

CASE REPORT

Pulmonary Hemorrhage Associated With Severe Leptospirosis – The Role Of Low Dose Intravenous Methylprednisolone

Thiam Seong Christopher Lim¹, Tan Yi Jun², Then Ru Fah³

1 Unit of Nephrology, Department of Medicine, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia

2 Department of Medical, Serdang Hospital, Jalan Puchong, 43000 Kajang, Selangor, Malaysia

3 Department of Nephrology, Serdang Hospital, Jalan Puchong, 43000 Kajang, Selangor, Malaysia

ABSTRACT

Leptospirosis has a wide range of presentation which ranges from mild flu-like symptoms, to severe form including renal failure, liver failure, and hemorrhage. Pulmonary involvement can progress from subtle clinical features to life threatening pulmonary hemorrhage and acute respiratory distress syndrome. Although benefits of corticosteroids in adult respiratory distress syndrome have been proven and accepted, evidence for use of corticosteroids in pulmonary leptospirosis is still limited. Given the vasculitic nature of severe leptospirosis, it has been proposed that addition of intravenous corticosteroid therapy, particularly in cases of pulmonary involvement is beneficial. We report a case of leptospirosis with suspected pulmonary hemorrhage which deteriorates after a few days of admission in our tertiary hospital. We have demonstrated that the prescription of a lower dose of corticosteroid than what was widely reported in the literature can equally led to a satisfactory recovery of the pulmonary hemorrhage.

Keywords: Leptospirosis, Pulmonary hemorrhage, Acute respiratory distress, Leptospirosis pulmonary hemorrhage syndrome

Corresponding author:

Christopher Lim

Tel: +60389472568

E-mail: drchrislim@gmail.com

INTRODUCTION

Leptospirosis, known to be a zoonotic disease, is caused by pathogenic spirochetes of genus *Leptospira*, which occurs in both temperate and tropical regions. Human transmission is usually through exposure of abraded skin or mucous membranes to fresh water or soil contaminated with the urine of an animal that is a chronic carrier. Patients can present with predominant pulmonary symptoms, ranging from breathlessness, cough, hemoptysis, and chest pain to acute respiratory distress syndrome (ARDS). These frequently happen during fourth to sixth days of illness.

The exact cause of pulmonary hemorrhage is still debatable. Toxin mediated process induces vascular injury causing vasculitis have been proposed to be the main causative factor in the pathogenesis of leptospirosis. This vascular injury primarily affects capillaries. It is found that linear deposition of immunoglobulins like IgA, IgM and IgG and complements on the alveolar surface may be part of the pathogenesis of LPHS.

The administration of intravenous methylprednisolone in a severely ill patient with LPHS is based on the immune mediated pathogenesis of the disease which can potentially decrease the morbidity and mortality. Hence, early administration of methylprednisolone in Leptospirosis pulmonary hemorrhage syndrome has been proposed as part of the treatment plan.

CASE REPORT

A twenty-two-year old gentleman with history of swimming at a water fall presented to the emergency department with a history of fever and diarrhea of four days duration. Upon examination, he was dehydrated and lethargy. His vital signs revealed blood pressure of 120/80mmHg, heart rate of 120 beats per minute and temperature of 38.3 Celcius. Abdominal and neurologically examination was unremarkable.

His systemic examinations were unremarkable. Initial blood investigations shows hemoglobin 13g/dL, hematocrit 37%, total white blood cell $3.8 \times 10^9/L$, platelet $103 \times 10^9/L$, urea 7 mmol/L, creatinine 132 $\mu\text{mol/L}$ and creatinine kinase 800 U/L. Leptospirosis IgM Antibody was positive. He was diagnosed as having leptospirosis with acute kidney injury. Intravenous ceftriaxone 2 gram once daily was promptly started.

On day three of admission, patient was found to be tachypnoeic and was intubated for impending respiratory collapse. Further investigation shows patient develops pulmonary hemorrhage as evidence by chest X-ray findings of bilateral diffuse alveolar space shadowing (Fig. 1) and the presence of fresh blood upon suctioning of the endotracheal tube. There was worsening of blood parameters with reducing platelet count and rapid drop of hemoglobin to 10.9 g/dL, platelet $26 \times 10^9/L$ and total white $6.1 \times 10^9/L$. Intravenous methylprednisolone 500mg once daily was started and continued for three days. His condition improved and he was extubated within one week. Repeated chest X-ray (Fig. 2) showed drastic improvement after intravenous methylprednisolone. He was discharged subsequently well.

