

Scrub Typhus Presenting as Meningitis Multiorgan Dysfunction Syndrome

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INTRODUCTION

Scrub typhus is a rickettsial infection caused by *Orientia tsutsugamushi* of *Rickettsiaceae* family. It is common in Asia. Clinical presentation may range from a mild, nonspecific fever to catastrophic multiorgan dysfunction syndrome involving central nervous system, kidneys, lung, and liver. We present a case of a 32-year-old female who presented to us with high grade fever, headaches, respiratory distress with failure and eschar. Investigations confirmed meningitis, ARDS. IgM antibodies against *Orientia tsutsugamushi* were positive by enzyme-linked immunosorbent assay (ELISA). Later she developed refractory shock and multiorgan failure and succumbed to her illness despite appropriate antibiotic therapy. *Orientia tsutsugamushi* of *Rickettsiaceae* family the causative organism of Scrub typhus is an obligate intracellular bacterium. Scrub typhus is transmitted by trombiculid mite bite and field rodents act as reservoirs.^[1] In the first week after the mite bite the clinical symptoms usually are fever, headache, myalgia, arthralgia, vomiting and diarrhoea. Serious complications like renal failure, acute respiratory distress syndrome (ARDS), sepsis, meningitis, meningoencephalitis and multiorgan failure usually occur in the 2nd week of illness.^[2]

PRESENTATION OF CASE

A 32-year-old woman, presented to us with fever, chills, myalgia, severe headache, and diarrhoea since 8 days and cough with breathlessness since 2 days. There was no history of vomiting, abdominal pain, blood in stools, melena, haemoptysis, convulsions. There was no pallor, icterus, lymphadenopathy, rash, or oedema. Physical examination revealed pulse rate of 122/bpm, respiratory rate of 35/min, patient was using all accessory muscles of respiration. Temperature was 104°F, blood pressure of 88/50 mm Hg, and a circumscribed eschar was seen on right iliac fossa just above the anterior superior iliac spine (figure 1). CVS examination was normal, RS examination revealed bilateral coarse crepitations all over the lung fields. Per abdomen examination was normal. Neurological examination revealed stupor GCS: (E-2 M-4 V- 3,) neck stiffness, and positive Kernig' sign. There were no focal neuro-deficits.

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Laboratory investigations: TLC- 11,200 cells/ mm³, with polymorphonuclear predominance; haemoglobin: 11 gm/dl, platelet count 1.5 lakhs cells/mm³, blood urea 160 mg/dl; serum creatinine 2.6 mg/dl; bilirubin 4.8 mg/dl; alanine aminotransferase (ALT) 235 IU/L; aspartate aminotransferase 148 IU/L; alkaline phosphatase 86 IU/L; total protein 6.8 g/dl; IgM antibodies against *O. tsutsugamushi* by enzyme-linked immunosorbent assay (ELISA) were positive. Blood and urine cultures were negative. Quantitative buffy coat for malaria, and IgM and IgG antibodies for leptospirosis and dengue were negative.

Chest X-ray revealed bilateral infiltrations (figure 2). PaO₂/FiO₂- 188, ECG showed sinus tachycardia. 2 D echo was normal. Abdominal ultrasound was normal. Computerized tomography of the brain with contrast revealed features of developing leptomeningitis. (Figure 3). Cerebrospinal fluid (CSF) analysis showed: TLC -82 cells with lymphocytic pleocytosis, protein 198 mg/dl, sugar 68 mg/dl, normal adenosine deaminase (4 U/L). CSF QuantiFERON-TB Gold assay was negative for tuberculosis and CSF RCR for herpes simplex virus was also negative.

