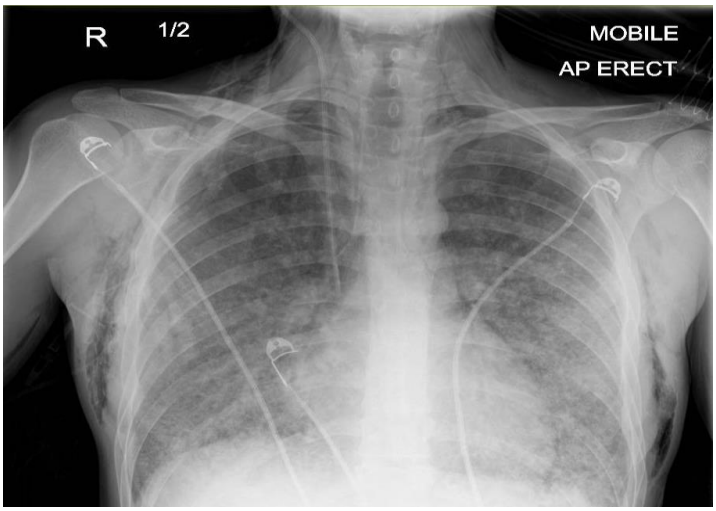

Fig 2: Day 3 – Extensive diffuse bilateral hazy ill-defined opacities, with subcutaneous emphysema projected over the lateral chest wall tracking along the lateral aspect of the neck

Table 1: Laboratory parameters

Laboratory parameters (Reference range)	On admission	Day 1	Day 2	Day 3	Day 4	Day 5
Hemoglobin (130-165 g/L)	89	81	83	79	81	81
White cell count (4-11*10^9/L)	3.1	2.5	6.8	7.9	17.6	13.1
Platelets (150-450*10^9g/L)	37	63	61	73	165	188
PT (9-14 seconds)	11.7	10.5	10.7	11.6	11.0	11.4
APTT (26-38 seconds)	27.9	21.7	21.8	21.1	21.8	22.2
INR (0.8-1.2)	1.0	0.9	0.9	1.0	0.9	1.0
CRP (0-4.9 mg/L)	260	168	72	42	19	9.6
Procalcitonin (0-0.49ng/ml)	>100	55.7	-	-	-	-
Urea (2.5-7.8 mmol/L)	10	10.9	9.0	10.6	9.3	8.3
Creatinine (62-107 mmol/L)	120	110	90	86	63	55
S. Sodium (133-146 mmol/L)	136	141	141	137	139	143
S. Potassium (3.5-5.3mmol/L)	4.0	3.7	3.4	3.8	4.4	4.6
T. Bilirubin	20	42	52	59	58	53
Alkaline phosphatase (30-130 U/L)	80	63	80	101	95	85
Alanine aminotransferase (0-40 U/L)	50	65	55	65	61	59
Magnesium (0.7-1mmol/L)	0.76	0.81	0.60	0.55	0.67	0.64
Phosphate (0.8-1.5mmol/L)	0.94	0.69	0.86	0.96	0.77	1.06
pH (7.35-7.45)	7.44	7.47	7.50	7.51	7.505	7.48
SaO_2 (92-100%)	92.6	96	97	93	92	95
PaO_2 (12-15kPa)	8.44	8.7	9.4	10.4	11.1	8,35
$PaCO_2$ (4.5-6.1kPa)	4.7	4.75	4.98	4.53	4.32	4.64
HCO_3- (22-29mmol/L)	24.5	27.3	29.2	26.6	24.4	26.1
Lactate (0.6-2.5 mmol/L)	2.3	1.0	1.8	3.4	2.8	0.74

CT images on day 2 (Fig 3-7)

Diffuse severe patchy bilateral ground glass opacities, pulmonary consolidative changes, peribronchovascular nodules and peri bronchial thickening.