DISCUSSION

Leptospirosis is one of the most prevalent zoonosis in the world, especially in tropical country. It is a transmissible disease caused by pathogenic spirochetes of the genus *Leptospira* which is present in animals' urine such as mice, cows and buffaloes. Although occupational exposure in farm workers, pet shop owners, veterinarians as well as field agricultural workers accounts for majority of human case of leptospirosis, lately it has also well known to be a disease of recreation. On the other hand, urban dwellers may be infected through exposure to rat urine. The disease can be transmitted through open wound, skin, and even through mucous membrane of the eyes and mouth, that has been in the contaminated water for a prolong period of time. Our

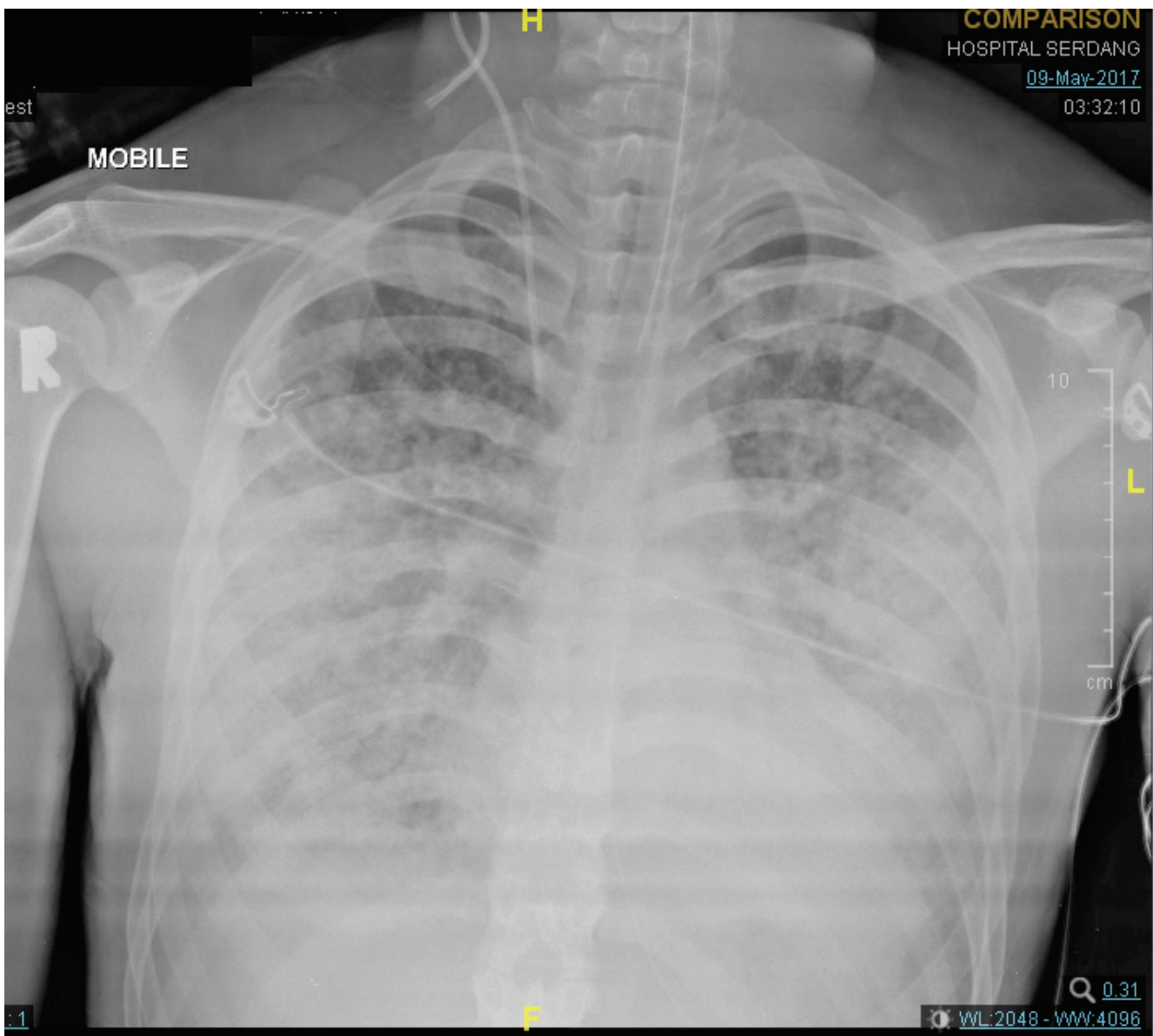


Fig. 1 Chest X-ray where it showed sudden and diffuse lung infiltration

patient has a history of jungle trekking and swimming in the waterfall that makes him high risk to be infected with leptospirosis. The diagnosis was confirmed with *Leptospira* antibody serology.

