

The Scrub Typhus Septet: A Case Series Highlighting Clinical Variability Beyond the Eschar

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ABSTRACT

INTRODUCTION: Scrub typhus is a zoonotic infection caused by *Orientia tsutsugamushi*, transmitted through the bite of infected chiggers. It is an emerging public health concern in many tropical regions, including South and Southeast Asia, and is often underdiagnosed due to its nonspecific clinical presentation. The disease spectrum ranges from mild febrile illness to severe multi-organ dysfunction, contributing significantly to morbidity and mortality if untreated.

CASE PRESENTATION: We describe seven cases of scrub typhus presenting with varied clinical manifestations and outcomes. One patient developed neurological involvement, another progressed to acute respiratory distress syndrome (ARDS), and one experienced acute kidney injury (AKI). Two patients had concurrent co-infections that modified their disease progression, while the remaining two presented with mild, self-limiting illness and responded rapidly to doxycycline therapy. The diversity in presentation underscores the diagnostic challenges associated with this infection.

CONCLUSION: Scrub typhus should be considered in the differential diagnosis of acute undifferentiated febrile illness, particularly in endemic areas. Early recognition, appropriate serological testing, and timely initiation of specific antimicrobial therapy are essential to prevent complications. Increased clinical awareness and improved diagnostic capacity are key to reducing the burden of this potentially life-threatening but treatable disease.

Keywords: Scrub Typhus, Opsoclonus-Myoclonus Syndrome, Acute Kidney Injury, Respiratory Distress Syndrome, *Orientia Tsutsugamushi*

INTRODUCTION

Scrub typhus, caused by the intracellular bacterium *Orientia tsutsugamushi*, is an emerging vector-borne illness transmitted through the bite of infected larval mites (chiggers). In recent years, it has gained increasing attention due to its ability to cause a wide range of clinical manifestations and

potentially life-threatening complications involving multiple organ systems. The nonspecific and overlapping nature of its early symptoms—often resembling other endemic febrile illnesses—poses a considerable diagnostic challenge, particularly in tropical regions with a high burden of infectious diseases.

Despite these challenges, scrub typhus remains

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a highly treatable disease when recognized early, with timely initiation of appropriate antibiotic therapy leading to rapid clinical recovery in most cases.

The disease is geographically concentrated within the so-called "tsutsugamushi triangle," which encompasses parts of South and Southeast Asia, the Western Pacific, and northern Australia. Multiple Indian states have reported rising incidence, including Himachal Pradesh, Uttarakhand, West Bengal, Assam, Kerala, Maharashtra, and Tamil Nadu [1,2]. Rural and agricultural populations remain at the highest risk due to environmental exposure to mite habitats in fields and forested areas, particularly during the post-monsoon months from July to November. The increased use of serological and molecular diagnostic tools, such as IgM ELISA and PCR, has led to improved detection rates across endemic regions.

CASES PRESENTATION

Case 1: A 40-year-old man with no comorbidities presented with acute febrile illness, severe myalgia, dry cough, and breathlessness for one day. On admission, he was febrile, tachycardic, and tachypneic, with bilateral crepitations on chest examination. Despite empirical antibiotics and supportive care, his respiratory distress worsened, requiring mechanical ventilation. Initial blood tests revealed thrombocytopenia, raising suspicion of a tropical infection. His platelets were $57,000 \times 10^3/\mu\text{L}$ and his serum glutamic-oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) were 195 and 89 u/L, respectively, and ALP was 261 u/l. His urea was 46 mg/dl and creatinine 1.06mg/dl. His Electrocardiogram (ECG) showed sinus tachycardia. A High-Resolution Computed Tomography (HRCT) of the chest showed diffuse ground glass densities with interlobular septal thickening in bilateral lung fields, mostly in peribronchial and peribronchovascular distribution (atypical viral pneumonia). Bilateral mild pleural effusion with basal consolidation and atelectasis in the lingula and bilateral lower lobes. A comprehensive infectious workup was negative for malaria, dengue, leptospirosis, and Coronavirus Disease 2019 (COVID-19); however, scrub typhus IgM serology turned positive, and intravenous doxycycline was initiated. As his respiratory status stabilized, he developed sudden bilateral limb jerks

involving both proximal and distal along with rapid, multidirectional eye movements. Neurological evaluation confirmed opsoclonus–myoclonus syndrome (OMS), a rare complication of scrub typhus. Magnetic resonance imaging (MRI) of the brain and an Electroencephalogram (EEG) were normal, and cerebrospinal fluid analysis showed lymphocytic pleocytosis with elevated protein levels, consistent with scrub typhus meningoencephalitis.

