# Successful utilization of plasma exchange and corticosteroids in the management of thrombotic microangiopathy and acute respiratory distress syndrome secondary to leptospirosis-a case report

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## ABSTRACT

**Background:** Leptospirosis, a zoonotic infection caused by *Leptospira* bacteria, presents with symptoms ranging from mild flu-like signs to severe multiorgan failure. A rare but serious complication of leptospirosis is thrombotic microangiopathy (TMA). This case report discusses the treatment of a 52-year-old female with leptospirosis complicated by TMA, highlighting the effectiveness of plasma exchange and corticosteroids in her recovery.

**Case Presentation:** A 52-year-old female presented with a five-day history of fever and progressive shortness of breath. Upon admission, she had tachypnoea, a partial pressure of oxygen in arterial blood (PaO2) to the fraction of inspiratory oxygen concentration (FiO2) ratio of 61, and bilateral lung infiltrates, requiring invasive mechanical ventilation and prone positioning. Laboratory tests revealed anemia, thrombocytopenia, schistocytes, and elevated lactate dehydrogenase, suggesting TMA. The patient also showed elevated liver enzymes and signs of a potential diagnosis of thrombotic thrombocytopenic purpura, though serological tests for tropical infections, including leptospirosis, were initially negative. The patient was treated with plasma exchange and corticosteroids, leading to improvements in her hematological parameters and acute respiratory distress syndrome (ARDS). However, she developed unexplained blood pressure and heart rate fluctuations, and electroencephalogram confirmed focal seizures, which were treated with levetiracetam and propofol. Subsequent serological testing confirmed leptospirosis with positive Immunoglobulin M antibodies and Leptospira polymerase chain reaction testing. The patient was treated with doxycycline and ceftriaxone, resulting in significant improvement, successful extubation, and eventual discharge.

**Conclusion:** This case highlights the challenges of managing leptospirosis complicated by TMA and severe ARDS. Plasma exchange and corticosteroids were essential in the patient's recovery. The initial delay in diagnosis due to negative serological tests underscores the importance of maintaining a high index of suspicion for leptospirosis in severe tropical illness cases with TMA. The patient's positive response to treatment, including resolution of seizures and hemodynamic instability, demonstrates the value of prompt and targeted interventions. The case emphasizes the need for a multidisciplinary approach in managing complex leptospirosis cases with severe complications.

**Keywords:** Plasma exchange, corticosteroids, thrombotic microangiopathies, acute respiratory distress syndrome, leptospirosis

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## Background

Leptospirosis, an infection caused by the spirochete Leptospira, is a zoonotic disease with a wide range of clinical manifestations, from mild flu-like symptoms to severe multiorgan failure [1]. One of its rare but significant complications is thrombotic microangiopathy (TMA) [2,3]. This case report details the management of a 52-year-old female with leptospirosis complicated by TMA, focusing on the therapeutic roles of plasma exchange and corticosteroids in her treatment and recovery.

## Case Presentation

A 52-year-old female with no notable past medical history presented to the emergency department with a 5-day history of fever and progressive shortness of breath over the previous 3 days. Upon admission, she had tachypnoea (a respiratory rate of 32/minute) with partial pressure of oxygen in arterial blood (PaO2) to the fraction of inspiratory oxygen concentration (FiO2) ratio of 61 and bilateral lung infiltrates. She required invasive mechanical ventilation and prone positioning to optimize respiratory function.

Initial laboratory tests revealed anemia (hemoglobin 9.0 gm/dl), thrombocytopenia (platelet count: 21,000 cells/mm$^3$), and the presence of schistocytes (>2%) on the peripheral blood smear along with high lactate dehydrogenase (LDH) (1781 U/l) suggesting TMA. Patient had elevation in liver enzymes (SGOT: 579, SGPT: 201 IU/L, and bilirubin: 1.35 mg/dl) with normal prothrombin times (PT: 12.8) and activated plasma thromboplastin time (30.4). These findings, combined with an elevated plasmic score (7 points) and an increased LDH-to-hemoglobin ratio (197), suggested a probable diagnosis of thrombotic thrombocytopenic purpura (TTP) [4,5]. Despite initial negative serological tests for tropical infections, including leptospirosis, scrub typhus, and dengue conducted at an external facility, a diagnosis of tropical fever was suspected, with leptospirosis and scrub typhus as differential diagnoses.

Pending results for ADAMTS13 levels, the patient was started on two sessions of plasma exchange (1.2 × plasma volume) to address the suspected TTP. Platelet counts, schistocytes, and LDH levels were closely monitored to assess treatment efficacy (Table 1). Concurrently, she received moderate-dose corticosteroids (80 mg/day for 3 days, followed by tapering). The patient showed improvement following plasma exchange and steroid treatment, along with supportive care.

Despite improvements in hematological parameters and acute respiratory distress syndrome (ARDS), the patient experienced unexplained fluctuations in blood pressure and heart rate. Given her need for neuromuscular blockers, nonconvulsive seizures were suspected in the context of TMA. An electroencephalogram (EEG) confirmed focal seizures, leading to the initiation of levetiracetam (2 g/day) and propofol infusion. Subsequent hemodynamic stabilization and resolution of epileptic activity were achieved, with repeat EEG showing no further epileptic discharges.

