INSTRUCTIVE CASE

14 year old male with oliguria and respiratory distress- What is your diagnosis?

AUTHORS: James Robertson C. Pichel, MD*, Dolores D. Bonzon, MD*, Francisco E. Anacleto Jr., MD*
*University of the Philippines College of Medicine- Philippine General Hospital

CORRESPONDENCE:
Dr. James Pichel
Email: docpichel@yahoo.com

CASE PRESENTATION

A 14 year old male from Quezon City Manila was admitted due to oliguria. He presented with 7 days of intermittent fever associated with malaise, photophobia with redness of the eyes. A few hours before admission, he developed repetitive vomiting with decreased urine output. He denied any muscle pain, change in his sensorium or seizure episode. He had a history of wading in flooded waters.

On physical examination, the patient was lethargic and in hypovolemic shock. The heart rate was 110 beats per minute, blood pressure then was 70/40mmhg, respiratory rate was 25 breaths/minute, and axillary temperature of 37.2 ^{0}C. After receiving a total volume of 60ml/kg of isotonic solution, his vital signs were stable and he was well-hydrated. However, he was still oliguric. A furosemide bolus (2mkdose) was given with no initial improvement of urine output.

Initial laboratory results showed: haemoglobin 124mg/dl, hematocrit 0.35, white blood cell count (WBC) 11,900/mm^3, and platelet count of 117,000/mm^3. Blood chemistries were the following; sodium of 135 mmol/l, potassium 3.1 mmol/l, chloride 97mmol/l, calcium 1.86 mmol/l, albumin 24 g/L, aspartate aminotransferase 50 U/L, alanine transaminase 95 U/L, alkaline posphatase 73 U/L, blood urea nitrogen 17.5 mmol/L, creatinine 460 umol/L, total bilirubin 151 umol/L, direct bilirubin 33.4 umol/L , indirect bilirubin 19 umol/L, protime with inr of 1.2, activated partial thromboplastin time 51.6 (control 34.7) and glucose 5mmol/L. Urinalysis showed glucosuria, albuminuria, with coarse, waxy, and fine granular cast. Sonography of the kidneys reveals bilateral enlarged kidneys but with normal parenchymal echogenicity. Chest radiography is described as having bilateral infiltrates (See Figure 1). His paO^2/fiO^2 ratio 508 mmhg. 2D echocardiography was unremarkable. Emergency acute peritoneal dialysis (PD) was initiated due to oliguria and azotemia using a rigid catheter insertion. However, on the 12th hour of hospital stay, he showed signs of respiratory distress with neck vein engorgement with rales on both lung fields. Endotracheal (ET) intubation was done and he received ventilator support. There was note of massive bloody pulmonary secretions per ET. The arterial blood gas shows uncompensated respiratory acidosis (ph 7.04, pco2 73.9) with uncorrected hypoxemia (50.8). What is your diagnosis?

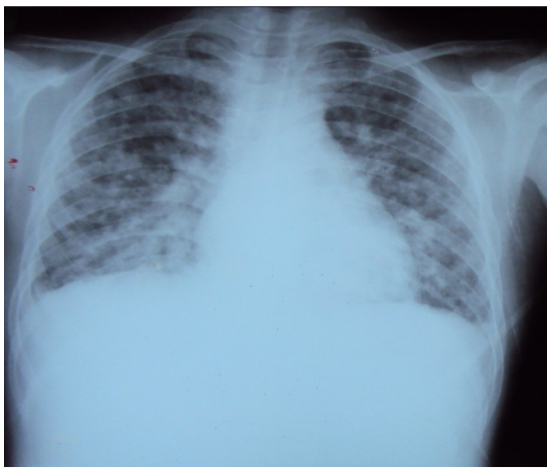

Figure 1. Chest x-ray of 14 year old teen presenting with oliguria and hemoptysis.

Downloaded from www.pidsphil.org

DIAGNOSIS

Leptospirosis with acute kidney injury and pulmonary hemorrhage

CONFIRMATION OF DIAGNOSIS:

A microscopic agglutination test (MAT) was performed which showed a fourfold increase between the acute and convalescent phase.

DISCUSSION

Leptospirosis is a spirochetal zoonotic disease, and in severe cases it can involve most organ systems of the human body. Globally, more cases are seen in tropical and developing countries[1]. Incidence rates are underestimated, due to the lack of awareness of the disease and relatively inaccessible and insufficiently rapid diagnosis[1].

