A rare presentation of scrub typhus: myocarditis, acute liver failure and leukemoid reaction

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Abstract

Scrub typhus is a mite borne zoonosis, caused by Orientia tsutsugamushi, a gram-negative intracellular organism. This infection usually presents in high prevalence in the rural areas of East Asia and Western pacific islands. It usually presents with fever, chill, myalgia, headache, skin rashes, having pathognomonic and skin lesion i.e. eschar in ~10% cases in Indian subcontinent. It can present with life-threatening complications on occasional. The simultaneous presentation of more than two complications is uncommon, rarely reported in literature. Here we report a case of 37-year-old woman with acute febrile illness, complicated with myocarditis, acute liver failure and leukemoid reaction. She was diagnosed promptly and successfully treated with doxycycline with full recovery of the complications.

INTRODUCTION

Scrub typhus is an acute febrile illness, caused by Orientia tsutsugamushi, transmitted to human by bite of trombiculid mite [1]. The incubation period is usually 6–21 days. The infected patient commonly presents with fever, chill, headache, myalgia, skin rashes, eschar and lymphadenopathy. The delay in diagnosis and treatment of scrub typhus may lead to develop serious complications like acute respiratory distress syndrome, myocarditis, acute kidney injury, liver dysfunction, meningoencephalitis and rhabdomyolysis, which pre-dominate in second week of untreated infection. Mortality is very variable, ranging from 0% to 70% in untreated patients (median 6%), for unknown reason [2].

Here we report a case presenting with a combination of complications like myocarditis, acute liver failure and a rarity-like leukemoid reaction, which was managed by timely diagnosis and prompt initiation of therapy.

CASE REPORT

A 37-year-old woman, residing in a village in India, without any comorbidities, presented with fever for 10 days, jaundice for 3 days, disorientation along with chest pain for 2 days prior of admission. Fever was moderate grade, intermittent without any chill and rigor. The jaundice was gradually progressive. The chest pain was dull aching, diffuse and non-radiating, not associated with sweating. The patient disoriented 2 days prior to admission. There was no history of abdominal pain, vomiting, joint pain, skin rashes, oral ulcers, cough, shortness of breath, gastrointestinal bleeding, headache and convulsion. Her menstrual history was normal. She had no history of ischemic heart disease, blood transfusion, intake of alcohol, any chronic drug use (steroid), over the counter or traditional medications and herbs before and after admission.

On physical examination, patient was drowsy, Glasgow Coma Scale was 10/15 (E2V4M4), pulse rate was 120/min, blood pressure was 100/70, respiratory rate was 22/min, axillary temperature was 102° F and there were no rashes on skin. The patient was icteric (Figure 1) and had mild pallor. There was diffuse tenderness over right hypochondrium on abdominal examination. She had bilateral extensor planter. S3 gallop was found on cardiovascular examination. Considering these clinical scenario infections, which are commonly diagnosed in

Figure 1. Photograph showing icterus.
India, malaria, dengue, leptospirosis, viral hepatitis and scrub typhus were thought of but autoimmune diseases were also kept in mind.

Complete hemogram revealed anemia (hemoglobin 9.2 g%), marked leukocytosis (90,400/cmm), thrombocytopenia (platelet 1 lac/cmm) and left shift on peripheral blood smear (neutrophils and band forms 70%, myelocytes 2%, metamyelocytes 10%, monocytes 2%, eosinophils 2%). She had normal serum electrolytes (serum Na+ 138 mEq/l, K+ 3.8 mEq/l) and renal functions (Ur 22 mg/dl, Cr 0.7 mg/dl). There was conjugated hyperbilirubinemia (total bilirubin 7.6 mg/dl, direct/indirect 5.6 mg/dl/2 mg/dl), marked transaminitis (aspartate aminotransferase [AST] 3552 U/l, alanine aminotransferase [ALT] 4055 U/l) with normal serum albumin and globulin level on liver function test, which suggested acute hepatitis. There was coagulopathy with prothrombin time (PT, 54.2 s) international normalized ratio (INR, 6.45) and activated partial thromboplastin time (aPTT, 34.2 s). Serum ammonia was 94.4 mcg/dl, which suggested of hepatic encephalopathy. She had lactate dehydrogenase (1032 U/l), C-reactive protein (32.2 mg/dl), erythrocyte sedimentation rate (84 mm first 1 h) and procalcitonin was negative (0.4 ng/ml). Serum triglyceride was 176 mg/dl. Ultrasonography of abdomen showed increased liver echogenicity. Her blood and urine were sterile. Autoimmune workup like antinuclear antibody was negative.