Initial negative results for leptospirosis and other tropical infections complicated the diagnostic process. However, serological testing eventually revealed positive leptospirosis Immunoglobulin M antibodies, and Leptospira polymerase chain reaction testing of blood and urine samples confirmed the presence of Leptospira DNA, confirming the diagnosis of leptospirosis.

## Discussion

Severe leptospirosis involves a complex interplay of immune responses and metabolic disturbances. The infection leads to excessive release of inflammatory cytokines and antigen–antibody complexes, causing significant endothelial damage and multiorgan dysfunction [6,7]. Unlike many gram-negative bacteria that activate Toll-like receptor 4 (TLR-4), Leptospira endotoxin signals through Toll-like receptor 2 (TLR-2), which does not effectively induce nitric oxide production. This altered signaling contributes to the disease's pathophysiology [8]. In addition, glycolipoprotein (GLP-1) inhibits the Na-K ATPase pump, causing fluid accumulation in the lungs, bland cholestasis in the liver, and electrolyte loss in the kidneys. Potassium depletion within cells further activates inflammasome pathways, exacerbating inflammation [9]. Although TTP is rarely reported in leptospirosis, the disease can cause endothelial damage and platelet aggregation that mimic TTP [6].

Therapeutic plasma exchange (TPE) is effective in removing circulating toxins, inflammatory mediators, and immune complexes from the bloodstream. By clearing these harmful substances, TPE reduces systemic inflammation and mitigates tissue damage associated with severe leptospirosis [10,11]. A critical feature of severe leptospirosis is endothelial damage, which disrupts vascular function and leads to fluid leakage and organ dysfunction [12]. Plasma exchange helps restore endothelial integrity by eliminating factors responsible for endothelial injury, thereby enhancing vascular stability and reducing leakage [13]. Observational studies suggest that TPE is associated with significant mortality benefits in patients with severe leptospirosis, particularly those with pulmonary

***Table 1.*** *Trend of clinical and laboratory parameters during the hospital stay.*

| LABORATORY PARAMETERS | DAY 1 | DAY 2[A] | DAY 3[A] | DAY 4 | DAY 5 | DAY 9 |
|---|---|---|---|---|---|---|
| Hemoglobin | 9.0 g/dl | 8.0 g/dl | 8.3 g/dl | 9.1 g/dl | 8.7 g/dl | 9.6 |
| Platelets | 21.0*10$^3$/µl | 25.0*10$^3$/µl | 37.0*10$^3$/µl | 106.0*10$^3$/µl | 156.0*10$^3$/µl | 240*10$^3$/µl |
| LDH | 1781 U/L | 1327 U/L | 1281 U/L | | 577 U/L | |
| Schistocytes | +++ | +++ | ++ | + | - | - |
| Inj. methylprednisolone/day | 80 mg/day | 80 mg/day | 80 mg/day | 40 mg/day | 40 mg/day | 10 mg/day |
| P/F ratio | 61.3 | 68.7 | 152.4 | 186 | 236 | 428 |

The patient was subsequently treated with a 10-day course of intravenous doxycycline and ceftriaxone. Over the course of treatment, the patient's condition improved, culminating in successful extubation and discharge.

[a]1.2 l plasma volume exchange done.

hemorrhage [10,11]. In addition, several case reports have documented successful management of severe leptospirosis with TMA using plasma exchange [14].

In our case, the patient exhibited pulmonary involvement without hemorrhage but had evidence of TMA (anemia, thrombocytopenia, high LDH and schistocytes on peripheral smear). Pending further diagnostic results, the patient was initiated on plasma exchange (1.2 plasma volume) along with corticosteroids, which led to significant improvement.

## Conclusion

In summary, this case underscores the complexity of managing leptospirosis complicated by TMA and severe ARDS. The therapeutic use of plasma exchange and corticosteroids played a crucial role in the patient's recovery. The delay in diagnosis due to initial negative serological results highlights the need for a high index of suspicion for leptospirosis in severe tropical illness cases presenting with TMA. The patient's response to plasma exchange and the resolution of her complications, including seizures and hemodynamic instability, demonstrate the effectiveness of timely and targeted therapeutic interventions. This case emphasizes the importance of a multidisciplinary approach in managing complex cases of leptospirosis with severe systemic complications.

### What is new?

Early diagnosis and targeted treatment with plasma exchange and corticosteroids are crucial in managing severe leptospirosis complicated by TMA and ARDS. Timely intervention can improve outcomes and highlights the need for rapid, comprehensive care for complex infections.

### List of Abbreviations

| | |
|---|---|
| ARDS | Acute respiratory distress syndrome |
| EEG | Electroencephalogram |
| LDH | Lactate dehydrogenase |
| TMA | Thrombotic microangiopathy |
| TTP | Thrombotic thrombocytopenic purpura |

### Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

### Funding

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### Consent for publication

Written consent was obtained from the patient's family member (son).

### Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report.

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## Summary of case

| | | |
|---|---|---|
| 1 | Patient (gender, age) | 52 years, female |
| 2 | Final diagnosis | Severe leptospirosis complicated by thrombotic Microangiopathy and ARDS |
| 3 | Symptoms | Fever, Flulike symptoms, jaundice |
| 4 | Medications | Antibiotics, corticosteroids |
| 5 | Clinical procedure | Plasmapheresis |
| 6 | Specialty | Infectious diseases/Tropical medicine |