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## **Dengue and Scrub Typhus Coinfection in a 17-Year-Old Male with Associated Meningoencephalitis: A Case Study**

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### **Abstract**

Dengue fever and scrub typhus are common causes of acute febrile illness especially in the post monsoon season. Due to many overlapping clinical features, scrub typhus infection may be missed in presence of dengue. Concurrent infection with those two pathogens is very rare and articles on dengue and scrub typhus coinfection are distinctly limited. In this study, we discuss a rare medical case of dengue fever and scrub typhus co-infection of a 17-year-old male admitted to RG Kar Medical college and hospital for treatment. Distinctive clinical features of the patient included thrombocytopenia, low albumin, significantly increased levels of Aspartate Transaminase and Alanine Transaminase, altered sensorium, increased intracranial pressure and acute meningoencephalitis. Timely diagnosis

of the patient followed by treatment with the antibiotics, vancomycin, ceftriaxone, doxycycline, antiviral acyclovir and intravenous fluids resulted in complete recovery from both the diseases. The present case illustrates the clinical importance of early recognition of coinfection in unremitting febrile illness to prevent their fatal complications. High degree of suspicion has to be made for coinfection in a patient presenting with febrile illness with thrombocytopenia and deranged laboratory parameters in post monsoon season in endemic regions in Asia. In case of coinfection with dengue and scrub typhus, vigilant monitoring of vitals, platelets transfusion, and timely treatment are necessary.

**Keywords:** Dengue Fever, Scrub Typhus, Coinfection, Acute Meningoencephalitis, Thrombocytopenia, Doxycycline

### **1. Introduction**

Dengue and scrub typhus are common tropical diseases causing non-specific febrile illness. Dengue is a mosquito-borne self-limiting viral disease of the tropics, and is transmitted by the bite of female *Aedes* mosquito <sup>[1]</sup>. *Aedes aegypti* is the most common vector of Dengue viruses. Dengue can present from mild illness with fever, headache, myalgia and rash to severe disease manifesting with shock, narrow pulse pressure, pleural effusion, ascites and bleeding <sup>[1]</sup>.

Scrub typhus is another non-specific febrile disease caused by the organism *Orientia tsutsugamushi* and is spread to people through bites of infected chiggers (larval mites). The organism is inoculated into the skin after the bite and disseminates widely to target organs infecting the host cells, causing host cell injury. It can range from milder disease with fever, headache, myalgia to severe disease with complications such as acute respiratory distress syndrome, acute kidney injury, disseminated intravascular coagulation, meningoencephalitis, myocarditis, hemophagocytic syndromes or multi organ dysfunction <sup>[2]</sup>. A wide spectrum of clinical manifestations, affecting nearly every organ system of the body have been described with scrub typhus <sup>[3]</sup>. If not promptly identified and treated, scrub typhus causes complications and increased mortality.

Both diseases have several clinical and laboratory features in common, including rash, thrombocytopenia and hepatic dysfunction. However, concurrent infection with both pathogens is rare, which may be due to involvement of different vectors, low level of suspicion or a lack of adequate diagnostic facilities. There have been many studies on coinfections of various vector-borne diseases, but there are distinctly limited articles on the coinfection of dengue and scrub typhus <sup>[4]</sup>. Co-infections may influence disease severity, treatment outcomes, and the development of drug resistance. In this study, we present a medical case report of a 17-year-old male diagnosed with dengue and scrub typhus coinfection. He had fever for 8-9 days along with altered sensorium and acute meningoencephalitis. Besides, the patient suffered from thrombocytopenia, low albumin content and significantly elevated levels of Aspartate Transaminase and Alanine Transaminase. Treatment with the antibiotics, vancomycin, ceftriaxone, doxycycline, antiviral acyclovir and intravenous fluids resulted in complete recovery

from both the diseases.