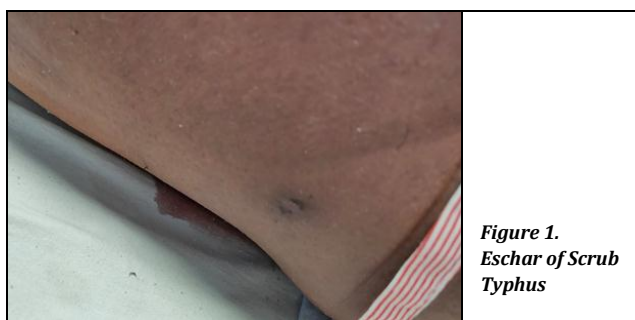


Figure 1.
Eschar of Scrub Typhus

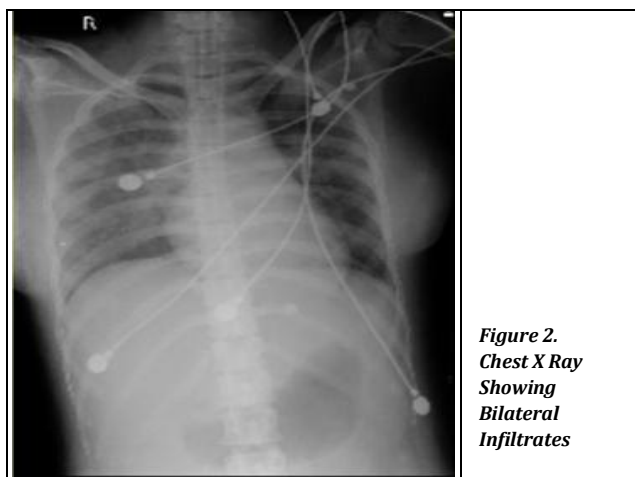


Figure 2.
Chest X Ray Showing Bilateral Infiltrates



Figure 3. CECT Brain Showing Features of Leptomeningitis

With a diagnosis of Scrub typhus with MODS and meningitis, she was started on Volume replacement with IV fluids, Inj. Noradrenaline, IV Azithromycin 500 mg/day, Tab. Doxycycline of 100 mg twice daily through RT, Mechanical

ventilation as per ARDS protocol, empirical Inj. Ceftriaxone as per creatinine clearance twice a day. Irrespective of treatment she succumbed to her illness.

DISCUSSION

Scrub typhus usually occurs in rainy season in India.^[3] The name “typhus” is derived from the Greek word, typhos that means stupor. The infection caused by *O. tsutsugamushi* spreads by blood and lymphatics and cause generalized vasculitis. The clinical symptomatology may range from maculopapular rash, generalized lymphadenopathy, hepatitis, pneumonitis, meningitis/meningoencephalitis, AKI, and septic shock.^[4] A study showed association of pneumonitis was with the occurrence of scrub typhus meningitis and meningoencephalitis.^[5]

Meningitis is actually a rare manifestation of Scrub typhus. In a study conducted in Thailand only one patient out of 30 diagnosed cases had meningitis.

The CSF findings in scrub typhus resemble those in viral meningoencephalitis, leptospirosis, and tuberculous meningitis.^[6] Eschar, is the pathognomonic sign of scrub typhus, which is a non-pruritic, nontender ulcer surrounded by red areolae and is covered by dark scabs. It is present in up to 50-60% of cases.^[6]

Scrub typhus is grossly under-diagnosed in India may be due to its vague clinical presentation, low index of suspicion, overlapping features with other tropical infectious diseases like malaria, leptospira and dengue and also lack of diagnostic facilities.^[7] India has an annual incidence of approximately one million cases.^[7] In a published study MODS was reported in one third of patients (17 out of 50). Hypotension (16%), renal impairment (12%), ARDS (8%) and meningitis (14%) were some of the important complications noted. They reported dramatic response to doxycycline in nearly all the patients.^[8] Our patient did not respond to the therapeutic regimen may be because of late arrival.

In a retrospective study of scrub typhus cases, conducted at a university teaching hospital, including 623 patients admitted between 2005 and 2010, MODS was seen in (34%) of patients.^[9] 5 Features of acute lung injury were observed in (33.7%) and (29.5%) required ventilator support. Shock requiring vasoactive agents, CNS dysfunction and renal failure were independent predictors of mortality.^[9]

The serologic diagnosis of scrub typhus is made by various tests. A single indirect immunofluorescent antibody (IFA) titer against *O. tsutsugamushi* of 1/400 or a 4-fold or greater rise in IFA titer is diagnostic. IgM ELISA based on the detection of 56 Da antigen has high specificity (~90%) and sensitivity (~90%) when compared to IFA. A standard PCR targeting the 56-kDa outer membrane protein will be useful but not widely available.^[10]

The treatment of choice for Scrub typhus is Doxycycline 200 mg/day for 7 days. Our patient did not respond to oral doxycycline. Failure of Doxycycline can be due bacteriostatic action, lower penetration into CSF (only 15–30%), and resistance to the drug. Azithromycin (10 mg/kg/day) has been proven to be more effective in both doxycycline-susceptible and resistant scrub typhus.^[11] Our patient did not respond to both the drugs.

CONCLUSIONS

Complications of scrub typhus can occur in the 1st week of illness and severity of complications ranges from a mild illness to myriad of life-threatening events. A high index of suspicion is required to diagnose scrub typhus in the early phase of the disease because delay in diagnosis can be catastrophic. Though eschar is pathognomonic, it is present only in half of the cases. A meticulous clinical examination is mandatory. In developing countries, where scrub typhus is endemic, the need for the development of rapid highly sensitive and commercially available diagnostic tests is very important. Especially in endemic areas treatment of all acute febrile illness with empirical doxycycline seems prudent.

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