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CASE REPORT

# Role of Low Dose Intravenous Methylprednisolone in Pulmonary Hemorrhage Associated with Severe Leptospirosis

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## ABSTRACT

Leptospirosis, an emerging zoonosis endemic in Malaysia, presents with diverse clinical manifestations, ranging from mild to potentially fatal illness. Pulmonary involvement in leptospirosis, particularly pulmonary hemorrhage, poses a significant risk of mortality, prompting exploration of various treatment strategies. While high-dose corticosteroid therapy has demonstrated efficacy in some studies, data on the use of low-dose corticosteroids in pulmonary leptospirosis remain scarce. Here, we report a case of successful treatment with low-dose methylprednisolone in a patient diagnosed with Weil's disease and pulmonary hemorrhage. The patient, initially presenting with fever, vomiting and hemoptysis, rapidly deteriorated, necessitating intubation due to respiratory distress. Prompt initiation of low-dose methylprednisolone alongside antibiotic therapy resulted in clinical improvement, resolution of pulmonary hemorrhage, and normalization of laboratory parameters. This case highlights the potential efficacy of low-dose corticosteroid therapy in managing severe pulmonary involvement in leptospirosis, offering insights into alternative treatment modalities for this challenging condition. Further studies are warranted to elucidate the optimal dosing and timing of corticosteroid therapy in leptospirosis-associated pulmonary complications.

## INTRODUCTION

The fluctuating incidence rates of leptospirosis in Malaysia from 2010 to 2020, ranging between 8.63 and 17.2 cases per 100,000 individuals, emphasize the critical importance of studying this disease. (Philip & Ahmed, 2023). Most cases of leptospirosis are self-limited while some progressed to severe disease with multi-organ involvement. Two clinical syndromes have been described, icteric or anicteric. Anicteric leptospirosis is typically a biphasic illness, with acute (septicemic) phase and immune phase. Icteric leptospirosis, also known as Weil's disease, occurring in 5-10% of cases, are often rapidly progressive and have a fulminant course. Pulmonary hemorrhage can often happen in icteric leptospirosis and carries a high mortality rate.

Literature reviews have demonstrated that high dose steroid (IV Methylprednisolone 1g OD) used in the early phase of illness reduce mortality and morbidity (Shenoy et al., 2006; Trivedi et al., 2001). Nevertheless, it is crucial to acknowledge that high-dose steroid therapy is associated with potential adverse effects, particularly an elevated susceptibility to infection among critically ill patients. In our case report, we present the application of low-dose steroid therapy in a young male diagnosed with leptospirosis and pulmonary hemorrhage.

## CASE REPORT

A 30-year-old gentleman with no known medical illness, presented to the emergency department ten days after jungle trekking and swimming in a river. His main complaints were fever, arthralgia, myalgia, vomiting and redness of both eyes for five days. The alarming symptom that brought him to medical attention was one episode of hemoptysis.

On examination, the patient was restless with acidotic breathing. He was noted to be jaundiced with conjunctival suffusion, blood pressure 88/60 mm Hg, heart rate 140 beats per minute, temperature 38.6 , oxygen saturation 98% under room air and respiratory rate 28 breaths/min. Other systemic examinations were unremarkable.

Fluid resuscitation was commenced and intravenous (IV) Ceftriaxone 2g was served, however the patient soon deteriorated and desaturated to oxygen saturation of 80% under room air, requiring high flow mask oxygen 15 L/min.

Blood investigation revealed thrombocytopenia (Platelet 59X10^3 µmol/L), acute kidney injury (Serum creatinine 395 µmol/L) and direct hyperbilirubinemia (40 µmol/L). Arterial blood gas showed severe metabolic acidosis with pH 7.01, bicarbonate 8.6 mmol/L and lactate 14 mmol/L. Liver enzymes and coagulation parameters were within normal range. Chest X-ray was unremarkable. Leptospirosis IgM ELISA test was negative. Nonetheless, severe leptospirosis was still suspected, taking into consideration of recent water activities.