## 2. Materials and methods

A 17 years-old male patient having fever for 8-9 days with episodes of epistaxis and melena stool was admitted to R.G. Kar Medical college and hospital, Kolkata, on November 2022. He had altered sensorium, increased intracranial pressure (ICP), neck rigidity and was suspected with meningitis. The patient had blood pressure=96/68 mm Hg, capillary blood glucose (CBG) =135 mg/dl, oxygen saturation (SpO<sub>2</sub>) =98%, pulse rate= 101/min and GCS= 9/15 (E3-V2-M4). In addition, the patient's hemoglobin content was 8.6 g/dl, packed cell volume (PCV)= 25.7%, total leucocyte count= 6200/mm<sup>3</sup>, neutrophil content 51%, lymphocyte content 33%, eosinophil content 8%, monocyte content 8%, platelet count=71000/mm<sup>3</sup> (as recorded on 11.11.2022). On the following day (12.11.2022), the patient exhibited the following parameters: blood pressure=94/62 mm Hg, capillary blood glucose (CBG) =139 mg/dl, oxygen saturation (SpO<sub>2</sub>) =98%, pulse rate= 101/min. The parameters recorded on 16.11.2022 and 17.11.2022 were as follows: pulse rate=84/min, blood pressure= 130/70 and 120/72 respectively, SpO<sub>2</sub>=94% and 96% respectively, respiration rate= 18/minute, chest b/l ae positive and cvs s1s2 positive.

Serum of the patient was tested for leptospirosis and scrub

typhus infection at Virus Research & Diagnostic Laboratory (VRDL), Department of Microbiology, RG Kar Medical College and Hospital, Kolkata, after obtaining ethical clearance from the institution and informed consent. Serum IgM antibodies to leptospirosis or scrub typhus were detected by ELISA method following standard kit protocol (J. Mitra & Co. Pvt. Ltd.) according to the manufacturer's instructions. Calculations were done as per kit instructions as follows:

Sample O.D. ratio = Sample O.D. ÷ Cut off Value [Cut off Value =0.569 for Leptospira IgM, and 0.372 for Scrub Typhus IgM, respectively] (Calculation of Leptospira or Scrub Typhus IgM units=sample O.D. ratio×10)

The patient was also tested for dengue virus infection at the serology division, RG Kar Medical College and Hospital. Serum IgM antibodies to Dengue antigen were detected by ELISA method following standard kit protocol (J. Mitra & Co. Pvt. Ltd.) according to the manufacturer's instructions. Calculations were done as per kit instructions as follows:

Sample O.D. ratio = Sample O.D. ÷ Cut off Value [Cut off Value =0.525 for Dengue IgM] (Calculation of Dengue IgM units=sample O.D. ratio×10)

## 3. Results

The laboratory investigation report of the biochemical parameters of the patient is shown in Table 1.

**Table 1:** Laboratory investigation report of patient

Laboratory investigations	Result
<b>(a) Laboratory parameters (with reference values in parenthesis)</b>	
Total Protein (6-8 g/dl)	5.0
Albumin (3.2-5.0 g/dl)	2.7
Total bilirubin (0.1-1.0 mg/dl)	4.2
Direct bilirubin (0-0.3 mg/dl)	2.0
Urea (10-40 mg/dl)	120
Creatinine (0.5-1.5 mg/dl)	2.0
ALT (5-35 IU/L)	184
AST (5-35 IU/L)	269
ALP (adult 110-310 IU/L)	277
Sodium (135-145 mmol/l)	140
Potassium (3.5-5.0 mmol/l)	4.3
<b>(b) Other investigations</b>	
MPDA	Negative
Dengue NS1	Positive
HBsAG	Non-reactive
Anti-HCV antibody	Non-reactive
ICTC	Negative

**Table 2:** Results of CSF study

Appearance	Cell count	Cell type	Glucose (reference value 40-74 mg/dl)	Microprotein (reference value 10-50 mg/dl)	ADA (reference value < 10 U/L)
Mild haemorrhagic	120/mm <sup>3</sup>	Stained smear showed predominantly lymphocytes and few neutrophils in the background of red blood cells	54	121	4.0

Cerebrospinal Fluid (CSF) examination study is shown in Table 2.

