

Scrub typhus and dengue infected pregnancy: A rare encounter

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ABSTRACT

Pregnancy is associated with many physiological and biochemical adaptations in the body of the women. Many immunological changes occurring during various trimesters of pregnancy make pregnant women more vulnerable to infectious agents. Infections acquired during pregnancy adversely affect the maternal and foetal wellbeing. Immediate detection and treatment of infections play an important role for good maternal and foetal outcome. Scrub typhus also known as tropical Rickettsioses are one such rare bacterial infection caused by *Orientia tsutsugamsuhi* transmitted by mites. Similarly, dengue viral fever might also occur during pregnancy by the bite of aedes mosquito.

Keywords: Pregnancy, Acute undifferentiated fever, Rashes, Thrombocytopenia, Scrub typhus, Dengue.

1. INTRODUCTION

Fever during pregnancy i.e., body temperature of 38 degree Celsius or more requires early diagnosis of aetiological cause due to its adverse effect on foetal maternal outcome (Bhatt et al., 2021). Pregnant women are more susceptible to infectious diseases caused by various bacterial, viral, fungal or protozoal invasion in the body. This is due to various physiological and immunological adaptations in a normal pregnancy (Swamy, 2014).

Dengue fever is caused by single stranded RNA virus belonging to Flaviviridae family and is transmitted by the vector mosquito *Aedes aegypti* (primarily) and *Aedes albopictus* (Brar et al., 2021). Clinically it manifests as mild asymptomatic infections to severe life-threatening dengue or dengue shock syndrome (Rathore et al., 2022). Scrub typhus is caused by the bacteria *Orientia tsutsugamushi* transmitted by the larval stage of mites (chiggers) of Trombiculidae family. Its clinical course may range from spontaneous recovery without any treatment to multiple organ failure (Watthanaworawit et al., 2016).

A seasonal increase in dengue cases and concomitant scrub typhus infection in endemic regions may lead to diagnostic dilemma. This is due to similarity in clinical and laboratory characteristics in both the infectious diseases. Both are associated with development of rash, thrombocytopenia

and hepatic dysfunction (Subedi et al., 2021). During pregnancy, concomitant infection of dengue and scrub typhus if not diagnosed and treated early may lead to adverse maternal and foetal outcomes. Here we present a rare case of 25-year-old near term pregnant female with acute febrile illness, diagnosed of having dengue and scrub typhus co infection.

2. CASE PRESENTATION

A 25-year-old primigravida, residing in a village and was involved in farming and cattle handling was brought to casualty of our tertiary rural hospital with history of high-grade fever since past 2 days. The fever was intermittent in nature and was associated with chills, rigors and dry cough. The patient also gave history of difficulty in breathing, nausea, vomiting, headache and body ache. There was no history of yellowish discoloration of eyes, joint pain, diarrhoea, urinary symptoms or bleeding manifestations. There was no history of hypertension, diabetes, thyroid disorder or bronchial asthma. Obstetric history revealed patient was primigravida and duration of marriage of was 2 years. Her menstrual history revealed patient's gestational age to be 33 weeks 5 days.

On general examination patient's vitals revealed pulse of 114 bpm, blood pressure of 110/70 mm hg in right arm supine position, respiratory rate of 22/min, spo2 of 92 on room air and temperature of 102-degree Fahrenheit which only subsided following intravenous paracetamol injection. Pitting edema was present and there was no evidence of any pallor or lymphadenopathy. She had a small popular crusted lesion on her feet as shown in figure 1 and maculopapular rashes all over her body (Figure 2). On systemic examination patient was conscious and oriented to time place and person but dyspnoeic and tachypnoeic. On auscultation breath sounds on both sides were present and occasional crackles were heard in the basal regions of both the lungs. Heart sounds were normal. On per abdomen examination uterus 32 to 34 weeks size, relaxed, breech presentation and foetal heart rate was regular of 158 bpm, liver was palpable just below right costal margin suggestive of mild hepatomegaly.



Figure 1 An atypical eschar on right sole of the patient

Routine laboratory investigations as in Table 1 were suggestive of thrombocytopenia and mildly elevated liver enzymes (aspartate transaminase, alanine transaminase and alkaline phosphatase). Serological tests revealed a positive IgM antibody for dengue and scrub typhus. Serological tests for leptospirosis, typhoid, Hepatitis B, Hepatitis C were negative. Peripheral smear did not show malarial parasite.

Ultrasound revealed a single intrauterine live foetus of gestational age of 33 weeks 5 days with 2177 grams weight. Liquor index was 4.5 suggestive of severe oligohydramnios. Foetal vessels Doppler was normal and did not reveal any uteroplacental insufficiency. Liver was of size 15 cm suggestive of mild hepatomegaly. A provisional diagnosis of full term primigravida pregnancy with severe oligohydramnios with acute co infection of scrub typhus and dengue was made. Foetal monitoring was done with DFMC and NST twice a day.