The patient was managed with doxycycline, antibiotics, and anti-epileptics. Over the next 12 days, he showed steady clinical improvement, was extubated, and recovered completely without residual neurological deficits.

Case 2: A 60-year-old female presented with complaints of high-grade fever associated with chills for the past twelve days, along with loose stools for two days and an acute onset of breathing difficulty.

On examination, the patient was conscious and oriented. She was febrile with a temperature of 103°F . Her pulse rate was 120 beats per minute, respiratory rate 24 cycles per minute, and blood pressure 90/60 mmHg. Oxygen saturation was 86%, and she was started on 4 liters of oxygen per minute. A characteristic eschar measuring approximately $2 \times 1 \text{ cm}$ was noted on the anterior abdominal wall (Figure 1). Her examination revealed bilateral coarse crepitations. The Quick Sequential Organ Failure Assessment (qSOFA) score was calculated to be 2, indicating a high risk of sepsis.



Figure 1: Eschar on the anterior abdominal wall of the patient in case 2

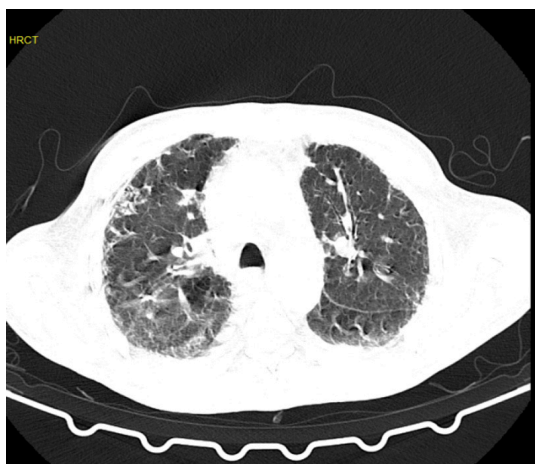


Figure 2: High-Resolution Computed Tomography (HRCT) of the chest showing bilateral ground-glass opacity in case 3

Her renal function was deranged. Her platelets were 82000 x10³/micL. Her SGOT was 164 µ/L, SGPT was 78 µ/L, and ALP was 441 µ/L. Her renal parameters were urea of 131 mg/dL and creatinine of 2.43mg/dL. Her ECG showed sinus tachycardia, and Chest X-ray –increased bronchovascular markings in bilateral lung fields- More on the right side.

In light of the clinical presentation and the presence of an eschar, a diagnosis of scrub typhus was confirmed by a positive Immunoglobulin M enzyme-linked immunosorbent assay (IgM ELISA). Given the diagnosis of scrub typhus with systemic inflammatory response syndrome (SIRS), acute kidney injury, and transaminitis, intravenous doxycycline was initiated. Supportive management included oxygen supplementation, intravenous fluids for hydration, and hepatoprotective agents. Her renal parameters and liver enzymes normalized over the course, confirming a favorable outcome.

Case 3: A 71-year-old man with a history of diabetes mellitus and bronchial asthma presented with a 10-day history of high-grade fever with chills and rigors and a productive cough. On examination, his temperature was 104°F. Blood pressure was 100/60 mmHg while on a noradrenaline infusion at 2.5 ml/hr. Pulse was 114 beats per minute, low volume. Respiratory rate was 24 breaths per minute. Oxygen saturation was 92% with 4 liters of oxygen. General examination revealed an eschar on the left side of his neck. He had thrombocytopenia of 48000 x 10⁹/mic

and SGOT, SGPT, and Alkaline Phosphatase (ALP) were 167 u/L, 95 u/L, and 150 u/L, respectively. His urea was 59mg/dl and creatinine 1.17mg/dl. ECG showed a normal sinus rhythm with low-voltage complexes. Auscultation of his lungs detected bilateral wheezes and crepitations, while other systemic examinations were normal. He was started empirically on intravenous meropenem and doxycycline. Bronchodilators and antihistamines were also administered.