ELISA results indicated the patient was positive for both scrub typhus and dengue viral infection. In addition, CSF study confirmed that the patient suffered from acute meningoencephalitis. The patient had blood pressure=96/68 mm Hg, capillary blood glucose (CBG) =135 mg/dl, oxygen saturation (SpO<sub>2</sub>) =98%, pulse rate= 101/min and GCS= 9/15 (E3-V2-M4). The patient's hemoglobin content was 8.6 g/dl, packed cell volume (PCV)= 25.7%, total leucocyte

count= 6200/mm<sup>3</sup>, neutrophil content 51%, lymphocyte content 33%, eosinophil content 8%, monocyte content 8%, platelet count=71000/mm<sup>3</sup> (as recorded on 11.11.2022). On the following day (12.11.2022), the patient exhibited the following parameters: blood pressure=94/62 mm Hg, capillary blood glucose (CBG) =139 mg/dl, oxygen saturation (SpO<sub>2</sub>) =98%, pulse rate=101/min. The parameters recorded on 16.11.2022 and 17.11.2022 were as follows: pulse rate=84/min, blood pressure=130/70 and 120/72 respectively, SpO<sub>2</sub>=94% and 96% respectively,

respiration rate=18/minute, chest b/l ae positive and cvs s1s2 positive.

#### 4. Discussion

Scrub typhus infection has been associated with several neurological manifestations, which includes meningitis, meningoencephalitis, seizures and altered sensorium as observed in previous studies [5, 6]. In a recent study, we reported a case of scrub typhus infection associated with acute meningitis for a 14-year-old male patient [7]. Central nervous system (CNS) involvement is a known complication of scrub typhus which ranges from aseptic meningitis to frank meningoencephalitis [8]. Cases of acute encephalitis syndrome due to scrub typhus infection has been reported in an earlier study [5]. A case series of scrub typhus from Pondicherry reported meningitis as a common CNS complication [9]. Cases with meningitis have been reported to be associated with a lower rate of mortality (6.2%), than the higher rates among cases with renal impairment (57%), pulmonary complications (68%), hypotension requiring inotropes (84%), and hepatitis (59%) [10]. Incidence of CNS dysfunction and meningoencephalitis in cases of scrub typhus have been reported to range from 9.5% to 23.3% as reported in earlier studies [9-11].

Studies on the comparative incidence and dissemination of dengue have shown that maximum *Aedes aegypti* larval indices were found during the monsoon and post-monsoon period [12-14]. The highest cases of these diseases were found positive in the post-monsoon season. The stagnant water in low-lying areas during post-monsoon season acts as the breeding ground for mosquitoes. So, there is a high surge in dengue cases in these months. In the current case study, the patient exhibited a rare case of dengue fever and scrub typhus co-infection associated with thrombocytopenia, low albumin and significantly increased levels of Aspartate Transaminase (AST) and Alanine Transaminase (ALT). In addition, increased levels of urea and creatinine for the patient indicated kidney infection associated with the diseases.

A low leukocyte count and platelet count are more commonly associated with dengue infections. Low platelet count is also a feature of scrub typhus but usually associated with leukocytosis. AST > ALT is found in both the diseases but in scrub typhus, elevated levels of alkaline phosphatase is also seen [15]. Elevated levels of AST and ALT indicating abnormal liver function has been associated with patients with scrub typhus in earlier study [16]. Severe thrombocytopenia, high AST and ALT with low albumin have been reported in cases of coinfections [17-19]. Additionally, patients with co-infection reportedly had lower hemoglobin levels [20], an observation similar to the present case study.

The patient was treated with the antibiotics, namely, vancomycin, ceftriaxone, doxycycline, antiviral acyclovir along with additional medications (Levipil-500, Pan-40, Zofer-4, Trenaxa-500 and Paracetamol) and intravenous fluids which resulted in complete recovery from both the diseases. As *Orientia tsutsugamushi* lacks a proper cell wall, the cephalosporin group of antibiotics is virtually ineffective against scrub typhus [21, 22]. The treatment of choice for scrub typhus is doxycycline. The antirickettsial drugs, azithromycin and doxycycline have both been shown to be effective in the treatment of scrub typhus, but the resolution of symptoms has shown to be faster in doxycycline

compared to azithromycin [23].

