

Dengue and Scrub Typhus Coinfection: Timely Diagnosis for Proper Management

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Abstract

Introduction: Dengue and Scrub typhus infection are common causes of acute infective febrile illness in India especially in the post-monsoon season. There are some overlapping clinical features of both these infections like rash, thrombocytopenia and transaminitis which can lead to delay in diagnosis and hence treatment of the other. Here we discuss a case of a 27 years old woman with a coinfection of both Dengue and Scrub typhus infection and how we could timely diagnose her for proper management.

Methods and Materials: We selected a patient from a tertiary care hospital and all required investigations were done accordingly.

Conclusion: It is important to have a high suspicion of coinfection of both dengue and scrub typhus during the post-monsoon season in India and accordingly know which Dengue test (Dengue NS1 and Dengue IgM/IgG) should be done at what time in order to correctly diagnose Dengue infection.

Keywords: Dengue; Scrub Typhus; Dengue NS1; Dengue IgM/IgG; Case Report

Introduction

Scrub typhus is caused by the bite of trombiculid mite (*Lep-totrombidium deliense*) transmitting the organism *Orientia tsutsugamushi* and annually almost 1 million new cases are reported in the world [1]. The disease is characterised by acute episodes of fever associated with rash and in some cases an eschar which shows a dramatic response to antibiotics. In some cases, it leads to a significant illness resulting in multiple organ involvement and death. Although very little is known about the pathogenesis of the disease, it is assumed that the manifestations of the disease occur due to systemic vasculitis as a result of direct effects of the organisms causing an exaggerated immune reaction. A wide spectrum of clinical manifestations, affecting nearly every organ system of the body have been described with scrub typhus [2].

Dengue infection is one of the foremost frequent causes of febrile disease in tropical climates. Infections are caused by the fla-

vivirus Dengue viruses (type 1 to 4) transmitted by the *Aedes* species mosquito. *Aedes aegypti* mosquito is the most common vector of Dengue viruses. Symptom severity varies and may range from a light, flu-like clinical picture to severe haemorrhage and shock. The most common symptoms experienced by travellers include fever, muscular pain, headaches and skin rash [3].

Dengue fever and tsutsugamushi disease are common causes of acute febrile illness of unclear origin in Asia. Both the diseases have some clinical as well as laboratory features in common which creates a diagnostic dilemma such as rash, thrombocytopenia and hepatic dysfunction⁴. 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 [4].

Here we discuss a case report of a young Indian female aged 27 years having coinfection with both Dengue and Scrub typhus and how we could correctly diagnose it at the right time.

Case Presentation

A 27-year-old female residing in Kolkata, India presented to the emergency department of our hospital with a complaint of intermittent high-grade fever without chills and rigor for 5 days along with nausea, myalgia, anorexia and generalized weakness for 2 days. She also had an episode of vomiting on the day of admission. On examination, she was alert, conscious, cooperative and febrile. Her BP was 100/70 mmHg, Pulse-98/min, SpO₂-98%@ room air, Chest auscultation-bilateral vesicular breath sound, Per abdomen-soft, non-tender and she had signs of dehydration. Her initial investigations revealed mild anaemia, leukopenia, mild thrombocytopenia, transaminitis and no other significant findings (Table 1). We sent several investigations for her fever. Malaria parasite dual antigen and WIDAL tests were negative. Dengue IgM/IgG was non-reactive by ELISA (IgM dengue units 1.57 and IgG dengue units 1.30) but Scrub typhus IgM antibody was reactive by ELISA (0.71).

She is a high school teacher who was working from home. But recently she had gone to a friend's house who had a big garden. The USG whole abdomen did not reveal any obvious abnormality. She did not complain of any eschar like lesion on admission, so we did a thorough search of her body and found an eschar on the lateral side of her left upper thigh (Figure 1).

Since she had a low platelet count and the dengue IgM test (reported non-reactive) was sent on the fifth day of her fever, we decided to order a Dengue NS1 test in addition to all the above investigations later on that day of her admission itself. To all our surprise Dengue NS1 was indeed reactive (Dengue unit-52.46), by Dengue NS1 antigen enzyme immunoassay test. To exclude any possibility of false-positive Dengue NS1 we decided to do a repeat Dengue IgG/IgM test on the 10th day of her fever (There is a 0.5-2% chance of false-positive Dengue NS1). Her repeated Dengue IgM was reactive (IgM dengue unit-41.5) and IgG was non-reactive (Dengue unit-0.48).

The platelet count since admission changed in the following sequence from the day of admission: 102000 (Day 1) > 90000 (Day 4) > 135000 (Day 5) > 225000 (Day 6). The typical dengue rash was missing in her case. She was treated with Injection Doxycycline for 7 days, IV fluids and other conservative treatments. She became apyrexial on the 4th day of her admission.