The symptoms of leptospirosis are usually mild in about 90% of cases. They tend to appear suddenly about seven to fourteen days after infected by the *leptospira* bacteria. However, symptoms can develop as early as 2 and as late as 30 days after exposure. The symptoms consist of mild headache, myalgia, cough, loss of appetite, nausea and vomiting. These symptoms will resolve within 5 to 7 days. However, about 10% of cases progress to severe leptospirosis, which is also called Weil's disease. Severe leptospirosis usually develops one to three days after the milder symptoms have resolved. In severe cases

organs such as brain, liver, kidneys, heart and lungs are involved.

Patients with leptospirosis may present with mainly respiratory symptoms and they usually develop between fourth and sixth day of illness. The disease deteriorates rapidly and may be life threatening in less than 72 hours. Although LPHS is not uncommon, it has a rapid and severe course with high mortality rates of 30-60%.

Evidence is rather unclear for the use of corticosteroids in the treatment of severe leptospirosis. The rationale for their use in such situation is that, severe immunological response that is triggered can results in multi-organ dysfunction. Glucocorticoid-based therapy such as intravenous methylprednisolone can reduce the

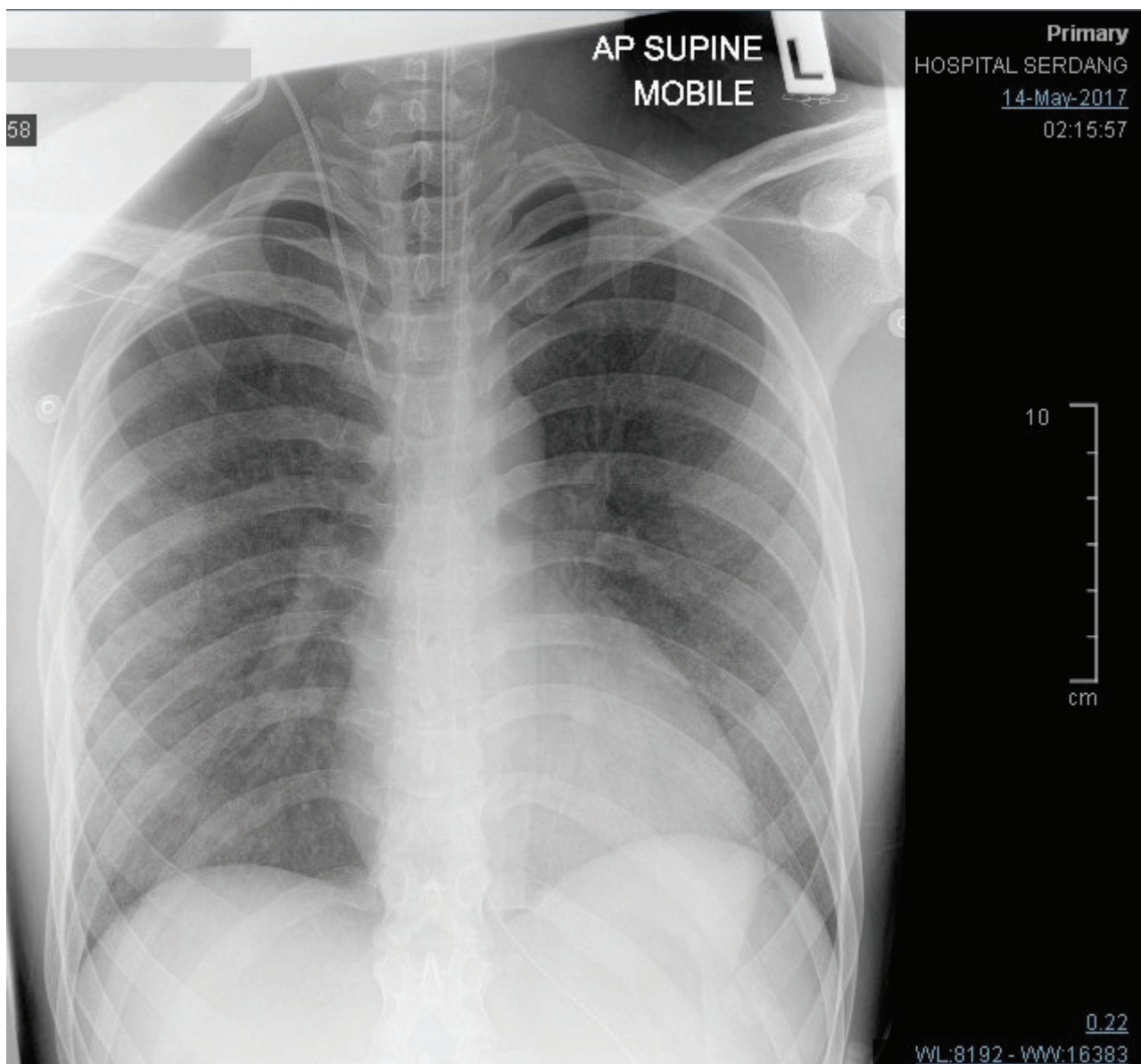


Fig. 2 Rapid resolution of the lung infiltration after intravenous methylprednisolone was given

production of cytokine and TNF- α , which in turn tone down the inflammatory response of the disease, and therefore, ameliorate the adverse effect of immune-mediated response. In fact, there are a number of cases reported supports the role of methylprednisolone in LPHS (1).

