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A case of Scrub Typhus presenting with high fever, eschar, septic shock, ARDS, acute kidney injury, thrombocytopenia, hypoalbuminemia and transaminitis in 50-year-old man coming back from Delta region of Myanmar

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Abstract

A 50-year-old gentle man, coming back from Delta region, presented with, septic shock, ARDS and acute kidney injury following 8 days history of high fever. Eschar was noted on right forearm. His temperature was 105°F; very ill and toxic with SaO2 90% on air. He was hypotensive (80/50 mmHg), tachycardic (128/ min), tachypneic (respiratory rate 32/min) with low SaO2 (90% on air); crackles were audible in both lungs. Chest radiograph showed patchy opacities in both lungs. He had low Platelet count (34 x 109/mm3), raised serum creatinine (160 µmol/L), raised liver enzymes (SGOT 121 U/L & SGPT 86 U/L) and low serum albumin (22 mg%). Rapid test for Scrub Typhus IgM was positive. The patient recovered with oxygen therapy, fluid replacement, inotropes, cefopyrazone/salbactam and doxycycline.

Keywords: Fever; septic shock; ARDS; acute kidney injury; hypoalbuminemia; eschar; scrub typhus; doxycycline.

Background

Scrub typhus, or tsutsugamushi fever, is a zoonotic disease, caused by *Orientia* (formerly *Rickettsia*) *tsutsugamushi*. It is first described in Japan in 1899; it is transmitted to humans by mite, an arthropod vector of the *Trombiculidae* family. Morbidity and mortality caused by rickettsioses have had a major influence on military activities and public health for over 2000 years [1].

Myanmar has been one of the endemic countries since 1947 [2] and sporadic cases were reported both from Myanmar and neighboring countries [3, 4]. As of variants, phenotypic and genotypic variants *Orientia tsutsugamushi* were reported in the Asia-Pacific region [5] and Thai-Myanmar border [6]; genotypic heterogenicity was also recovered in Myanmar recently [7]. Therefore, different variant or new variant of *Orientia tsutsugamushi* may have changes in not only infectivity and clinical presentation but also antimicrobial sensitivity. Mortality rates for scrub typhus range from 1% to 50% depending on timing of proper antibiotic treatment, host immunity, co-morbidities

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and the strain of O. *tsutsugamushi* encountered.

Case presentation

A 50-year- old man came with high continuous fever, cough and headache for 8 days. He had been to forest in Delta area which is the continuous with Bago Range a few weeks ago. He noticed history of tick bite. Eschar was noted on right forearm. (**Figure 1-a**) His temperature was 105°F; very ill and toxic with SaO2 90% on air. His blood pressure was 80/50 mmHg, pulse rate was 128/min. Crackles on both lungs. Blood for complete picture showed mild anaemia (hemoglobin 10.2 g/dl); normal total WBC (7.6 x 109/mm3) with normal differential count (Neutrophil 55%, Lymphocyte - 38%, Monocyte - 7%, Eosinophil - 0 %); and, low Platelet count (34 x 109/mm3). CXR (PA) revealed patchy opacities in both lung field suggestive of broncho-pneumonia with ARDS (Figure 2). ECG (12 leads) were normal. Ultrasonogram of abdomen was normal. Blood for malaria parasite was negative; Dengue IgG and IgM were negative. Blood for Widal test was negative. Urine RE was normal. Liver Function test revealed normal total bilirubin (0.3 mg/dl) with raised liver enzymes: SGOT 121 U/L (< 36 U/L); and, SGPT 86 U/L (< 40 U/L). Total protein was normal 54 mg% with low albumin 22 mg%. Serum creatinine was 160 µmol/L. Rapid test for Scrub Typhus IgM was positive. Retroviral serology, KT-VDRL and hepatitis screen (B and C) were negative. Sputum for acid fast bacilli was negative; Klebsiella species was grown in sputum and sensitive to cefopyrazone/salbactam and amikacin. He was treated with oxygen therapy, fluid replacement, inotropes, cefopyrazone/salbactam and doxycycline; temperature fell after 72 hours. The platelet count rose to 150 x 109/mm3 one week later; SGOT and SGPT normalized by two weeks. Acute kidney injury improved with fluid replacement. Eschar healed at one week (**Figure 1-b**).

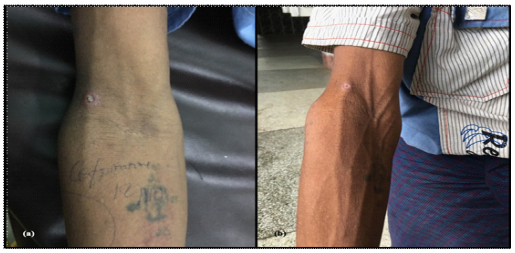

Figure 1: *(a) Showing eschar on flexor aspect of right forearm (Lt) and (b) showing healed eschar (Rt)*

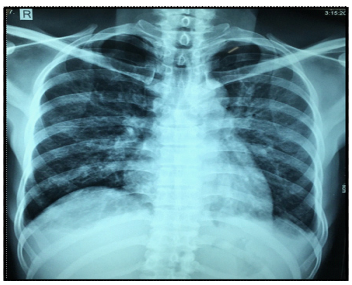

Figure 2: *CXR showing multiple patchy opacities in both lung field.*

Discussion

Scrub typhus is a neglected tropical disease; and, a leading cause of undifferentiated febrile illness in the areas of tsutsugamushi triangle caused by *Orientia tsutsugamushi*. Imported cases of scrub typhus was reported in those travelers coming back from tsutsugamushi triangle [8]. The prevalence of scrub typhus or the infectivity of mite/tick may be related with ecology; a sudden upsurge in scrub typhus cases was reported after the 2015 earthquake in Nepal [4].