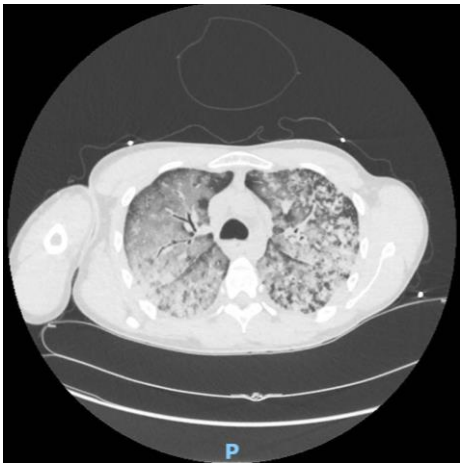

Fig 3: CT chest image.

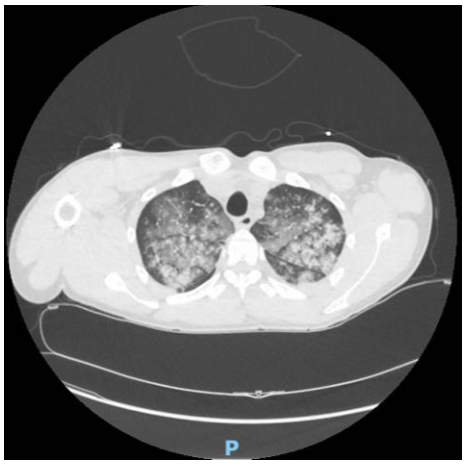

Fig 4: CT chest image

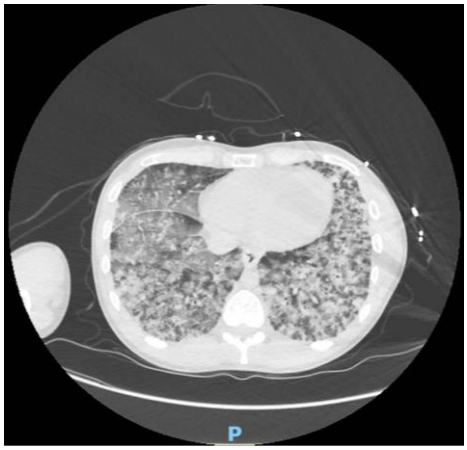

Fig 5: CT chest image.

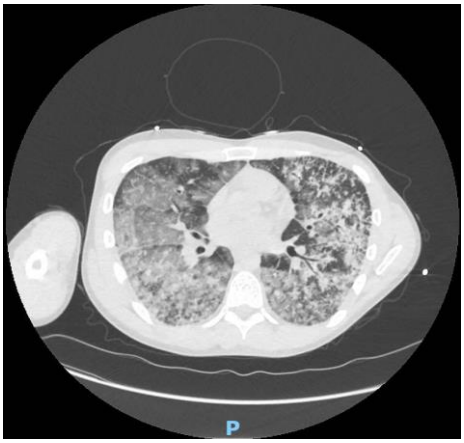

Fig 6: CT chest image

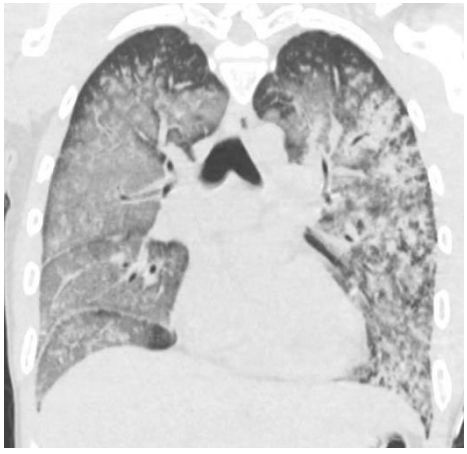

Fig 7: CT chest image

DISCUSSION

In this case report, we discuss a patient who developed pulmonary hemorrhage as the earliest manifestation of Leptospirosis which is a rare occurrence and there are very few mentions of the same in any of the

previous literature[10]. This patient, who even though had a severe pulmonary involvement, did not have the same severity of involvement of other organs such as kidney or liver which again is an unusual picture when we consider Weil's disease [11,12].

Leptospirosis is rare by itself in the UK as there were only 8 confirmed cases in the second quarter of 2023. The occurrence is on the rise as part of the globalization and due to indulgence in water sports [2].

