Case report

Massive splenomegaly in scrub typhus: A rare presentation

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Introduction

Scrub typhus, caused by rickettsial pathogen Orientia tsutsugamushi, is endemic and re-emerging in eastern and southern Asia, northern Australia and islands of the western Pacific and Indian oceans. Scrub typhus is a potential cause of Pyrexia of Unknown Origin (PUO) as reported in recent studies [1–3]. With an usual incubation period of 6–21 days, the illness varies from mild and self limiting to fatal. Patients who do not receive an appropriate treatment can have a high case fatality of around 30–70% while the median case fatality rate for untreated patients is 6% and for treated patient is 1.4% [4]. Hepato splenomegaly is not an uncommon occurrence in scrub typhus positive patients. Massive splenomegaly has been previously described in cases with scrub typhus and malaria coinfection [5]. Massive splenomegaly in isolated scrub typhus infection is rarely reported in literature. We report a case of PUO presenting with fever and massive splenomegaly posing a diagnostic challenge.

CASE REPORT

A 22 year old male from Sitapur district of the Indian state of Uttar Pradesh presented with a 15 day history of fever, abdominal pain, myalgia and headache. Clinically, patient was febrile (oral temperature - 101.2 °F), conscious and anicteric with no apparent skin rashes. His blood pressure was 128/70 mmHg, pulse rate was 112/min and oxygen saturation – 94% on room air. The patient had multiple, firm to rubbery, non tender, discrete lymph nodes in axillary region (largest in anterior axillary - measuring 2 cm × 2 cm). He also had palpable firm, non tender, discrete lymph nodes in inguinal region around 1.5–2 cm in diameter. Auscultation of chest revealed diminished breath sounds in basal regions of left side. Prominent splenomegaly, palpable up to 10 cm below the costal margin [Fig. 1] and a mild hepato megaly (liver span-14 cm) were the findings on abdominal examination. Cardiovascular and neurological examinations were essentially normal.

Complete blood counts revealed mild normocytic normochromic anemia (hemoglobin 12 g/dl), thrombocytopenia (90,000 cells/mm³) and normal leucocyte count 8200/cmm. Other blood investigations showed normal electrolytes, kidney function tests, liver function tests, sterile blood cultures, negative malarial parasite, rk 39 for kala-azar and IgM Dengue. A chest X ray was done that showed mild blunting of left costophrenic angle. Blood was taken for culture and sensitivity, using aseptic precautions before starting antimicrobial (injection ceftriaxone -1gm 12 hourly) which was found to be sterile. Patient developed puffiness of face and pedal edema on day 5 of admission. His oxygen saturation dropped to 88% on room air, while urine output was adequate (24 h – 1.5 l). Urinalysis revealed trace proteinuria (10 mg/dl), pyuria(4–6 WBCs/hpf) and absent hematuria. Urine culture was found to be sterile. An electrocardiogram showed sinus tachycardia and no evidence of vegetations or valvular regurgitations were found on 2 Dimensional echocardiogram. A contrast CT of abdomen and thorax was done that showed mild hepatomegaly, gross splenomegaly, mild left sub-pulmonic pleural

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effusion with collapse and consolidation in basal region of left lung. Facial puffiness and pedal edema resolved on diuretic treatment by day 12. C-reactive protein was elevated (96 mg/dL) and PPD (Purified Protein Derivative) test was negative.

A bone marrow aspiration was done on day 7 to exclude the possibility of lymphoma, which showed normal hemopoiesis without any immature cells. Lymph node biopsy was planned but could not be done due to patient’s unwillingness. In view of non resolving fever, thrombocytopenia, hepato-splenomegaly and lung consolidation, IgM antibody for scrub typhus was done which was found to be positive (OD = 2.538). A course of oral doxycycline was started on day 12 (100 mg BD), pyrexia resolved on 2nd day of treatment [Table 1] and patient showed rapid clinical improvement within 7 days of introducing doxycycline. Spleen regressed completely and lymph nodes in axillary and inguinal region were no longer palpable by day 18. He was discharged afebrile on day 20 post admission.