Within 12 hours of admission, he was intubated due to worsening respiratory distress. Post intubation, fresh blood was noted upon endotracheal suction. Repeated chest x-ray showed bilateral diffuse alveolar space shadowing, consistent with pulmonary hemorrhage. IV Methylprednisolone 500 mg daily was administered.

The patient developed another episode of hemoptysis the next day. Blood parameters revealed worsening thrombocytopenia (Platelet 16 µmol/L) and direct hyperbilirubinemia (217 µmol/L), deteriorating kidney function (Serum creatinine 463 µmol/L) as well as rhabdomyolysis (Creatine kinase enzyme 2188 u/L). Repeated leptospirosis ELISA test IgM turned out to be positive.

After three days of steroids and antibiotic, he was able to wean off ventilator with chest

X-ray showing resolution of pulmonary hemorrhage. Daily IV Methylprednisolone 500 mg was served for a course of three days and maintenance dose was deemed not indicated due to significant improvement in clinical condition. IV Ceftriaxone was continued for a total of seven days. Notably within the next few days, platelet count, bilirubin and creatine kinase had normalized, and acute kidney injury recovered without requiring dialysis. The patient was discharged well on day 10 of admission.

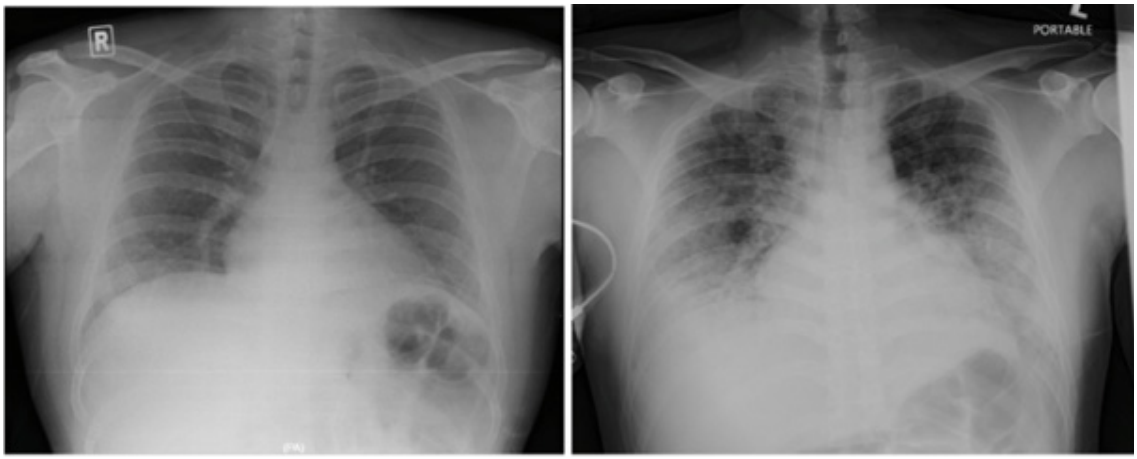


**Figure 1:** Chest X-ray (Left: Upon presentation, clear; Right: 12 hours post admission, bilateral diffuse alveolar shadowing).

## DISCUSSION

Our case report highlights the successful management of a 30-year-old male presenting with severe leptospirosis complicated by pulmonary hemorrhage. This case underscores the importance of early recognition and treatment initiation in combating this potentially fatal disease.

Leptospirosis, endemic in Malaysia, often presents with nonspecific symptoms, posing a diagnostic challenge. In our patient, the initial presentation of fever, arthralgia, myalgia, and vomiting rapidly progressed to pulmonary hemorrhage, necessitating prompt intervention. This progression is consistent with the literature, which underscores the need for heightened clinical suspicion and early initiation of appropriate therapy (Centers for Disease Control and Prevention, 2019).

While antibiotics like doxycycline and penicillin are recommended for leptospirosis treatment (Centers for Disease Control and Prevention, 2019), conflicting evidence regarding their efficacy necessitates exploring alternative therapeutic options (Brett-Major & Coldren, 2012; Charan et al., 2013; Watt et al., 1988). Despite initial negative serological tests, our patient received empirical antibiotic therapy, which likely contributed to his favorable outcome.