Leptospirosis is a zoonosis which has a potential to cause mortality[13]. The disease is caused by the spirochete species *Leptospira*. Humans incur the disease by coming into contact with the contaminated urine of infected animals. The animals that can transmit the disease include cattle, pigs, horses, dogs and wild animals such as raccoons. Theses animal may not exhibit the signs and symptoms of the disease but act as vectors for the disease[14]. The spirochaete enters the host by invading the abraded skin and mucous membranes. Once it enters the body of the vector, it travels through the lymphatics to reach the blood stream. Eventually, it gets settled in the kidneys and liver.

The disease can manifest in different ways such as a subclinical infection, febrile illness which might be undifferentiated and the most severe form; Weil's disease [5]. Leptospirosis can present in two forms; anicteric and the icteric form. Anicteric form comprises of 90% of patients, who have nonspecific flu-like self-limited illness and is rarely fatal. The icteric form involves the kidney, liver, heart, lung and brain [15]. Lung involvement in isolation is rare and this can mislead clinician to take a different diagnostic and treatment route.

Patients with involvement of the lung can clinically present as cough, dyspnea, chest pain, and hemoptysis. The worst manifestation of lung involvement is the alveolar hemorrhage, severity of which can be related to mortality [16]. The pathophysiology behind alveolar hemorrhage is small vessel vasculitis which is possibly toxin mediated [17]. Mortality with severe pulmonary hemorrhage can go up to 60% [18].

Laboratory investigations include a complete blood count which may reveal leukocytosis secondary to sepsis, thrombocytopenia, and sometimes pancytopenia secondary to macrophage activation syndrome. Liver and renal impairment with elevated levels of serum creatinine, blood urea, bilirubin, and transaminitis are found. Low levels of sodium, potassium and magnesium may be seen which can precipitate cardiac arrythmias. Urinalysis can point towards glomerulonephritis as it may evidence proteinuria, granular casts, and occasionally microscopic hematuria. Chest X-ray may reveal military mottling similar to ARDS and chest CT scan may reveal ground-glass opacities. Diagnosis of leptospirosis is mainly done by serology (IgM ELISA) which has a sensitivity and specificity of 89% and 94% respectively [19] or rapid blood PCR can also be used.

Treatment for leptospirosis is mainly supportive. The efficacy of antibiotics remains unclear but helps in decreasing the disease duration. Antibiotics are recommended, especially for severe disease. Empirically treatment is with a penicillin or doxycycline, but alternatives such as cephalosporins or azithromycin are acceptable [20].

Severe cases with respiratory failure need noninvasive ventilation (BiPAP) or if failing require mechanical ventilation with initiation of lung protective ventilation. Refractory hypoxia might go on to need Extracorporeal membrane oxygenation.

Patients with severe leptospirosis require correction of hypovolemia, hypotension and electrolyte abnormalities. Management of respiratory failure should be done with timely initiation of mechanical ventilation with positive end-expiratory pressure or NIV (BiPAP) and high concentration of inspired oxygen. Extracorporeal membrane oxygenator has been used in refractory hypoxia cases.

Use of steroids for immunomodulation has showed the reduction in need for ventilator support. In our patient, we used pulse dose of methylprednisolone initially followed by the tapering dose of prednisolone considering autoimmune vasculitis as the prime diagnosis of the condition. There were very less studies regarding the usefulness of steroids in severe leptospirosis but considering the clinical picture, it was always wise to start with high dose steroids to combat the initial insult. Whether this approach eventually reduces the severity of leptospirosis that is the matter of further evaluation.

Other helpful immunomodulatory strategies tried including plasmapheresis and immunoglobulin administration [21,22]. Other modalities which were tried in resistant cases of leptospirosis were inhaled nitric oxide, desmopressin, hemofiltration and activated factor VII [23].

CONCLUSION

Leptospirosis should be considered as a differential by clinicians when patient present with the triad of fever, jaundice and renal failure. With the clinical context of exposure to contaminated water, physician should promptly treat it in a timely manner [9]. Severe leptospirosis may lead to pulmonary hemorrhage with mild hepatic or renal impairment and clinicians should be aware of the pulmonary forms.

Declaration by Authors

Ethical Approval: This case report was made from the patient admitted to Luton and Dunstable University Hospital, UK and informed consent was taken from the patient for sharing the anonymous case and necessary images for the sake of educational publication and presentation.

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Conflict of Interest: The authors declare no conflict of interest.

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