Differential diagnosis:
- Lymphoma
- Malaria
- Visceral Leishmaniasis
- Enteric Fever
- Acute Leukemia
- Infective endocarditis

Discussion

Scrub typhus is an acute febrile illness caused by obligate intracellular gram-negative bacterium Orientia tsutsugamushi transmitted to rodents (primary host) and humans (accidental host) by the bite of the larval form of trombiculid mite. Scrub Typhus can have diverse clinical manifestations ranging from fever, headache, myalgia, generalized or regional lymphadenopathy to meningo-encephalitis, acute respiratory distress syndrome and multiple organ dysfunction syndrome with hepatic and renal failure. The classical “eschar” as described in scrub typhus is found only in a few proportion of the patients. Scrub typhus has emerged as a potential cause of prolonged fever in recent years and it is known to be endemic within the geographical confines of the “tsutsugamushi triangle” extending from northern Japan and far-eastern Russia in the north to northern Australia in the south and to Pakistan in the west [6]. The Indian subcontinent owing to its very location represents one of the largest tropical and subtropical regions with high prevalence of many of these infections [7].

Hepatomegaly and splenomegaly may be found in patients of scrub typhus as reported in previous studies [8–11]. Splenomegaly is “massive” when it is palpable >8 cm below the costal margin or its drained weight is >1000 g [12]. Diseases associated with massive splenomegaly include chronic myeloid leukemia, lymphomas, hairy cell leukemia, polycythemia vera, sarcoidosis and infections like malaria and visceral leishmaniasis. Massive splenomegaly in scrub typhus is rarely reported in literature.

Our patient had fever, moderate hepatomegaly, massive splenomegaly and axillary and inguinal lymphadenopathy on presentation. The closest differential that we considered was lymphoma. A normal peripheral blood examination, gradual resolution of lymphadenopathy and a normal bone marrow examination negated its possibility. Being a highly endemic zone, odds of malaria and kala-azar in our case were high, but were eventually ruled out by negative smear examination and immunochromatographic tests for malaria and a negative rk 39 dipstick test for kala-azar. A 2D Echocardiography done to rule out infective endocarditis showed an absence of valvular regurgitation or vegetations.

Fever in our case was unresponsive to conventional broad spectrum antibacterials. CT thorax and abdomen revealed subpulmonic pleural effusion and collapse and consolidation of basal region of left lung in addition to hepatosplenomegaly. In view of prolonged non responsive fever and high endemicity, we ordered IgM antibody for scrub typhus by ELISA which showed a positive result with subsequent rise in optical density values (OD values) on day 18. Our case had a transient anasarca that could be attributed to the capillary leak induced by the infection. A course of oral doxycycline resolved fever, hepatosplenomegaly and lymphadenopathy in our patient dramatically which further confirmed our diagnosis.

Scrub typhus is a grossly underdiagnosed cause of undifferentiated fever in our country. Lack of awareness and a low index of clinical suspicion combined with lack of availability of adequate

Table 1

| Day 1 | Day 5 | Day 10 | Day 12 | Day 14 | Day 16 | Day 18 | Day 20 |
|-------|-------|--------|--------|--------|--------|--------|--------|
| 104   | 102   | 100    | 98     | 96     | 97     | 99     | 100    |

Fig. 1. Figure showing enlarged spleen, measuring upto 10 cm below right costal margin in mid clavicular line on day 1 of hospital stay.

Table 1

Table showing temperature spikes of the patient during hospital stay. Doxycycline was added on day 12; note the gradual drop in temperature spikes in day 12 till day 20 (day of discharge).
and effective serological assays contribute to diagnostic delay. We should always keep scrub typhus in our differentials in a febrile patient with splenomegaly who is not responding to routine antibacterials.

Authors contribution

Virendra Atam: Conceptualisation, planning, supervision, data analysis and review of final submission
Avirup Majumdar: Write up of article, data acquisition, planning, analysis, reviewing literature, conceptualisation, submission of article
D. Himanshu: Conceptualisation, analysis of data, supervision, final review before submission
Vivek Kumar: Review of literature, Data acquisition and planning
Isha Atam: Data acquisition and planning

Informed Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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ETHICAL APPROVAL

Not applicable

Declaration of Competing Interest

None

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