

Scrub Typhus: A Case Series Highlighting Diverse Clinical Manifestations

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ABSTRACT

This case series presents three patients with scrub typhus, highlighting diverse clinical manifestations such as fever, arthritis, meningoencephalitis, respiratory involvement, thrombocytopenia, and renal dysfunction. Diagnostic challenges stem from varied symptoms and absence of eschar. All patients responded well to doxycycline therapy. The report emphasizes the importance of considering scrub typhus in endemic areas, especially among patients with prolonged fever and atypical presentations, and advocates for early diagnosis and treatment to prevent severe complications and improve outcomes.

Key words: Scrub typhus, clinical manifestations, endemic, meningoencephalitis, arthritis, multi-organ involvement, early diagnosis, India.

INTRODUCTION:

Scrub typhus is a life-threatening zoonotic infection caused by *Orientia tsutsugamushi*, an obligate intracellular Gram-negative bacterium. The disease is transmitted to humans through the bite of larval *Leptotrombidium* mites (chiggers) and primarily targets endothelial cells, monocytes, and other cells, leading to vasculitis and endothelial dysfunction (1). Its clinical presentation ranges from mild, self-limiting illness to severe, potentially fatal disease. Typical symptoms include high-grade fever, headache, rash, lymphadenopathy, myalgia, and sometimes jaundice or thrombocytopenia. However, the classic eschar found at the site of the mite bite is seen in fewer than half of cases, and a rash occurs in less than 40% (2).

Scrub typhus is endemic in the "tsutsugamushi triangle," a geographically distinct region covering much of the Asia-Pacific, including India, where the disease is increasingly reported from diverse ecological zones ranging from southern metropolitan areas to the Himalayan belt (3). Recent case series highlight a wide spectrum of presentations, from gangrene and meningoencephalitis to anemia and hematuria, underscoring the diagnostic challenges and potential for multi-organ involvement (4).

This case series aims to explore the varied clinical manifestations, diagnostic method, and management of scrub typhus, thereby adding to the understanding of its disease spectrum and informing effective healthcare strategies in endemic regions.

CASE 1:

A 56 years old male, came to the outpatient department with complaints of fever since 3 days, low grade, intermittent, relieved on antipyretics and complaints of swelling and pain of right knee, right hand and left ankle since 3 days. No history of exposure to farm animals, pet dogs or cats. Patient was admitted one and a half months back in view of joint swelling and pain, diagnosed gout secondary to alcohol use. Patient was in complete remission and was discharged.

Since using TAB and Amlong 5 mg OD for two years, the patient has been recognized to have systemic hypertension. He also drinks 140 milliliters of whisky a day, making him a recognized alcoholic. The patient had been drinking for the past eight years, but he hasn't had any in the last one and a half months. The patient had a fever, a pulse rate of 98 beats per minute, a blood pressure of 110/70 mm Hg, and a SpO₂ of 98% at room air when examined. The results of the systemic evaluation were within normal range. Upon local inspection, the right knee, right hand, and right ankle showed swelling and a localized increase in warmth, along with a painfully limited range of motion.