This case represents an unusual clinical course because the patient had severe disease yet was without jaundice, muscle pain, or meningitis. The patient showed evidence of acute involvement of the kidneys and lungs. With fever, hypotension, and thrombocytopenia, severe dengue was suspected. Other differential diagnoses for his rapidly progressive renal failure were hemolytic uremic syndrome and thrombocytopenic purpura. However, he did not show any evidence of microangiopathic anemia or neurologic manifestations. The platelet count increase rapidly with no evidence of rhadomyolysis yet hemoptysis occured. Clinical manifestation of leptospirosis can range non-specific urinary findings to acute renal failure. Pulmonary involvement may range from a simple cough to pulmonary hemorrhage and acute respiratory distress syndrome. Renal involvement in leptospirosis is usually due to the icterohemorrhagiae serogroup[7].Thus MAT results could suggest which serogroup caused the infection[8].

The renal involvement usually affects the tubulo-interstitial area which can cause acute tubular necrosis. Glomerular changes may be present but are not remarkable. Hemodynamic alterations, immune response and direct nephrotoxicity are responsible for the development of renal lesions[3]. Interstitial nephritis with tubular necrosis is the basic pathology, and vasculitis is observed in the acute phase of the disease[3]. Reports have shown that the pathogenesis of renal lesion is related to the migration of the organism and production of their virulent toxin including those that are released from the lysis of the microorganism[8]. Other than the invasiveness of leptospires, there are several bacterial components, including lipopolysaccharides, peptidoglycans and outer membrane proteins consisting mainly of glycolipoproteins, can activate monocytes through receptors, especially CD3. Pro-inflammatory cytokines, including tumour necrosis factor alpha (TNFα) and interleukins, are released and induce the inflammatory process through generation of several vasoactive and inflammatory mediators and adhesion molecules[3].

The case fatality rate of leptospirosis with acute renal failure is high in spite existing treatments, including dialysis, plasma exchange, and continuous renal replacement therapy[9]. The 1995 outbreak in Nicaragua has raised awareness that leptospirosis can lead to severe pulmonary form of leptospirosis (SPFL) or severe pulmonary hemorrhagic syndrome (SPHS). It was first identified in South Korea (10) and is now recognized in other parts of the world.

The reason for the emergence of SPHS is still not understood. There was a report of the emergence of severe pulmonary hemorrhagic syndrome (SPHS) in slum communities in Salvador, Brazil. In their report, it did not identify SPHS before 2003, although 47 cases were identified from 2003 through 2005; the case-fatality rate was 74%. By 2005, SPHS caused 55% of the deaths due to leptospirosis[4]. The SPHS is fatal which can lead to death in less than 72 hours. The respiratory symptoms usually observed on the 4^{th} to 6^{th} day of illness. This can be due to leak into the capillary endothelium. Others consider thrombocytopenia as a cause of bleeding but it

Downloaded from www.pidsphil.org

was not significantly low in our patient. The toxic substance produced by leptospirosis such as endotoxins or cytokines such as tissue necrosis factor (TNF), seems to play an important role in the pathogenensis of this syndrome[11].

In leptospirosis, dengue, Hantavirus infections and sepsis, there is an intense leak of fluid and proteins into the intravascular space. However, in leptospirosis, there is also extrusion of erythrocytes, resulting in a picture of widespread hemorrhagic infiltrates. In the lungs, the capillary endothelium lesion is manifested as pneumonitis with hemorrhagic infiltrates and edema in the alveoli and septa[5]. Alveolar invasion by edema fluid and erythrocytes importantly alter gas exchange, ultimately leading to hypoxemia. In our patient, he initially showed only a mild respiratory problem and had unremarkable chest x ray findings. The evolution, was very rapid, and in few hours he developed dyspnea, respiratory distress, accompanied by massive bleeding per endotracheal tube. At this point his arterial blood gas showed severe hypoxemia and repeat chest x-ray showed extensive bilateral infiltrates with areas of alveolar filling. These radiologic findings can also be seen in viral pneumonia, bacterial pneumonia, military tuberculosis, pulmonary haemorrhages, and in acute respiratory distress syndrome (ARDS)[12]. Nicodemius and colleague considered that there is a presence of direct action of the microorganism on the lung parenchyma and vascular endothelium[13].

Clinical suspicion of alveolar hemorrhage is fundamental in initiating early intervention with hemodynamic and respiratory support including corticosteroid therapy. The benefits of corticosteroids has been extensively studied and accepted in acute lung injury and ARDS. The evidence for its use in pulmonary leptospirosis is confined to case reports and brief studies from single bolus to pulse therapy[14].

