

## Scrub Typhus Case Report; Acute Febrile Illness in a Young Lady

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## Abstract

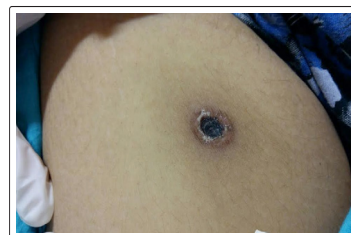
We are reporting a case of young Indian lady with history of recent travel to India, presented with acute febrile illness. Initially she was treated with antibiotics with diagnosis of sepsis but she did not respond. Thorough investigations were done to find out the cause of her illness but all the workup was negative. Later on detailed examination revealed an eschar on the right thigh. Based upon the fact that she has a history of recent travel to Andhra Pradesh that is endemic for scrub typhus, with the presence of eschar on the right thigh, empirical treatment with doxycycline was started. Patient responded very well to the treatment and was discharged home. High clinical suspicion of scrub typhus is necessary for early diagnosis and treatment in patients coming from endemic area. Presence of eschar is pathognomonic but its absence does not make the disease unlikely. Early diagnosis is associated with better outcomes.

**Keywords:** Fever, Eschar, Scrub Typhus

## Case Report

28 year old Indian lady with no previous significant medical history presented with headache for 5 days and fever for same duration. Headache was gradual in onset generalized, persistent and not relieved by analgesics. Fever was high grade associated with rigors and chills. Past medical history was insignificant apart from iron deficiency anemia. She is a school teacher, mother of 2 kids. Family history was unremarkable. Travel history was significant for travel to India, stayed there for 4 weeks, returned one week back. Stay in India was unremarkable. On examination she was febrile 39°, apart from that vitals were stable and examination was unremarkable. CBC shows leucopenia, WBC 2.2 with ANC 1.6, lymphocytes 0.5, hemoglobin 11.6, platelets 86. Peripheral smear shows mild anemia with marked leukopenia and thrombocytopenia, presence of toxic neutrophils. Malaria parasite was negative. Other biochemical test revealed normal kidney function test and liver function test. CRP was 30 with pro-calcitonin and 0.14 and ESR 3. Patient admitted in medical floor with presumptive diagnosis of meningitis. LP was not done due to thrombocytopenia and patient was started empirically on ceftriaxone and acyclovir. However patient remained febrile and symptomatic and did not improve to treatment. Infectious disease team was consulted for advice. Thorough examination was done that revealed a small discolored painless skin lesion on the right thigh 0.5 cm? Bruise. Reviewing case summary, Young lady with fever and headache and bicytopenia with low inflammatory markers and recent travel to India, differential diagnosis was to rule out CNS infections like meningitis or encephalitis, typhoid fever, dengue fever, leptospirosis, brucellosis. Advised to do CSF analysis that came out as completely normal picture. Dengue and Brucella serology were negative. Blood cultures were negative. Ceftriaxone and acyclovir was stopped however patient continued to spike high-grade fever reaching 40° with persistent picture of bicytopenia and

severe headache. Liver functions tests started to get impaired with ALT 91 and AST 114. CRP started to rise and reaching 246. Patient was started on IV Tazocin empirically. Viral panel including CMV, Epstein-Barr virus, HIV serology was sent that came negative MRI head was done that was unremarkable. Patient started to become hypotensive and desaturated, IV hydration was started. Thorough examination revealed black eschar on right thigh, at the site of previous discolored skin lesion. Since patient had travel history to Andhra Pradesh, empirical diagnosis of SCRUB TYPHUS was made and doxycycline was started. IV Tazocin was stopped. Test for serology for *Orientia tsutsugamushi* is not available in our Center. It was tried to send to a reference lab but could not be done. Patient stayed in medical ICU for one day for observation, her blood pressure was stabilized and she was sent back to the floor. Patient started to improve, became afebrile and symptoms resolved. Blood counts for WBC and platelets became normal. CRP decreased from 246 to 13 and patient was discharged home on doxycycline to continue for total 10 days.