Though scrub typhus and dengue fever share many common characteristics causing diagnostic dilemma, concurrent infection with both of them are very rare. A case of dengue and scrub typhus coinfection presenting as acute febrile illness in a 50-year-old female from southern belt of Nepal was reported by Sapkota S *et al* [4]. A 17-month-old was diagnosed in Kolkata to have coinfection of dengue fever and scrub typhus [24]. Other cases of co-infection of scrub typhus and dengue fever have also been reported in some studies [25-28].

#### 5. Conclusion

In the current study, we report a rare case of dengue fever and scrub typhus coinfection of a 17-year-old male patient who recovered completely on treatment with antimicrobials and suitable medications. Both Dengue and Scrub typhus infection is endemic in India with thousands of Indians getting infected annually with these two diseases especially in the post-monsoon season. The overlapping clinical features of both the infections sometimes cause underreporting of such cases. Overlooking of co-infection of these diseases or delay in diagnosis and treatment may lead to increased mortality rate among patients. It is therefore important to have a high suspicion of coinfection of both dengue and scrub typhus during the post-monsoon season in India. As a result, it is very crucial to properly diagnose for such coinfections of the zoonotic disease with dengue viral fever prevalent during the post-monsoon season so that timely administration of antibiotic therapy may save lives.

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#### 7. Disclosure of conflict of interest

The author has no potential conflicts of interest to disclose.

#### 8. Statement of ethical approval

The studies on patient samples were carried out after obtaining ethical clearance from the institution and informed consent.

#### 9. Statement of informed consent

Informed consent was obtained from the patient and his families included in the study.

#### 10. References

1. Simmons CP, Farrar JJ, van Vinh Chau N, Wills B. Dengue. *N Engl J Med*. 2012; 366:1423-1432.
2. Paris DH, Shelite TR, Day NP, Walker DH. Unresolved problems related to scrub typhus: A seriously neglected life-threatening disease. *Am J Trop Med Hyg*. 2013; 89:301-307.
3. Rajapakse S, Weeratunga P, Sivayoganathan S, Fernando SD. Clinical manifestations of scrub typhus. *Trans R Soc Trop Med Hyg*. 2017; 111:43-54.
4. Sapkota S, Bhandari S, Sapkota S, Hamal R. Dengue