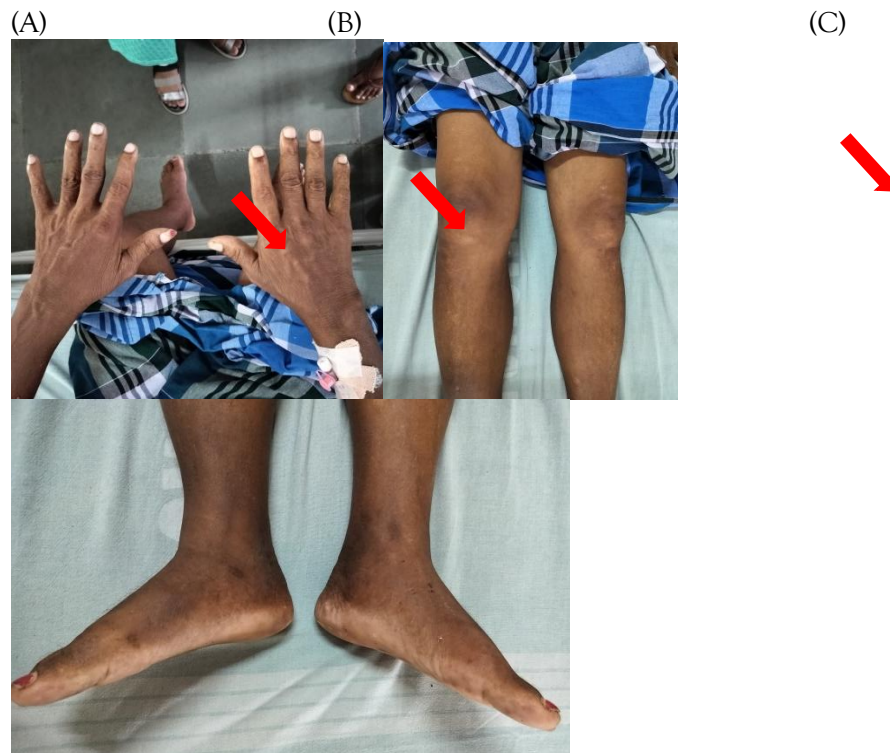


Figure 1: A- Arrow shows Right hand swelling of wrist, metacarpophalangeal and interphalangeal joints with painful restriction of movements. B- Arrow shows Right knee diffuse swelling with painful restriction of movements. C- Arrow shows Right ankle diffuse swelling with painful restriction of movements. The results of routine tests showed mild neutrophilic leukocytosis (11,200/mm³), 1,71,000/ μ L platelets, 64 mg/dL urea, 2.41 mg/dL creatinine, and 9.2 mg/dL uric acid. In addition to synovial fluid from the knee, blood and urine cultures were sent for examination and microscopy. With a suspicion of bacterial etiology, ceftriaxone was prescribed to the patient.

Analysis of synovial fluid showed needle-shaped crystals. The patient received treatment for gouty arthritis. Because NSAIDs were prohibited due to severe kidney impairment, the patient received intravenous fluids, oral prednisolone and probenecid.

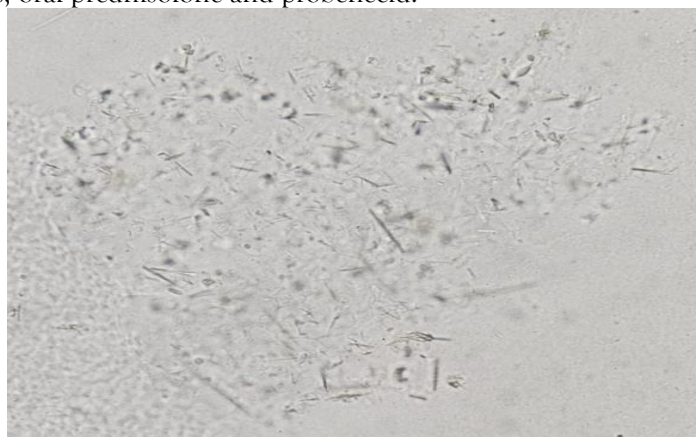


Figure 2: D- Shows presence of needle shaped crystals under light microscopy. After two days, a repeat blood sample revealed thrombocytopenia with platelets of 1,48,000/ μ L, and the patient continued to have fever spikes. Scrub typhus was found to be ELISA IgM positive in the vector-borne disease panel that was sent. The patient began taking 100 mg of doxycycline orally every day.

On the fifth day of doxycycline, the patient was in the hospital and had improved symptoms, including no pain, edema, or restriction of range of motion in the afflicted joints. Oral doxycycline, a tapered dosage of oral prednisolone, and febuxostat with probenecid were given to the patient upon discharge.

CASE 2:

A 42 years old male, who is a construction worker, was brought to the casualty by the patient's attenders at 4 pm in the afternoon, with a history of fever since 5 days, complaints of agitated behavior an altered sensorium since afternoon and an alleged involuntary movements of both upper and lower limbs associated with up rolling of eye balls which lasted for 1 minute, at around 2 pm. No history of exposure to farm animals, pet dogs or cats.