Clinical presentation may be typical [9] or rare presentation if early diagnosis could not get or the patient came late; thus, complicated by ARDS [10], multiorgan failure and thrombocytopenia [11]. It may presented with acute abdomen, septic shock and DIC rarely [12]. This patient came to hospital late; he had fever for almost 7 days- septicemic state. Thus, he had septic shock, ARDS, acute kidney injury, thrombocytopenia, hypoalbuminemia and transaminitis.

In 2017, serologic and molecular surveillance of 152 suspected scrub typhus patients in central region of Myanmar revealed *Orientia tsutsugamushi* of genotypic heterogeneity. In addition, potential co-infection with severe fever with thrombocytopenia syndrome virus was observed in 5 (3.3%) patients. Both scrub typhus and severe fever with thrombocytopenia syndrome were endemic in Myanmar [13]. Therefore the presence of thrombocytopenia in this patient supported their findings. Eschar was seen in 95% of cases. Eschar is pathognomonic; the underlying erythema may varies with ethnicity/ skin color- more prominent in white skin; multiple eschars may be seen [14].

Rickettsial infections are widespread in Myanmar; recent serological study on 700 leftover blood samples from primary care clinics and hospitals of central and northern regions of Myanmar revealed that IgG seroprevalence for scrub typhus was nearly 20%, for murine typhus was 5% and for spotted fever group was 3% [15]. This patient came back from Delta area, southern regions of Myanmar; therefore, the seroprevalence of rickettsial infections may be wide spread.

History of travelling or exposure along with tick bite gave clue to diagnosis if the patient was fully conscious; otherwise, physical examination was extremely important. Eschar is the single most useful diagnostic clue; pathognomonic**.** The eschar begins as a small, painless papule at the site bitten by chigger and develops during the 6 to 18days (median 10 days) incubation period. It enlarges, undergoes central necrosis with a black crust; the border is surrounded by reddish erythema.

In endemic area, the tick may be attached to skin of patients. The common presentations were fever, headache, myalgia, and non-specific malaise; hearing loss concurrent with fever was seen in one third of cases. Conjunctival suffusion/congestion was remarkable as seen in this patient. Generalized lymphadenopathy is seen in majority of cases. Cough sometimes accompanied by infiltrates on the chest radiograph is one of the commonest features; common findings in CT chest are ground glass opacity, mediastinal lymphadenopathy and

inter-lobular septal thickening [16]. In chest radiograph of this patient, multiple ground glass opacities were seen. However, CT chest was not done in this case. The serious complications are pneumonitis, myocarditis, meningoencephalitis, acute renal failure, gastrointestinal bleeding and ARDS. Cases with multi-organ failure and immune thrombocytopenia were reported [11]. In this patient, hypoalbuminemia and transaminitis were present in addition to septic shock, ARDS, acute kidney injury and thrombocytopenia. The study by Aung Thu reported hypoproteinaemia, elevation of SGOT, SGPT, and alkaline phosphatase in cases of scrub typhus in Myanmar. Thus, having hypoalbuminemia and transaminitis in this patient confirmed the report.

Diagnosis of scrub typhus is challenging as its symptoms mimic with other acute febrile illnesses. Several methods are used for diagnosis of scrub typhus: enzyme-linked immunosorbent assay (ELISA), immunofluorescence assay (IFA), immunochromatographic test (ICT), Weil–Felix, polymerase chain reaction (PCR) and loop-mediated isothermal amplification (LAMP). PCR based methods are good for early-stage diagnosis with higher specificity and sensitivity; however, it is less applicable in circumstances of scrub typhus due to the variegated genetic makeup of *Orientia tsutsugamushi* among its serotypes [17]. In resource limited setting, all the diagnostic tests are difficult. In this case, the diagnosis was mainly based on eschar, positive rapid test for scrub typhus IgM and exclusion of other common causes of fever of antimicrobial therapy, the treatment of choice is oral tetracycline 500 mg four times daily or oral doxycycline 100 mg twice daily for 7 days. The alternative is oral chloramphenicol 500 mg QID for 7 days. Oral ciprofloxacin or rifampicin can also be used. In severe cases, parenteral doxycycline/parenteral chloramphenicol (50-75 mg/kg/day) should be given. One of efficacy and safety studies on scrub typhus revealed that clarithromycin may be safe [18]. The mortality rate is 50 % without treatment.

Conclusion

In cases with acute febrile illness, focused history taking particularly travelling history and tick bite is important. Thorough physical examination is essential; not to miss pathognomonic features, eschar. As the confirmatory tests, Immunofluorescent assay (IFA) and the immunoperoxidase test (IP), are not easily available in low-resources setting; history taking and physical examination are the only tools to get diagnosis early. Treatment is very simple and very cheap; early treatment not only gives dramatic clinical response but also prevents fatal complications. It is not responsive to conventional antibiotics.

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Declaration of conflict of interest

The authors declared no potential conflicts of interests with respect to authorship and publication of this article.

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