# Scrub Typhus with Unusual Presentation

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Case Report

## ABSTRACT

Scrub typhus is an acute, febrile zoonosis caused by an obligate intracellular bacterium Orientia tsutsugamushi. The clinical manifestations of the disease range from subclinical to fatal organ failure. The common symptoms are fever, chills, headache, myalgia, dry cough, lymphadenopathy, and gastrointestinal disturbances. The presentation with complications is usually due to delay in diagnosis and treatment. We report three cases of scrub typhus that presented with features of meningo-encephalitis, which is very unusual, and all patients recovered with empirical doxycycline treatment.

**Keywords:** Chigger, eschar, meningo-encephalitis, *Orientia tsutsugamushi*, Weil-Felix test

## INTRODUCTION

Scrub typhus is an acute febrile illness caused by *Orientia tsutsugamushi,* which is transmitted to humans by the bite of a larval-stage trombiculid mite or chigger and is an important consideration in the differential diagnosis of acute febrile illness especially from endemic areas.[1] The common symptoms are fever, chills, headache, myalgia, dry cough, lymphadenopathy and gastrointestinal disturbances.[2] The clinical and laboratory features are non-specific in scrub typhus and eschar is the single most useful diagnostic clue, and is pathognomonic for *O. tsutsugamushi* but is seen in less than 10% of cases in the Indian subcontinent.[3] The delay in diagnosis and treatment results in development of complications which is usually seen in the 2nd week of illness.

## CASE REPORTS

### Case 1

A 30-year-old housewife presented with 7 days history of fever with chills, headache and with four episodes of generalized tonic clonic seizures for 2 days prior to hospital admission. On examination, there was eschar on the right neck region [Figure 1] and the vitals were stable. The central nervous system (CNS) examination showed no focal neurological deficits

and there was terminal neck rigidity. The other system examination was within normal limits. Laboratory examination revealed normal renal and liver function tests. The peripheral smear and total count was normal. Cerebrospinal fluid (CSF) was clear with elevated protein (100 mg/dl) and there were few lymphocytes. The enzyme-linked immunosorbent assay for *O. tsutsugamushi* was positive. The CSF, blood and urine cultures were sterile.

Leptospira serology and WIDAL were negative. Magnetic resonance imaging brain was normal. She received acyclovir for 1 day and on day 2 she was started on empirical doxycycline (100 mg BID). Her symptoms completely resolved in 48 h and were discharged from the hospital on day 8.

### Case 2

A 50-year-old farmer presented with history of fever, headache for 6 days and history of seizures and altered sensorium for 1 day. On examination, patient was confused and disoriented. There was palpable purpura predominantly on the lower limbs and eschar was seen in the right axillary region [Figure 2]. The CNS examination showed terminal neck rigidity and there was no focal neurological deficit. The vitals were stable and systemic examination was normal. Laboratory examination revealed positive Weil-Felix test (WFT). The peripheral smear showed reduced platelet count (80,000/dl) with normal total count. The CSF analysis showed protein of 90 mg/dl, sugar 50 mg/dl (corresponding blood sugar 120 mg/dl) and 50 lymphocytes. The blood, urine and CSF culture were sterile. His symptoms completely resolved with empirical doxycycline (100 mg BID oral). His platelet count returned to normal within a week.

### Case 3

A 23-year-old female presented with a history of fever, chills, and headache for 5 days and altered sensorium for 1 day. Her pulse rate was 98/min, blood pressure 100/70 mmHg, temperature 39°C, and no lymph node enlargement. The CNS examination showed neck rigidity. Her other system examination was normal. The peripheral smear showed platelet count of 200,000/dl with normal hemoglobin and normal total count. The WFT was positive for scrub typhus. The CSF study showed elevated protein (120 mg/dl) and 100 lymphocytes. The leptospira serology and WIDAL were negative. The renal and liver function tests were normal. The patient was treated empirical with doxycycline (100 mg BID orally for 7 days). Her fever subsided on day two and discharged from the hospital on day 7.