Pulmonary hemorrhage in leptospirosis, particularly in icteric forms (Weil's disease), is a severe complication with high mortality (Taylor et al., 2015). High-dose corticosteroids have been traditionally used to manage this, reducing mortality and morbidity when administered early. Intravenous methylprednisolone at 1g daily for three days, followed by oral prednisolone at 1mg/kg/day for seven days, has been shown to effectively treat pulmonary leptospirosis, reducing the need for ventilator support and improving outcomes if given within the first 12 hours of symptoms (Shenoy et al., 2006; Trivedi et al., 2001).

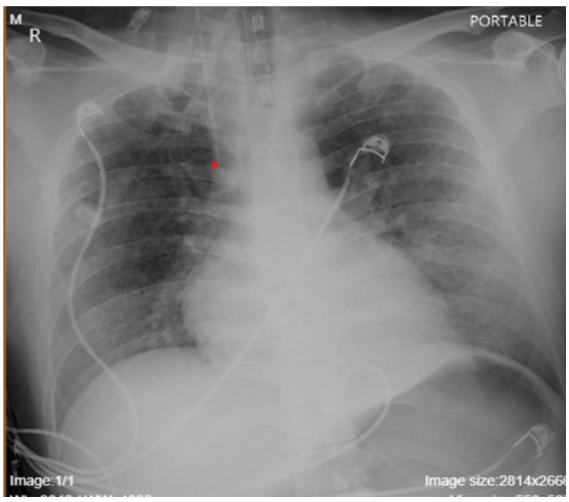


**Figure 2:** Resolution of chest X-ray changes after three days of IV Methylprednisolone 500mg OD.

However, caution is necessary when using high-dose corticosteroids due to the risk of nosocomial infections. Hingorani et al. (2016) reported two cases of severe invasive fungal infections following steroid treatment for pulmonary leptospirosis. One patient received IV methylprednisolone 125 mg every 8 hours for six days, and the other received two bolus doses of 250 mg. Notably, only these two patients among others in the same ICU developed severe fungal infections. Further research is needed to determine the causal relationship between steroid use in leptospirosis and invasive fungal infections. Therefore, steroid use in pulmonary leptospirosis should be judicious, employing the lowest effective dose for the shortest duration possible.

Recent studies and case reports have suggested that lower doses of corticosteroids might be equally effective while potentially reducing the risk of adverse effects. For instance, Lim et al. (2018) reported successful treatment of pulmonary hemorrhage with a lower dose of 500 mg methylprednisolone once daily for three days without a maintenance dose, achieving complete recovery. Similarly, Kularatne et al. (2010) demonstrated the efficacy of 500 mg IV methylprednisolone daily for three days followed by 8 mg orally for five days in a cohort of severely ill patients, showing reduced mortality and improved outcomes.

Further supporting our approach, Thunga et al. (2012) and Pedro (2020) reported successful outcomes using tapering doses of methylprednisolone and equivalent hydrocortisone dosing, respectively, underscoring the flexibility and potential efficacy of various low-dose corticosteroid regimens.

Our patient's management aligns with these findings. The administration of 500 mg IV methylprednisolone daily for three days resulted in significant clinical improvement, resolution of pulmonary hemorrhage, and normalization of laboratory parameters without the need for a prolonged maintenance dose. This result suggests that lower doses of corticosteroids can be effective in managing severe pulmonary leptospirosis, potentially offering a safer alternative to high-dose regimens.

The successful outcomes observed across various steroid regimens underscore the adaptability of treatment approaches in managing pulmonary hemorrhage associated with leptospirosis. Despite differences in dosing and administration, these regimens share a common goal of modulating the immune response to mitigate pulmonary damage.

## CONCLUSION

Our case report demonstrates the successful use of low-dose methylprednisolone in managing severe leptospirosis with pulmonary hemorrhage. The findings underscore the potential of low-dose methylprednisolone as a viable treatment option for pulmonary complications in leptospirosis, offering a balance between efficacy and safety. However, it is crucial to note that our patient, like those in similar case reports, was young and without comorbidities. Further research is needed to

validate these results across diverse patient populations and to establish standardized protocols for dosing and duration.

## CONFLICT INTEREST

We have no conflict of interest to disclose.

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