After the fever resolved, the anorexia, nausea, and myalgia resolved. She continued to have some degree of generalized weakness which ultimately subsided after another 7 days. Her latest blood report on the 7th day follow up after discharge revealed Hb-10.2 gm/dl, T.C- 6200 cells/cubic mm, PCV- 31.8%, Platelet count- 423000/ul, SGPT-51 U/L and SGOT 37 U/L.

Lab value interpretation

Dengue virus Antibody IgM and IgG Capture ELISA Interpretation

Dengue IgM and IgG unit

- <9- Negative
- 9-11- equivocal
- >11- Positive

Dengue NS1 antigen enzyme immunoassay interpretation

Dengue unit

- <9- Negative
- 9-11- Equivocal
- >11- Positive

Scrub typhus IgM antibody Interpretation

- >0.55- Reactive
- 0.45-0.55- Equivocal
- <0.45- Non reactive

Figure 1: Eschar seen on the lateral side of her left upper thigh.

Lab Values at the time of admission along with the reference ranges		
Hematologic	Values	Reference range
Hb	11.2gm/dl.	11-15 gm/dl
Total leukocyte count	4000-11000/cumm	1800/cu.mm.
Platelets	102000/cu.mm	150000-400000/ cu.mm
SGPT	243 U/L.	9-52 U/L
SGOT	516 U/L.	14-36 U/L
Creatinine	0.57 mg/dl.	0.52-1.04 mg/dl
C Reactive protein	28 mg/dl.	< 10 mg/dl
Serum sodium	131 mmol/l.	137-145 mmol/l
Serum potassium	3.6 mmol/l.	3.5-5.1 mmol/l

Table 1

Discussion

Based on cartographic approaches, 390 million dengue infections were estimated annually in the world of which 96 million manifest apparently with any level of severity which is over thrice of the WHO data [5]. There is a 38.3% prevalence of laboratory-confirmed dengue infection among clinically suspected patients in India [6]. The article called "The global burden of disease in 2013" and WHO both identify India as an epicentre of Dengue (Stanaway, *et al.* 2016, World Health Organization, 2012). This data is much lower than the national data on Dengue collected by the National Vector Borne Disease Control Programme (NVBDCP) in India because of the lack of an efficient systemic surveillance system [7].

According to a cohort study, there were 18,781 confirmed Scrub typhus cases reported in 138 hospital-based studies and two community-based studies in India during the last 10 years [8]. In an open cohort study conducted at a tertiary care hospital in Himachal Pradesh, among 1164 patients attending hospital with acute undifferentiated fever, 10 patients were diagnosed with coinfection with Dengue and Scrub typhus infection [9]. Coinfection of Dengue and Scrub typhus is rare and there is no reported prevalence of the coinfection in Eastern India anywhere to the best of our knowledge.

Given the endemic of Dengue and Scrub typhus in India, especially in the post-monsoon season i.e. July-December, we witness a significant number of Dengue and Scrub typhus infections during this time. Our patient is an urban dweller with low contact with the

woods, yet she had a scrub typhus infection. During the management of patients with fever, we normally do not think of coinfection with both the above-mentioned organisms. Our patient had Scrub typhus IgM positive in the blood test we had sent on her admission. Initially, her Dengue IgG and IgM tests were non-reactive on the day of her admission which was the 5th day of her fever. Her routine blood test showed thrombocytopenia and mild transaminitis which prompted us to suspect Dengue as a coinfection.

Considering the fact that Dengue IgM becomes positive 4th-5th day after the onset of symptoms and remains positive up to approximately 12 weeks post symptom onset whereas Dengue NS1 antigen is detected during the first 7 days of symptoms, we decided to go for a Dengue NS1 antigen test as well [10,11].

Ironically her Dengue NS1 antigen test was positive confirming our suspicion. Scrub typhus infection can also cause mild thrombocytopenia and transaminitis which could have misled us into not considering Dengue infection at all.

Among scrub typhus patients, approximately 20% of patients get admitted to the ICU, 17.4% present with Multiple Organ Dysfunction Syndrome and it possesses a case fatality rate of 6.3% [8]. Untreated severe dengue fever can have a mortality rate as high as 10 to 20% due to the development of complications and even in the presence of supportive treatment, it carries a mortality rate of roughly 1% [12]. Therefore early diagnosis and treatment of scrub typhus and dengue infection is important to prevent the development of complications and mortality. In the post-monsoon season in India, it is important to have a high degree of suspicion for coinfection of both Dengue and Scrub typhus.

Conclusion

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. Some overlapping clinical features of both these infections can sometimes deceive us into not considering the other. Delay in diagnosis and hence treatment can lead to complications and high mortality from these infections. Therefore it is important to have a high suspicion of coinfection of both dengue and scrub typhus during the post-monsoon season in India. It is also vital to know which Dengue test (Dengue NS1 and Dengue IgM/IgG) should be done at what time in order to not miss the diagnosis at the right time.

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