## DISCUSSION

The complications of scrub typhus usually develop after the 1st week of untreated illness. The clinical severity of scrub typhus ranges from mild to fatal organ failure. *O. tsutsugamushi* targets the endothelial cells and macrophages through which it disseminates into the multiple organs via hematogenous and lymphogenous routes and predominantly locates in the macrophages of the liver and spleen.[4] The

**Figure 1:** Photograph showing eschar in the neck region (case 1)

**Figure 2:** Photograph showing eschar in the axillary region (case 2)

bacteria then cause focal or systemic vasculitis and perivasculitis in multiple organs, with various complications. The various complications known to occur with this disease are acute renal failure, acute hepatic failure, interstitial pneumonitis, acute respiratory distress syndrome, septic shock, myocarditis, pericarditis, meningo-encephalitis and also acute hearing loss is reported.[5,6]

The CNS manifestations of scrub typhus vary from aseptic meningitis to meningo-encephalitis. Patients may present with confusion, delirium and may develop seizures. Focal neurological signs are very rare but are known to occur. CSF profile may show changes similar to viral or tuberculous meningitis.[7]

The WFT, which detects antibodies produced during *O. tsutsugamushi* infection, is the most common and commercially available test for the diagnosis of scrub typhus in developing countries like India. The sensitivity and specificity of WFT is low and is usually positive during the 2nd week of illness. The gold standard confirmatory tests like indirect immunoperoxidase test and the immunofluorescent assay are costly and not easily available in developing countries like India. Hence the diagnosis of scrub typhus is mainly by clinical suspicion and by characteristic clinical finding, eschar and serology.

The preferred drugs in the treatment include doxycycline and chloramphenicol. Doxycycline is usually given as 100 mg PO twice daily for 7-14 days. The alternative drugs used in scrub typhus include rifampin (600-900 mg/day) and azithromycin. Early treatment shows better outcomes and faster resolution than delayed treatment[7] and delayed administration of antibiotics is independently associated with major organ dysfunction.[8] Patients treated with appropriate antibiotics typically become afebrile within 48 h of starting therapy.

In our case series all presented with features of viral encephalitis (clinical and CSF study) within the 1st week of untreated illness, which is very rare and unusual. The CSF examination revealed predominant lymphocytes with elevated protein level similar to viral encephalitis. All responded to treatment with empirical doxycycline within 48 h. In addition case 2 had thrombocytopenia that resolved over a week.

The interventions for prevention of scrub typhus can be undertaken at four levels, i.e. primordial, primary, secondary and tertiary. The trombiculid mites (chiggers) are found mainly in areas of heavy scrub vegetation. The primordial preventive measures would be to avoid going to such places like farms, areas of heavy scrubs and contact with rodents and domestic animals.[9] The primary prevention methods include health promotion and specific protection. The awareness and education activities should be targeted at groups in endemic areas and to people at risk along with the general population. Rodent population can be controlled by measures like rodent poisoning and rat trapping. At present, there are no effective vaccines for scrub typhus. The specific protection measures include wearing protective clothes, using insect repellents and chemoprophylaxis.

The secondary prevention includes early diagnosis and treatment. Early diagnosis and optimal treatment can reduce many life-threatening complications. Since the sensitivity and specificity of the WFT for early diagnosis is low and gold standard confirmatory tests are not easily available in rural health settings, the diagnosis of scrub typhus mainly should focus on characteristic clinical findings. Therefore, thorough search for eschar over all areas of the body is very important in the clinical examination for early diagnosis and optimal treatment.[10] The treatment of all acute febrile illness with empirical doxycycline can be considered pending diagnosis, especially in endemic areas of scrub typhus and in high-risk population.

## CONCLUSIONS

The scrub typhus can present with unusual presentation in the 1st week of illness. Hence, scrub typhus should be included in the differential diagnosis of all causes of aseptic meningitis/encephalitis especially from endemic areas and treatment with empirical doxycycline can be considered pending diagnosis.

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