Initial chest X-ray showed multiple opacities scattered across both lung fields. A serological test returned positive for scrub typhus IgM. A high-resolution Computed Tomography (CT) scan of the chest (Figure 2) revealed small amounts of pleural fluid, patchy interlobular septal thickening, and ground-glass opacities. High-resolution CT chest also showed small honeycomb cysts consistent with a Usual Interstitial Pneumonia (UIP)-like pattern. Given the patient's background history of asthma, these findings were considered more likely related to an undiagnosed chronic interstitial process rather than acute scrub typhus. The possibility of a pre-existing lung disease was therefore recognized. Such findings highlight the importance of considering underlying chronic pulmonary pathology when interpreting radiological abnormalities in acute infections. His Arterial Blood Gas (ABG) showed respiratory alkalosis and hypoxemia.

The patient's clinical condition was concerning, with a qSOFA score of 2, indicating a high risk of sepsis. He was closely monitored and managed accordingly. He gradually improved over the following days.

Case 4: A 28-year-old male presented with complaints of high-grade fever for the past 20 days. He had a history of loose stools for 3 days. On examination, he was febrile with signs of dehydration. His platelets were 192000 x10³/micL. His SGOT was 101 µ/L, SGPT was 76 U/L, and ALP was 32 U/L. His renal parameters were urea of 14 mg/dL and creatinine of 1.04 mg/dL. Chest X-ray was Normal. ECG showed sinus tachycardia with no ST-T changes.

Scrub typhus IgM ELISA was positive, and doxycycline was initiated. Despite the initiation of antibiotics, fever spikes persisted, prompting further evaluation. His echocardiogram revealed no vegetations. Subsequently, blood cultures grew carbapenem-resistant *Klebsiella pneumoniae*.

Appropriate antibiotics were added.

A co-infection with scrub typhus and carbapenem-resistant *Klebsiella pneumoniae* was established, and he improved clinically with no further fever spikes.

Case 5: A 44-year-old female presented with high-grade, intermittent fever for 7 days, along with myalgia and headache. She also complained of a dry cough and breathlessness for 2 days. She had been evaluated outside and was found to be Dengue IgM positive. On examination, an eschar was noted below the left breast. Vitals were stable with a temperature of 100.4°F. Systemic examination revealed bilateral air entry with mild basal crepitations in the lungs, and a soft abdomen with mild epigastric tenderness. ECG showed a normal sinus rhythm with no ST-T changes. Hepatoprotectives were added for hyperbilirubinemia of 2.3 mg/dl and transaminitis. Her scrub typhus IgM was positive. She improved well with doxycycline. Her platelets were 170000 $\times 10^3/\mu\text{L}$. His SGOT, SGPT, and ALP levels were 635 u/L, 443 u/L, and 118 u/L, respectively. His Urea was 16mg/dL, and his creatinine was 0.47mg/dL. Chest X-ray showed increased bronchovascular markings in bilateral lung fields.

A final diagnosis of scrub typhus (IgM positive) and dengue fever (IgM positive) was made. The patient improved symptomatically and remained vitally stable throughout the hospital stay, with improving liver enzymes and normalization of complete blood count (CBC).

Case 6: A 16-year-old male with a past history of treated pulmonary tuberculosis presented with high-grade intermittent fever and headache for 10 days. On examination, he was febrile and mildly dehydrated, with generalized ichthyosis but no eschar or rash. Cardiovascular examination revealed a loud S1 with a non-ejection click. ECG showed a normal sinus rhythm

Initial workup for malaria, dengue, and enteric fever was negative. Given his history and elevated ESR, tuberculosis reactivation was considered; however, the chest X-ray was normal

Scrub typhus IgM serology returned positive, and doxycycline was initiated. Despite adequate therapy, the patient continued to have fever spikes, and repeat cultures remained sterile. Further evaluation with Positron Emission Tomography/Computed Tomography (PET)-CT scan revealed

hypermetabolic periportal and mesenteric lymphadenopathy and findings suggestive of abdominal tuberculosis. In light of the persistent fever and imaging findings, the possibility of abdominal tuberculosis was favored. The positive scrub typhus IgM may have represented a false-positive result due to serological cross-reactivity. This case highlights the diagnostic challenges in endemic regions, where serological overlap between tropical infections can complicate the interpretation of results.

