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## Dengue with Scrub Typhus Coinfection in Northern India

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### Authors' contributions

*This work was carried out in collaboration among all authors. Authors VS, SCM, NAA and BBR were involved in the management of the patient. All the authors contributed towards literature search. Authors VS and PS wrote the first draft of the manuscript. All authors read and approved the final manuscript.*

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Case Study

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### ABSTRACT

**Background:** Amongst the many vector and water-borne diseases prevalent in tropics, dengue occupies a prominent place. Dengue epidemics are frequent and at times, during such epidemic, coinfections may occur causing diagnostic dilemmas.

**Case Report:** A 36 years old lady, from a rural background, presented during the 2019 dengue epidemic with fever, vomiting, and non-colicky abdominal pain. The evaluation showed hepatosplenomegaly, leukocytosis, and thrombocytopenia. The investigations confirmed the diagnosis and she was treated conservatively as a case of dengue with warning signs. A longer than anticipated duration of fever and clinical deterioration prompted reassessment, which revealed the presence of an eschar over the right upper thigh. The Weil-Felix test using Proteus OX-K stain was positive at a titer of 1:320. Following treatment with oral doxycycline, she showed rapid defervescence and clinical improvement.

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**Conclusions:** Coinfection with scrub typhus is rare with dengue. If left untreated, it adversely affects the outcome. The key to diagnosing such coinfections includes a high index of suspicion, repeated clinical examination, and the knowledge of local endemicity.

**Keywords:** Dengue fever; scrub typhus; coinfection.

## 1. INTRODUCTION

Dengue is a common arbovirus infection with worldwide prevalence. Over the years there has been a global resurgence of dengue with the disease spreading to new geographical areas [1]. The epidemics are frequent and the magnitude vast. In a tropical country like India, with a myriad of vector and water-borne diseases, the risk of coinfection remains high. A vast majority of coinfections have overlapping clinical manifestations making the diagnosis challenging and the management difficult. If left undiagnosed and untreated, these coinfections may at times adversely affect the clinical outcome.

Scrub typhus is a major health care concern in the Asia-Pacific region, and the population at risk exceeds one billion [2]. It is an arthropod-borne disease caused by gram-negative bacillus *Orientia tsutsugamushi*. After an incubation period of 5-14 days, the disease manifests with fever, headache, myalgia, eschar, cough, and vomiting. If left untreated, the case fatality approaches 50% [3]. The tropical Indian climate provides an environment conducive for the propagation and transmission of both dengue and scrub typhus. Although both the diseases are individually prevalent, coinfections are rare. Here we present a case of dengue who developed coinfection with scrub typhus.

## 2. CASE PRESENTATION

In autumn of 2019, the northern part of India witnessed a major dengue epidemic. Our center,

a secondary level teaching hospital encountered numerous such patients. To manage this deluge within the available scarce resources, the evaluation, diagnosis, and the management was protocolized. All patients with acute febrile illness fulfilling the diagnostic criteria were screened for dengue using rapid-diagnostic card-based test followed by confirmation using an enzyme-linked immunosorbent assay (ELISA) based antigen detection test (Panbio Dengue Early ELISA, Standard Diagnostics Inc, 65, Borahagal-ro, Giheung-gu, Yongin-si, Gyeonggi-do, Republic of Korea). It was during this epidemic that our patients sought medical consultation.

The patient, a 36 years old lady from a rural Kanpur was apparently well till around 4 days prior to the hospitalization when she developed high-grade fever, headache, nausea, vomiting, and non-colicky pain over the right upper quadrant of the abdomen. At presentation her pulse was 106 beats per minute, blood pressure was 98/64 mm of Hg, the temperature was 102° F and the respiratory rate was 22 per minute. The clinical examination showed leg edema; mild gum bleeding and hepatosplenomegaly; the liver span was 17 cms and the spleen was palpable 2 cms below the left costal margin. She was screened for dengue using a rapid diagnostic test followed by confirmation using an ELISA base antigen detection test. The investigations showed leukocytosis, thrombocytopenia and an elevated liver enzyme (Table 1). She was hospitalized and treated with intravenous fluids, antipyretics, and proton pump inhibitors.

**Table 1. Laboratory values at the time of hospitalization**

Variable	Value	Reference range
Hemoglobin (g/dl)	13.8	12-15
Total leucocyte count (per mm <sup>3</sup> )	13,300	4000-1000
Platelets	44,000	1.5-4.5 x 10 <sup>5</sup>
Blood urea nitrogen (mg/dl)	15	8-23
Serum creatinine (mg/dl)	0.9	0.6-1.3
Serum bilirubin (mg/dl)	0.5	0.1-1.0
Aspartate aminotransferase	156	15-37
Alanine aminotransferases	201	12-78
Serum alkaline phosphatase (IU/L)	56	46-116
Total protein (g/dl)	6.6	3.8-7.6
Serum albumin (g/dl)	3.7	3.2-3.8
Serum lactic dehydrogenase	182	100-190