In this case, the patient is diagnosed to have suffered from LPHS on third day of admission. His respiratory symptoms developed rapidly and intravenous corticosteroid was administered for a consecutive of three days duration. Patient responded well to intravenous corticosteroid.

A study by Trivedi et al. showed that 61.53% of the pulmonary leptospirosis patients has significant improvement in the lung disease after receiving early course (within the first 12 hours) intravenous methylprednisolone 1 gram daily for 3 days. In the same study, intravenous methylprednisolone is also beneficial in severe cases whereby the mortality has decreased from 85.71% to 33.33% (2). Others studies has also concluded that pulmonary involvement in case of leptospirosis can be treated successfully with less expensive and less complicated interventions, which is corticosteroid (3). As for the dosing of methylprednisolone, many studies proposed that it should be given at a high dose of 1 gram IV daily for 3 days, followed by oral prednisolone at a dose of 1mg/kg/day for 7 days (4). Corticosteroids has been shown to reduce or delay the need for ventilator support and serves an important role in infrastructure limited settings. For our case, we are the first to report that usage of a much lower dose of 500mg once daily for 3 days without maintenance dose can equally lead to a full recovery from LPHS. In fact, our patient has made a complete and tremendous recovery from leptospirosis.

However, a recent systemic review studying the role of high dose corticosteroids in severe leptospirosis yielded mixed results. Four studies revealed a benefit of corticosteroids in treating severe disease with pulmonary involvement when administered early in the course of the disease, but these studies had several methodological limitations. Only the randomized controlled trial study showed that corticosteroids are ineffective and may increase the risk of nosocomial infections. The author concluded that there is no strong evidence to suggest that high dose corticosteroids are effective in severe leptospirosis, and a well-designed randomized clinical trial is needed to resolve this (5). Moreover, steroids used in LPHS carries the risk of opportunistic infections and adverse effects like hyperglycemia, abdominal discomfort, skin rash and hot flushes.

Other treatments proposed for LPHS include immunomodulation therapy like plasmapheresis, cyclophosphamide and plasma exchange. All patients with LPHS should be mechanically ventilated in a timely

manner. In fact, extracorporeal membrane oxygenation (ECMO), a method of cardiopulmonary support which relieves lungs of its gas exchange function, has been used to be given to patients that are difficult to ventilate in spite of maximal mechanical ventilation.

There is limitation in our study. Our results may not be able applicable to a wider or different population. Nevertheless, the outcome from our study, allow us to form hypothesis that a small dose of corticosteroids could be one of the viable treatment options for LPHS.

CONCLUSION

Our case highlights the need for suspicion of LPHS when patient develop hemoptysis or respiratory distress. Early recognition and high suspicious of diagnosis is important as administration of corticosteroid in time, in addition of broad-spectrum antibiotics, mechanical ventilation and early supportive care can lead to successful treatment, shortened hospital stays, reduction of morbidity and morbidity. Targeting the vasculitic nature of the disease via the smallest dose of corticosteroid has demonstrated to be effective as evidence by our patient's response and improvement to treatment.

ACKNOWLEDGEMENT

None.

REFERENCES

1. Thunga G, John J, Sam KG, Khera K, Khan S, Pandey S, et al. Role of high-dose corticosteroid for the treatment of leptospirosis-induced pulmonary hemorrhage. *J Clin Pharmacol*. 2012;52(1):114-6.
2. Trivedi SV, Chavda RK, Wadia PZ, Sheth V, Bhagade PN, Trivedi SP, Clerk AM, Mevawala DM. The role of glucocorticoid pulse therapy in pulmonary involvement in leptospirosis. *J Assoc Physicians India*. 2001;49:901-3.
3. Abraham Ittyachen VK, Lakshmanakumar CK, Eapen MR, Joseph. Methylprednisolone as adjuvant in treatment of acute respiratory distress syndrome owing to leptospirosis. *Indian J Crit Care Med*. 2005;9(3):133-136.
4. Shenoy VV, Nagar VS, Chowdhury AA, Bhalgat PS, Juvele NI. Pulmonary leptospirosis: an excellent response to bolus methylprednisolone. *Postgrad Med J*. 2006; 82(971):602-6.
5. Rodrigo C, Lakshitha de Silva N, Goonaratne R, Samarasekara K, Wijesinghe I, Parththipan B, Rajapakse S. High dose corticosteroids in severe leptospirosis: A systematic review. *Trans R Soc Trop Med Hyg*. 2014;108(12):743-50.