- and scrub typhus coinfection in a patient presenting with febrile illness. *Case Rep Infect Dis.* 2017; 3.
5. Kar A, Dhanaraj M, Dedeepiya D, Harikrishna K. Acute encephalitis syndrome following scrub typhus infection. *Indian J Crit Care Med.* 2014; 18:453-455.
  6. Misra UK, Kalita J, Mani VE. Neurological manifestations of scrub typhus. *J Neurol Neurosurg Psychiatry.* 2015; 86:761-766.
  7. Banerjee S, Latif A, Ghosh S, Chakraborty B, Ray (Ghosh) R, Ghosh S. Case Study of a 14-Year-Old Male Patient with Scrub Typhus Infection and Acute Meningitis. *Int j adv multidisc res stud.* 2023; 3:581-584.
  8. Drevets DA, Leenen PJ, Greenfield RA. Invasion of central nervous system by intracellular bacteria. *Clin Microbiol Rev.* 2004; 17:323-347.
  9. Kar A, Dhanaraj M, Dedeepiya D, Harikrishna K. Acute encephalitis syndrome following scrub typhus infection. *Indian J Crit Care Med.* 2014; 18:453-455.
  10. Vivekanandan M, Mani A, Priya YS, Singh AP, Jayakumar S, Purty S. Outbreak of scrub typhus in Pondicherry. *J Assoc Physicians India.* 2010; 58:24-28.
  11. Varghese GM, Trowbridge P, Janardhanan J, Thomas K, Peter JV, Mathews P, *et al.* Clinical profile and improving mortality trend of scrub typhus in South India. *Int J Infect Dis.* 2014; 23:39-43.
  12. Mahajan SK, Rolain JM, Kashyap R, Bakshi D, Sharma V, Prasher BS, *et al.* Scrub typhus in Himalayas. *Emerg Infect Dis.* 2006; 12:1590-1592.
  13. Sharma R, Panigrahi N, Kaul S, Barua K, Bhardwaj M. Status Report on DF/DHF During 1998 in the National Capital Territory of Delhi, India. Published online. 1999:109-112.
  14. Katyal R, Gill K, Kumar K. Seasonal variations in *Aedes Aegypti* population in Delhi, India. Published online, 1996.
  15. Kumar RR, Kamal S, Patnaik SK SR. Breeding habitats and larval indices of *Aedesaegypti* (L) in residential areas of Rajahmundry town, Andhra Pradesh. *J Commun Dis.* 2002; 34:50-58.
  16. Thap LC, Supananond W, Treeprasertsuk S, Kitvatanachai S, Chinprasatsak S, Phonrat B. Septic shock secondary to scrub typhus: Characteristics and complications. *Southeast Asian J Trop Med Pub Health.* 2002; 33:780-6.
  17. Hu ML, Liu JW, Wu KL, Lu SN, Chiou SS, Kuo CH, *et al.* Abnormal liver function in scrub typhus. *Am J Trop Med Hyg.* 2005; 73:667-668.
  18. Basheer A, Iqbal N, Mookkappan S, Anitha P, Nair S, Kanungo R, *et al.* Clinical and Laboratory Characteristics of Dengue-Orientia tsutsugamushi co-Infection from a Tertiary Care Center in South India. *Mediterr J Hematol Infect Dis.* 2016; 8:e2016028.
  19. Khetarpal N, Khanna I. Dengue Fever: Causes, Complications, and Vaccine Strategies. *J Immunol Res.* 2016; 6803098.
  20. Roy MG, Roy N, Pal AK. Dengue and Scrub Typhus Coinfection: Timely Diagnosis for Proper Management. *ASCR.* 2022; 3:50-53.
  21. Watt G, Jongsakul K, Chouriyagune C, Paris R. Differentiating dengue virus infection from scrub typhus in Thai adults with fever. *Am J Trop Med Hyg.* 2003; 68:536-538.
  22. Murray PR, Rosenthal KS, Pfaller MA. Inhibition of cell wall synthesis. *Medical Microbiology.* 7th ed., Ch. 19. Elsevier, 2012.
  23. McClain JB, Ballou WR, Harrison SM, Steinweg DL. Doxycycline therapy for leptospirosis. *Ann Intern Med.* 1984; 100:696-698.
  24. Fang Y, Huang Z, Tu C, Zhang L, Ye D, Zhu BP. Meta-analysis of drug treatment for scrub typhus in Asia. *Intern Med.* 2012; 51:2313-2320.
  25. Roy S, Chakrabartty S. Scrub typhus and dengue coinfection in a 17-month-old child. *Indian J Case Rep* 2017; 3:134-6.
  26. Basheer A, Iqbal N, Mookkappan S, Anitha P, Nair S, Kanungo R, *et al.* Clinical and Laboratory Characteristics of Dengue-Orientia tsutsugamushi co-Infection from a Tertiary Care Center in South India. *Mediterr J Hematol Infect Dis.* 2016; 8:e2016028.
  27. Garg A, Jain A, Kashyap R. Travel-acquired Scrub Typhus Infection Masked by Dengue Fever in a Patient from Nonendemic Area. *J Glob Infect Dis.* 2018; 10:114-115.
  28. Raina S, Raina RK, Agarwala N, Raina SK, Sharma R. Coinfections as an aetiology of acute undifferentiated febrile illness among adult patients in the sub-Himalayan region of north India. *J Vector Borne Dis.* 2018; 55:130-136.
  29. Subedi P, Ghimire M, Shrestha K, Ghimire K, Adhikari S, Tiwari B. Dengue and scrub typhus co-infection causing septic shock. *Oxf Med Case Reports.* 2021; 11:2021.