Not a known case of type 2 diabetes mellitus, systemic hypertension, bronchial asthma, epilepsy. Patient is a known alcoholic for 10 years. Last drink was 10 days back.

On examination, pulse rate was 80 beats/min, regular, Blood pressure was 130/90 mmHg, respiratory rate- 17/minute, SpO₂- 97% at room air, Capillary blood glucose was 278mg/dL. Bilateral pupils were 3mm and sluggishly reacting to light. Systemic examination was within normal limits. Brudzinski's sign was positive. CT brain was done in view of altered sensorium. There was no hemorrhage or space occupying lesions.

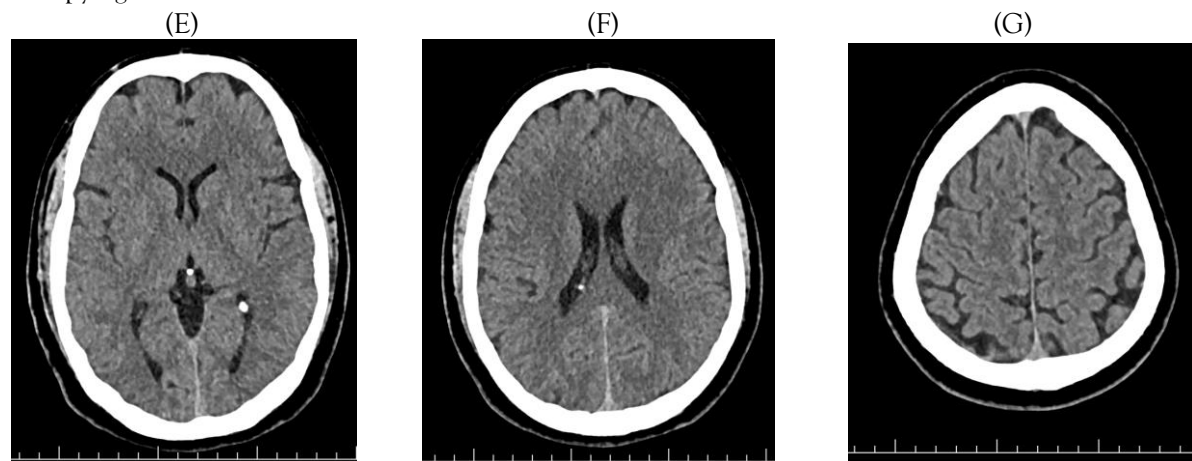


Figure 3: E, F & G- Shows Computed tomography of brain- plain- Normal study.

Fundus was normal. Investigations revealed mild neutrophilic leukocytosis (10,120/mm³), Platelets of 1,73,000/ μ L, mild transaminitis (AST-78 IU/L, ALT-91 IU/L, ALP-155 IU/L) and ongoing inflammation ESR- 60 mm, CRP48 mg/dL.

The patient was put on intravenous ceftriaxone after blood and urine cultures were received due to the presumed bacterial etiology of neutrophilic leukocytosis. After a lumbar puncture, the CSF was sent for examination. It revealed an acellular, colorless fluid that contained 182 proteins and 73 carbohydrates. Platelets dropped to 1,38,000/ μ L, according to a repeat CBC. A panel of vector-borne diseases was delivered. Scrub typhus ELISA IgM was found to be positive. Intravenous doxycycline 100 mg twice a day was used to treat the patient. After receiving intravenous doxycycline for 48 hours, the patient's sensorium improved and there were no more seizure occurrences. After being moved to oral doxycycline, the patient was ultimately released.

CASE 3:

A 34-year-old woman arrived at the outpatient clinic complaining of widespread myalgia, a dry cough that had been present for four days, and a fever that had been present for seven days. No noteworthy prior history. There are no such grievances in the family. No prior experience with farm animals, pets, or cats. No comorbidities are known. No past history of addictions or high-risk conduct.