In conclusion, medical practitioners should have a high index of suspicion of leptospirosis for all children who presents with high grade fever and flu-like symptoms but with no signs of glomerulonephritis, coupled with thrombocytopenia, and azotemia. BUN, serum creatinine and a complete blood count are mandatory laboratory tests in this case. Although, its is unusual in children, clinicians should be aware of the severe pulmonary complications of leptospirosis which can rapidly progress and may lead to death in less than 72 hours.

PROLOGUE

The patient was initially treated with IV crystalline penicillin at 3M IU/day given in 6 divided doses. Emergency acute peritoneal dialysis was performed. Pulse methylprednisolone therapy was given for the pulmonary problem.

On his 3rd hospital stay, there was clinical and laboratory improvement with better oxygen saturation. He was discharged after 9 days with normal renal and pulmonary function.

REFERENCES

1. Bharti AR, Nally JE, Ricaldi JN, Matthias MA, Diaz MM, Lovett MA, Levett PN, Gilman RH, Willig MR, Gotuzzo E, Vinetz JM. Leptospirosis: a zoonotic disease of global importance. Lancet Infect Dis 2003; 3: 757–771.
2. Coursin DB, Updike SJ, Maki DG. Massive rhabdomyolysis and multiple organ dysfunction syndrome caused by leptospirosis. Intensive Care Med 2000; 26: 808–812.
3. Visith S, Kearkiat P. Nephropathy in leptospirosis. J Postgrad Med 2005; 51: 184–188.
4. Gouveia E, John Metcalfe, Ana Luiza F. de Carvalho, Talita S.F. Aires, et al. Leptospirosis related Severe Pulmonary Hemorrhagic Syndrome, Salvador, Brazil. Emerging Infectious Diseases 2008; 14: (3): 505-508.
5. Yersin C, Bovet P, Merien F, Clément J, Laille M, Van Ranst M, et al. Pulmonary haemorrhage as a predominant cause of death in leptospirosis in Seychelles. Trans R Soc Trop Med Hyg 2000; 94:71–76.
6. Friedland JS, Warrell DA. The Jarisch-Herxheimer reaction in leptospirosis: Possible pathogenesis and review. Review of Infectious Diseases 1991; 13: 207-210.
7. Tappero JW, Ashford DA, Perkins BA. Leptospira species (leptospirosis). In Mandell GL, Bennet JE and Dolin R, editors. Principles and practice of infectious

Downloaded from www.pidsphil.org

diseases, 5th edn. McGraw-Hill, New York, 2000; p. 2495–2501.Levett PN.
8. Usefulness of serologic analysis as a predictor of the infecting serovar in patients with severe leptospirosis. Clin Infect Dis 2003; 36:447–452.
9. Peces R. Acute renal failure in severe leptospirosis. Nephrol Dial Transplant 2003; 18: 1235–1236.
10. Park SK, Lee SH, Rhee YK, Kang SK, Kim KJ, Kim MC, et al. Leptospirosis in Chonbuk Province of Korea in 1987: a study of 93 patients. Am J Trop Med Hyg 1989; 41:345–51.
11. Dobrina A, Nardone E, Vecile M, Cinco M, Patriarca P. *Leptospira icterohaemorrhagiae* and leptospire peptidoglycans induce endothelial cell adhesiveness for polymorphonuclear leukocytes. Infection and Immunity 1995; 63:2995-2999.
12. Gonçalves AJ, Carvalho JE, Silva JB, Rozembaun R, Vieira AM. Hemoptisis and the adult respiratory distress syndrome as the causes of death in leptospirosis. Changes in the clinical and anatomopathological patterns. Revista da Sociedade Brasileira de Medicina Tropical 1992; 25:261-270.
13. Nicodemo AC, Duarte MIS, Alves AF, Takamura CFH, Santos RTM, Nicodemo EL. Lung lesions in human leptospirosis: microscopic, immunohistochemical, and ultrastructural features related to thrombocytopenia. American Journal of Tropical Medicine and Hygiene 1997; 56**:**181-187.
14. Courtin JP, Carre P, Poubeau P, et al. Diffuse alveolar hemorrhage and myositis in icterohemorrhagic leptospirosis. Rapid control by a single bolus of Corticosteroid. Rev Mal Respir 1994; 11: 601-3.

Downloaded from www.pidsphil.org