Case 7: A 23-year-old lactating female, 4 months postpartum, presented with a two-week history of high-grade fever. She also reported vomiting for two days. On initial assessment, her vital signs were stable, and both general and systemic examinations were unremarkable. Following admission, a thorough local examination revealed the presence of an eschar on the trunk, which raised clinical suspicion for scrub typhus. ECG showed a normal sinus rhythm. Her platelets were around 230,000 $\times 10^9/\mu\text{L}$, and her SGOT and SGPT were 78 u/L and 113 u/L, respectively. Her urea was around 12mg/dl, and creatinine was 0.63mg/dl. Subsequent serological testing with Scrub Typhus IgM ELISA confirmed the diagnosis. Her renal function was normal. Liver enzymes were elevated at presentation (but showed improvement in due course). The patient was initiated on azithromycin therapy and showed clinical improvement.

DISCUSSION

The clinical features of scrub typhus overlap with many other tropical infections, making clinical differentiation difficult without laboratory support. Fever was the most consistent symptom across all cases, while vomiting, headache, abdominal pain, and breathlessness were also frequently observed. The absence of eschar may lead to delayed diagnosis, which, in turn, is associated with more severe disease complications.

Orientia tsutsugamushi primarily invades and multiplies within phagocytes and endothelial cells, leading to vascular endothelial injury and cytokine release [3]. This endothelial dysfunction underlies the multi-organ involvement characteristic of scrub typhus. Neurological involvement in scrub typhus ranges from meningitis, meningoencephalitis, and cerebellitis to rare features such as opsoclonus–myoclonus syndrome (OMS) and Parkinsonism. A

study published in the Journal of Neurosciences in Rural Practice evaluated a subset of 25 patients who underwent lumbar puncture despite the absence of overt neurological signs; 48% showed reactive cerebrospinal fluid (CSF) with mild mononuclear pleocytosis [4], a finding similar to that in Case 1.

D'Sa et al. [5] reported a patient who developed a gradual-onset headache and visual disturbances, accompanied by spontaneous, multidirectional saccadic eye movements (opsoclonus). The patient fully recovered with doxycycline therapy. Similar doxycycline-responsive cases were also described by Reddy et al. [6]. Pulmonary involvement in scrub typhus varies from mild bronchitis and interstitial pneumonitis to severe acute respiratory distress syndrome (ARDS), which is a potentially fatal complication. In a comprehensive study by Wang et al., the mortality rate associated with ARDS was approximately 25% [7]. Liver involvement is a common feature, as observed in our cases, presenting with elevated transaminases and hyperbilirubinemia. Severe hepatic dysfunction has been correlated with increased disease severity and poorer outcomes [8]. Renal involvement is frequently encountered, with incidence rates ranging from 10% to 60%. In a study by Attur et al., urinary abnormalities were present in 56.7% (147/259) of patients, and 23.2% (60 patients) developed acute kidney injury (AKI). Hemodialysis was required in 10% of these cases [9].

Diagnosing scrub typhus can be difficult due to its nonspecific clinical presentation and overlap with other tropical infections such as dengue, malaria, and leptospirosis. The absence of an eschar often leads to diagnostic delays. In one of the cases, persistent fever despite doxycycline and evidence of abdominal TB raise the possibility of false-positive scrub typhus serology or concurrent infection, highlighting diagnostic uncertainty as a limitation of this series. In one patient, his HRCT chest showed a small honeycomb cyst. It is plausible that these changes reflect an undiagnosed chronic lung process rather than disease-related fibrosis. This underscores the importance of recognizing co-existing pulmonary conditions as possible confounders in imaging interpretation. Despite occasional limitations related to cross-reactivity and the timing of the antibody response, multiple diagnostic modalities for scrub typhus were evaluated by Kundu et al. [10]. The ELISA and rapid diagnostic test (RDT)

detecting *Orientia tsutsugamushi*-specific IgM antibodies demonstrated excellent diagnostic accuracy, supporting the utility of serological testing as a reliable, accessible diagnostic tool in endemic regions.

CONCLUSION

Scrub typhus remains a significant yet often overlooked cause of acute febrile illness due to its varied clinical manifestations. This case series underscores the broad spectrum of disease severity, ranging from uncomplicated febrile episodes to life-threatening multi-organ dysfunction. Early diagnosis and rapid initiation of doxycycline therapy can significantly lower both morbidity and mortality. Enhancing clinical awareness and implementing early diagnostic measures are key to improving patient outcomes and preventing serious complications, especially in endemic areas.

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