The patient's examination revealed a fever of 101.4°F, a regular heart rate of 102/minute, blood pressure of 110/70 mm Hg, a regular respiration rate of 18/minute, and a SpO₂-98% at room air. Diffuse expiratory wheezing was found upon systemic assessment.

Thrombocytopenia of 1,16,000/ μ L, mild hemoglobin anemia of 10.2 mg/dL, and total counts of 6,018/mm³ without any neutrophilic or lymphocytic predominance were found during routine tests. An x-ray of the chest showed noticeable bronchovascular borders.

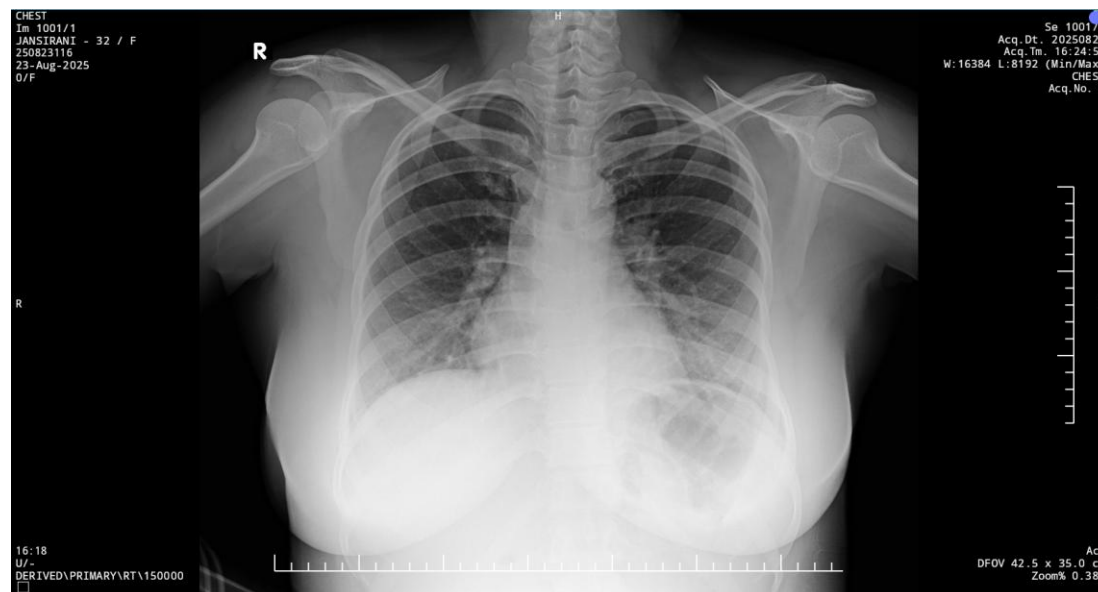


Figure 4: H- Showed chest X-Ray- PA view with increased bronchovascular markings in bilateral lung fields

In addition to an inhaled bronchodilator, analgesics, and other supportive drugs, the patient was empirically started on injections of ceftriaxone 1g IV Q12h and doxycycline 100mg P/O twice daily after a vector-borne illness panel was provided. There were high titers of IgM scrub typhus detected in the vector-borne illness panel. As the patient's platelet count increased and their symptoms improved during their hospital stay, they were released on oral doxycycline.

DISCUSSION:

Fever, headache, myalgia, and distinctive eschar are the most prevalent symptoms of scrub typhus, a potentially fatal rickettsial disease (5). If treatment is not received or is postponed, complications may affect the liver, kidney, lung, and nervous system (6).

Involvement of the central nervous system (CNS) can range from mild meningitis to frank meningoencephalitis (7) (8). Meningeal signs, headaches, seizures, delirium, and altered sensorium are examples of neurological symptoms that frequently appear subacutely. Analysis of cerebrospinal fluid (CSF) usually reveals variable high adenosine deaminase (ADA), lymphocytic pleocytosis, and elevated protein (9,10).

Because its symptoms can be confused with those of other CNS illnesses, like TB meningitis, scrub meningoencephalitis is not well known (11). Scrub typhus CNS illness mortality varies; some studies show that doxycycline improves prognosis, while other studies show that case fatality rates are substantial, particularly in patients with multi-organ failure. According to recent pediatric data, 10% of survivors may experience sequelae (9,7).