## Discussion

Scrub typhus is an acute febrile illness caused by *Orientia tsutsugamushi* (rickettsia tsutsugamushi) [1-3]. It is endemic in 'Tsutsugamushi triangle' which extends from northern Japan and far-eastern Russia in the north, to northern Australia in the south, and to Pakistan, India and Afghanistan in the west [4]. Incubation period is 7-10 days.

Presence of scrub typhus and other rickettsial diseases has been known to be pathogenic in Indian subcontinent for past several decades. Significant morbidity and mortality was seen among army troops deployed in Southeast Asia during World War II [5]. However, there has been a considerable decline in the incidence of scrub typhus in the later decades. Recent reports from several parts of India, including South India, indicate that there is a resurgence of scrub typhus. It remains grossly underdiagnosed due to nonspecific clinical presentation, limited awareness, low index of suspicion among clinicians and lack of diagnostic facilities [6].

*Orientia tsutsugamushi* is an obligatory intracellular Gram-negative coccobacillus [7]. There are several serotypes of *O. tsutsugamushi*, and infections with one serotype gives only transient cross-immunity to another. It is a zoonotic disease transmitted by the larval mites (chiggers) of the *Leptotrombidium deliense* group. These larval mites usually feed on the wild rats of the subgenus *Rattus*. The infection is acquired through agricultural activities in the oil palm, rubber plantation, rice fields, and recreational activities in the woods or mountainous areas [8].

Clinical manifestations include nonspecific febrile illness often accompanied by headache, myalgia, nausea, vomiting, diarrhea, cough and breathlessness. The pathognomic clinical sign of scrub typhus is “eschar” (40–50%) which may be inconspicuous as it is often present in areas like groin, gluteal folds, breast folds, and external genitalia and may go unnoticed in dark-skinned people [5,9-12]. Patients are usually unaware of the bite, as the eschar is painless and does not itch. Severity of disease varies from subclinical illness to severe illness with multiple organ system involvement, which can be serious enough to be fatal, unless diagnosed early and treated.

Scrub typhus lasts for 14 to 21 days without treatment. Severe infections may be complicated by interstitial pneumonia, pulmonary edema, congestive heart failure, circulatory collapse, signs and symptoms of central nervous system dysfunction, including delirium, confusion, and seizures [9,11,13,14]. Death may occur as a result of these complications, usually late in the second week of the illness. By contrast, patients treated with appropriate antibiotics typically become afebrile within 48 hours of starting therapy.

Lab findings can be leukopenia, thrombocytopenia, coagulopathy, elevation of liver enzymes and bilirubin indicating hepatocellular damage, Proteinuria, renal impairment, reticulonodular infiltrates (most common finding on chest radiograph or peribronchial interstitial infiltrates). CSF examination might show a mild mononuclear pleocytosis with normal glucose levels [8]. The indirect fluorescent antibody (IFA) test remains the mainstay of serologic diagnosis. A four-fold rise in titers over a 14-day period is conclusive [14]. The pathological hallmark of scrub typhus is a lymphohistiocytic vasculitis upon biopsy of eschar or generalized rash.

Treatment include doxycycline 100 mg orally or IV twice a day for 7-14 days as drug of choice. Azithromycin (500 mg orally for 3 days) is alternative [5,11]. Chloramphenicol was the first drug shown to be effective in the treatment of scrub typhus, and is still commonly used in endemic regions.

The case-fatality rate for untreated classic cases is 7%. Poor prognostic factors include requiring care in an intensive care unit, high APACHE-II scores, and the absence of an eschar (making

diagnosis more difficult).

Complications include acute respiratory distress syndrome, encephalitis, pneumonia, pericarditis, acute renal failure, acute hepatic failure, hematemesis, melena and diarrhea [5,12,13]

No vaccine is available to prevent the transmission of scrub typhus. Prevention is based on avoidance of the chiggers that transmit *O. Tsutsugamushi*, accomplished by insect repellents and by the use of protective clothing impregnated with benzyl benzoate.

## Conclusion

High clinical suspicion of scrub typhus is necessary for early diagnosis and treatment in patients coming from endemic area. Presence of eschar is pathognomic but its absence does not make the disease unlikely. Early diagnosis is associated with better outcomes.

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