Over the next 5 days of hospitalization, although the platelet counts improved, the fever and leukocytosis persisted. On day-6 she was noted to have a high-grade fever with chills and appeared unwell. A longer than anticipated duration of fever, clinical deterioration late in the course of illness, and the persistent leukocytosis led to the suspicion of a coinfection. A fresh set of investigations were sent. The peripheral blood smear did not show malaria parasites and the serology for hepatitis B and C, human immunodeficiency virus, Salmonella and Leptospira were negative; the blood and the urine culture were sterile. It was at this juncture that a repeat diligent clinical examination revealed the presence of eschar on the lateral aspect of her right upper thigh (Fig. 1). The history was revisited. The lady, in the absence of a home-based toilet, often resorted to open-air defecation in the farms. Seven days prior to the onset of her symptoms, during one such visit, she remembered having been bitten over the right thigh. In her preoccupation with day to day activities, the persistent local pain was deemed trivial and ignored. Following the discovery of eschar and pending the results of Weil-Felix test, oral doxycycline was started. She responded with rapid defervescence. The Weil-Felix test using Proteus OX-K stain received later was positive at a titer of 1:320. Lack of diagnostic precluded performance of a confirmatory test for scrub typhus. Following the defervescence, she was observed in-hospital for 2 days, and was subsequently followed as outpatient. The oral doxycycline was continued for a total of 7 days. Over the next 3 months of the dengue epidemic, now with heightened suspicion, one more similar case was encountered.



**Fig. 1. Eschar (arrow) over the lateral aspect of right upper thigh**

### 3. DISCUSSION

Dengue and scrub typhus are common infections of tropics and they share many common clinical features. Dengue, a mosquito-borne human arbovirus infection, has been endemic in India for many decades. After an incubation period of 4-10 days, the disease manifests and passes through three phases: febrile, critical and recovery. The spectrum of the disease is wide, and the clinical course and outcome are often unpredictable. Many coinfections including malaria, salmonella, chikungunya, leptospira, and acute viral hepatitis have been described with dengue. These coinfections if undiagnosed, may adversely affect the outcome. During an epidemic, the paucity of health care workers coupled with the deluge of patients often overwhelms the healthcare setup. This result in a hurried suboptimal clinical evaluation which provides an optimal milieu for missing the presence of a coinfection.

Scrub typhus is a potentially life-threatening, but treatable mite-borne infection. In India, it is endemic in the sub-Himalayan regions and southern states and preferentially affects the uneducated population residing in rural areas [4,5]. Humans acquire the infection on accidentally encroaching a zone of an infected mite. The chiggers while feeding introduces the organism into the human. Once introduced the rickettsia proliferates damaging the small blood vessels which in turn leads to fluid leak, platelet aggregation, inflammation, disturbance in microcirculation, and widespread microinfarction. The clinical manifestations are nonspecific with fever and headache being the commonest. Eschar at the site of the chigger feeding, the classical disease manifestations, often precedes the onset of fever and is commonly seen over the abdomen, lower extremities, axilla and anterior chest [6]. Late presentation and delayed diagnosis are the common causes of an adverse outcome [7].

The topical Indian climate provides an environment conducive for the propagation of both dengue and scrub typhus. Both these diseases peak during the monsoon and share common demographic and clinical features. Despite similarities, coinfections are exceedingly rare [8,9]. Whether this is because of the different vectors involved, a low index of suspicion or a lack of diagnostics remains unknown. Physicians worldwide tend to follow the principle of Occam's razor; a single-minded pursuit of an established diagnosis often leads to

disregarding the presence of an obvious clue pointing towards the presence of a coinfection. These coinfections, if left undiagnosed jeopardizes patient safety and outcome. Attempts have been made to differentiate dengue and scrub typhus based on the clinical and laboratory parameters. In one study, the authors noted that bleeding gums, thrombocytopenia and leucopenia favor a diagnosis of dengue, while leukocytosis and thrombocytopenia favor scrub typhus [10]. They also noted that those with coinfection had lower mean hemoglobin levels and normal leukocyte counts when compared to patients having dengue or scrub typhus alone. Contrary to the previous findings, we noted that our patient had a normal hemoglobin level and leukocytosis rather than the anticipated dengue associated leucopenia.

In our patient, the ongoing dengue epidemic coupled with overlapping clinical manifestations led to a delay in the diagnosis of scrub typhus coinfection. The index of suspicion was low and subtle clues like leukocytosis and hepatosplenomegaly were ignored. Further compounding the issue was the location of eschar in the upper thigh and the prevalent social custom which often prevents physicians from a diligent head to toe examination. It was the atypical disease course, late clinical worsening, and negative laboratory results for locally prevalent infections that led us to reevaluate, leading to the discovery of eschar.

#### 4. CONCLUSION

Amongst the many coinfections reported with dengue, scrub typhus is an uncommon disease. In a diverse country like India with a plethora of vector and water-borne disease, the key to identifying such coinfection includes a high index of suspicion (atypical presentation or course), diligent head to toe clinical examination and knowledge of local endemicity. The presence of an eschar should prompt an early empiric therapy pending the investigation results. Early diagnosis and prompt therapy reduce the risk of serious complications and mortality.

#### CONSENT

All authors declare that a written informed consent was obtained from the patient for publication of this case report and accompanying images.

#### ETHICAL APPROVAL

It is not applicable.

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#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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