Arthritis or reactive arthritis may rarely complicate scrub typhus. Pain and swelling in large joints, especially the knee and shoulder, have been described, occasionally in association with eschar and other classic symptoms. Arthritis often presents as aseptic synovitis and responds well to doxycycline or minocycline, supporting an infectious etiology rather than immune-mediated alone. Differential diagnosis includes septic arthritis, yet the resolution with antibiotics and absence of organisms in synovial fluid favor post-infectious/immune mechanisms (12).

Scrub typhus can precipitate gout and severe hyperuricemia, especially in cases with multi-organ involvement and renal dysfunction. Multiple studies now confirm that hyperuricemia is significantly more common and severe in patients with scrub typhus compared to other febrile illnesses (13). In case 1, a patient who had previously received treatment for gout brought on by alcohol use and had been in full remission for a month arrived at the hospital with severe kidney damage and hyperuricemia from scrub typhus-induced gout precipitation. According to studies, individuals with scrub typhus who have hyperuricemia had more severe symptoms, greater mortality rates, and higher rates of neurological dysfunction and organ failure (13). Symptoms improve when gout attacks are promptly identified and treated, usually with antibiotics plus colchicine, NSAIDs, or corticosteroids (13,14).

From mild bronchitis and interstitial pneumonia to more serious problems like acute respiratory distress syndrome (ARDS), scrub typhus can affect the respiratory system and cause a variety of pulmonary symptoms (15). Coughing, dyspnea, and hypoxemia are examples of respiratory symptoms. The most frequent radiological result is interstitial pneumonia, which frequently manifests as reticulonodular patterns and ground-glass opacities on chest imaging (16). In case 3, the patient had an acute bronchitis presentation along with a dry cough devoid of pneumonitis symptoms.

In both milder and more severe forms, elevated transaminase, bilirubinemia, and creatinine are common (17). Most cases can result in thrombocytopenia and anemia, which may indicate multi-organ involvement or severe disease (5). About 25–50% of individuals have macular or maculopapular rash, and lymphadenopathy is commonly observed (17). High mortality rates can result from MODS with shock, coagulopathy, and respiratory or renal failure in cases of severe illness (17). Eschar, which occurs in 7%–68% of instances, was once thought to be pathognomic. The absence of eschar is a risk factor for mortality, which can be attributed to delays in treatment, causing the onset of complications (15). Even after extensive examination, no eschar was found in all three of our cases.

The varied presentation of scrub typhus, absence of eschar in many cases, and overlap with other tropical infections frequently delay diagnosis. IgM ELISA and indirect immunofluorescence remain mainstays of laboratory diagnosis. Early doxycycline therapy is crucial and reduces mortality; azithromycin and chloramphenicol are alternatives in resistant cases or special populations (17,8).

In India, scrub typhus has been reported in at least 16 states (Jammu & Kashmir, Himachal Pradesh, Rajasthan, Haryana, Maharashtra, Karnataka, Andhra Pradesh, Kerala, Tamil Nadu, Pondicherry, West Bengal, Sikkim, Uttaranchal, Assam, Arunachal Pradesh, and Nagaland) (18,19,20). Coughing, dyspnea, and hypoxemia are examples of respiratory symptoms. The most frequent radiological result is interstitial pneumonia, which frequently manifests as reticulonodular patterns and ground-glass opacities on chest imaging (20). In case 3, the patient had an acute bronchitis presentation along with a dry cough devoid of pneumonitis symptoms.

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Key Findings:

- In endemic areas, it is necessary to consider scrub typhus as one of the differentials for an acute febrile illness or any prolonged fevers with unknown cause.
- As in some infectious diseases, reactive arthritis remains a possible localization with scrub typhus and can be confused with septic arthritis.
- Early and prompt treatment can avoid unnecessary complications.
- Medico-surgical consultation based on careful analysis of clinical, biological and radiological data with close clinical monitoring can avoid unnecessary invasive interventions.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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