She had towering liver enzymes with acute liver failure but serologically negative for hepatotropic virus (hepatitis B virus, hepatitis C virus, hepatitis E virus, hepatitis A virus). Serology for IgM dengue/IgM leptospira was negative. No malarial parasites were found on peripheral blood smear; Malaria Parasite Dual Antigen (MPDA) was also negative. But she had positive IgM for scrub typhus detected by enzyme-linked immunosorbent assay. Non-contrast CT (NCCT) of brain was normal; cerebrospinal fluid study was done to rule out any central nervous system (CNS) infection, but it was normal.

Her drowsiness was explained by hepatic encephalopathy after ruled out all possible metabolic and septic causes of encephalopathy, CNS infection and vascular events.

For chest pain, electrocardiogram (ECG) was done, showing ST-depression on lateral leads predominantly (V5, V6, lead 1, Augmented Vector Left (aVL)) (Figure 2) with elevated Troponin-T and Creatine Phosphokinase - MB (CPK-MB); there was global hypokinesia of left ventricle with ejection fraction 45% on transthoracic echocardiography, which suggested of myocarditis noninvasively supported by history of non-ischemic chest pain and normalization of ST-T changes, cardiac enzymes and echocardiographic findings later, after institution of disease directed treatment. Because of coagulopathy, with PT (54.2 s) INR (6.45) and aPTT (34.2 s), coronary angiography was not done.

For leukocytosis, to rule out myeloproliferative disorders, bone marrow aspiration and biopsy was done, which showed reactive marrow with myeloid: erythroid (M:E): 3:1 and no abnormal and hemophagocytic cells.

For reactive marrow and leukocytosis, we did leukocyte alkaline phosphatase (LAP) score, it came out 110, which is high, so leukemoid reaction was confirmed. The patient was hemodynamically stable with no history of hypotension; so this leukemoid reaction was not explained by hepatic necrosis.

Initially, the patient was treated symptomatically for acute liver failure and myocarditis. She was put on intravenous doxycycline for 14 days after positive scrub typhus report. The patient was improved gradually and became asymptomatic with normalization of liver enzymes (ALT 34 U/l and AST 28 U/l), thin-layer chromatography was 9800/cmm, cardiac enzymes (CPK-MB and troponin T) and ST-T changes on ECG on discharge and asked to take rest another few days, avoid strenuous activities and slowly increase exercise level.

DISCUSSION

Elevation of liver enzymes is common in scrub typhus but acute liver failure is rarely reported in literature [3]. Presentation of chest pain with tachycardia and S3 gallop suggested myocarditis, which was confirmed by ECG findings (ST depression, T inversion) and elevated troponin T and CPK-MB. Myocarditis rarely reported [4] and postulated to be caused by localized infection in endothelial cells of heart and cardiac myocytes [5].

Leukemoid reaction which, is very unusual following scrub typhus, can be explained as physiological response to overwhelming infection, which releases stimulatory molecules like growth factors (granulocyte colony-stimulating factor, granulocyte-macrophage colony-stimulating factor, Receptor tyrosine kinase (c-KIT) ligand), adhesion molecules (CD11b/CD18) and various cytokines (interleukin-1, 3, 6, 8, tumour necrosis factor) [3]. It often mimics hematological malignancy and could be differentiated by elevated LAP score [6, 7]. In a tropical country like India, scrub typhus serology should be done in acute febrile patient presenting with acute
liver failure and/or myocarditis. Scrub typhus infection has an excellent therapeutic response to inexpensive antibiotic doxycycline within 5 days of therapy [8]. Early therapeutic intervention with doxycycline should be intensified in endemic countries.

Scrub typhus has emerged as a common etiology of febrile illness in Southeast Asian countries. It is underrecognized infection, which may present with serious complications like myocarditis and acute liver failure. Leukemoid reaction may be seen in scrub typhus like other triggering infections. In patients with acute febrile illness with acute liver failure and/or myocarditis, scrub typhus should be ruled out in all cases. Timely diagnosis of disease and therapy with doxycycline/or azithromycin leads to excellent prognosis.

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CONFLICT OF INTEREST STATEMENT
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ETHICAL APPROVAL
None required.

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CONSENT
Written informed consent was obtained from the patient for publication of this case report and accompanying images.

GUARANTOR
Prof. Dr Soumitra Ghosh.