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Scrub Typhus

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Abstract
Scrub typhus is a rare and underdiagnosed disease caused by Orienta tsutsugamushi which results in multiorgan failure and has the case fatality rate of 70%. Here we present a case of a 25-year-old male who presented with vague symptoms of hepatitis and pneumonia but later, the development of ARDS and abdominal eschar led to diagnosis of this condition as scrub typhus infection. This patient was treated with parenteral ceftriaxone and oral doxycycline.

Keywords: laparotomy, intraabdominal mass, paediatric tumours

Introduction
Scrub typhus is caused by Orienta tsutsugamushi organism which is transmitted by the larval stage of Leptotrobidium mites, also known as chiggers [1]. Generally, the diagnosis is made by the history of eschar and/or a history of travel to endemic areas along with the patient's presenting clinical complains [1]. It has one million cases per annum and the antigenic heterogeneity of O tsutsugamushi is a threat as it precludes generic immunity and increases reinfection [1]. The larva mainly feeds on thin, wrinkled skin and takes the advantage of the hair follicles or pores on the skin rather than piercing it. It forms a black eschar like a cigarette burn on the site of chigger feeding [1]. The organism has been reportedly found in the salivary glands of the mites. When present, the eschar precedes fever and is usually present below the umbilicus in males. In females, anterior chest, head, and neck present as the usual pattern of developing eschars. The majority of the cases of scrub typhus are reported to be in the 'tsutsugamushi triangle' formed in the Asia-Pacific region [1]. The gold standard for diagnosing this condition is by performing immunofluorescence assay (IFA) [2]. Oral Doxycycline is the treatment of choice in mild cases, but severe cases may require parenteral administration [4]. Next-Generation sequencing is a new diagnostic tool that can help diagnose scrub typhus cases without the pathognomic eschar [5].

Case Presentation
A 25-year-old male patient presented with complaints of dry cough, high-grade fever, abdominal pain in the periumbilical region, breathlessness at rest, and yellowish discoloration of skin and sclera. He did not have any complain of decreased urine output, altered behavior, or bleeding from any site. He did not have a past history of any major medical illness. Patient had a history of occasional alcohol consumption over the last few years but didn't consumed it in last 6 months.
On general examination, the patient had evident icterus and his oxygen saturation was 76% on room air. All other general examination findings were unremarkable. On systemic examination of the per abdomen, the patient had a soft, tender abdomen with guarding present. On respiratory system examination, the patient had absent air entry in both the lower lobes of the lungs along with extensive crepitations in both the upper and middle lobes. Other systemic examination findings were normal.
The patient's routine investigative findings are mentioned in the table below. Total protein content was reduced. Serum albumin and sodium concentrations were decreased. The patient's activated plasma thromboplastin time was increased and prothrombin time was normal. The Dengue NS1 antigen and IgM, IgG antibody tests were reported to be negative. HIV1 & HIV2 antibody, HBsAg, IgM antibody against leptospira, HAV antigen, and HEV antigen were all found to be negative. The arterial blood gas analysis is narrated in the table below. The plasma fibrinogen level was normal. The fibrinogen degradation product was >5 µg/mL and was reported positive. The test for antibody IgM to scrub typhus by ELISA was indexed to be 3.6 and was reported highly positive. Anti-nuclear antibody (ANA) testing was found to be negative. Granzymes A and B levels in the plasma of this patient on admission were elevated (2200 pg/ml and 790 pg/ml respectively).

Table 1

Investigation	Value
Hemoglobin Concentration	10.6gm%
Red Blood Cell Count	3.5million cells/cmm
White Blood Cell Count	36000 cells/cmm

Total Platelet Count	39000 cells/cmm
Serum Urea Concentration	69mg/dL
Total Bilirubin Concentration	12.8mg/dL
Direct Bilirubin Concentration	6.7mg/dL
Indirect Bilirubin Concentration	6.1mg/dL
Serum Albumin	2.7gm/dL
SGPT (ALT)	187U/L
SGOT (AST)	220U/L
Alkaline Phosphatase	188U/L
Sodium Concentration	121mmol/L
Potassium Concentration	2.6mmol/L

Table 2

Arterial Blood Gas Analysis Parameter	Value
pH	7.43
pO_2	68mmHg
pCO_2	39.7mmHg
A-a Gradient	43.1mmHg
Plasma Bicarbonate Concentration	21.8mmol/L
Blood CO_2 Concentration	19.2mmol/L
Base Excess	-2.9mmol/L
Base Excess in Extracellular Fluid	-3.1mmol/L

On ultrasonography, the patient was found to have an enlarged liver and an enlarged spleen. Other Ultrasonographic findings were unremarkable.

On chest radiography, the patient was found to have inhomogenous opacification in the middle and lower zones of both the lungs which were suggestive of bilateral consolidation. Other chest x-ray findings were unremarkable.

This patient was treated for 10 days with injection ceftriaxone 1 gm twice a day and oral doxycycline 100mg twice daily. Other than this, the patient was treated with paracetamol and morphine for fever and pain. oxygen therapy by non-re-breather mask given initially and weaned as patient improved.

Discussion

Scrub typhus presents as nonspecific flu-like symptoms, fever, rash, headache, myalgia, cough, nausea, generalized lymphadenopathy, and abdominal pain as presented in this patient[2]. Scrub typhus can be misdiagnosed very frequently as malaria, dengue, rickettsial diseases, acute febrile conditions, leptospirosis, infectious mononucleosis, or HIV [2]. The lung is the most commonly affected organ due to scrub typhus infection and the majority of the mortality ensues due to development of ARDS. Although being the gold standard, IFA is expensive and complicated, and hence other serological tests such as indirect immunoperoxidase assay, Weil Felix test, ELISA, and immunochromatographic methods [3]. In this case, considering the ELISA cutoff value of >0.72 Madhya Pradesh, Central India [6], the patient's value of 3.6 indicates strong positivity of scrub typhus infection. Quantitative polymerase chain reaction is most sensitive in the early stage (<7days) of the disease when other serological tests are negative [7]. A study has shown that the serum levels of granzymes A and B increased during the acute phase of the disease, which was seen in our patient and reduced rapidly after treatment [8]. This can be suggestive of the role played by cytotoxic T-cells or natural killer cells in the pathology of scrub typhus. In a study, it was demonstrated that ANA positivity was significantly higher in patients with scrub typhus compared to those with other febrile illnesses [9], but here in this case ANA was reported to be negative. As scrub typhus is an infectious vasculitis, ANA positivity can be either causal or an epiphenomenon. One study has reported 44.8% sensitivity and 99.7% specificity for real-time PCR diagnosis of 16s rRNA [10], the rt-PCR report for this patient was also found to be negative. Doxycycline is the treatment of choice for scrub typhus. WHO recommends prophylaxis in endemic areas and 7 oral doses of doxycycline, tetracycline, or chloramphenicol over 35 days to be given every 5 days are proven to be effective for prophylaxis [11]. Rifampicin is more effective in patients that are poor responders to doxycycline. The recent upsurge in the cases of scrub typhus can be explained by population expansion which has led to increased urbanization, reduced sanitation, and increased the diversification of forest land for agricultural use [11]. Climate change has also affected the incidence of scrub typhus cases lately in India.

Conclusion

Scrub typhus is a rare but re-emerging disease of multi-organ failure due to mite larvae. It should always be kept in mind as a differential diagnosis if eschars are found during the general examination or if there is any history of travel to or residence in endemic areas it should be elicited properly. Proper prophylaxis should be suggested to people native to or traveling to scrub typhus prone areas.

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