Figure 2 Maculopapular rashes all over the body of the patient

Table 1 Routine laboratory investigations on admission

CBC	Hb-10.4gm/dl Mcv-76fl Tlc-17600/dl Plt-79,000lakhs/dl
Coagulation profile	Pt-13.5 Inr-1.08 APTT-30.8
KFT	Urea-16mg/dl Creatinine-0.4mg/dl Sodium-134mmol/dl Potassium-4mmol/dl
LFT	Total Protein-6gm/dl Albumin-2.8gm/dl Globulin-3.3gm/dl Aspartate aminotransferase-57 units/l Alanine aminotransferase-46 units/l AlkanlinePhophatase-100 IU/l Total Bilirubin: 0.6 mg/dl

Injection dexamethasone 12 mg was given 12 hours apart for foetal lung maturity. She was started injection ceftriaxone I/V 1 gram 12 hourly, injection paracetamol I/V 8 hourly and tablet azithromycin 500mg twice a day. After 24 hours elective LSCS was performed when patient was afebrile and well hydrated and a preterm alive male baby of 1.9 kg was delivered. Foetal serological tests did not reveal any vertically transmitted infection to the infant.

Postoperatively she was continued on the same antibiotics, injection ceftriaxone I/V 1gm 12 hourly and tablet azithromycin 500mg twice a day. Chest X-ray on day 2 of LSCS revealed mild opacities in lower lobes of lungs as in Figure 3 which was treated with chest physiotherapy and injection furosemide. Patient was discharged afebrile for 7 days and was discharged on day 9 of LSCS after suture removal. Both mother and baby were well in 3 week follow up visit.

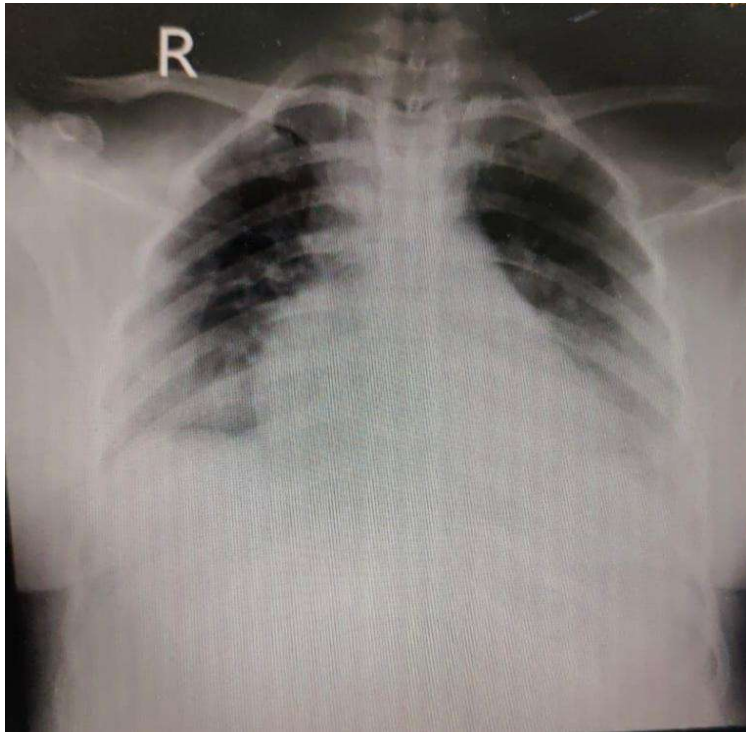


Figure 3 Chest X-ray showing bilateral lower lobes opacities

3. DISCUSSION

Dengue and scrub typhus both are associated with a complex interplay between the virus, host and host's immune system. Dengue ranges in clinical spectrum from mild asymptomatic infection to severe dengue haemorrhagic fever or dengue shock syndrome. The severe disease is due to third space fluid loss i.e., plasma leakage due to increased vascular permeability, platelets destruction and coagulation disorders. Its incubation period is 4-7 days (Bhatt et al., 2021). Risks associated with infection are similar in pregnant women as in a non-pregnant woman, if not treated aggressively may lead to maternal mortality. Studies show evidences of vertical maternal-foetal transmission. Dengue infection in new-borns results in fever, thrombocytopenia, coagulopathy, hepatomegaly and multiorgan failure (Chye et al., 1997).

Scrub typhus too ranges in clinical spectrum from mild febrile illness to severe multiorgan dysfunction. They primarily infect the endothelial cells of blood vessels and various organs like heart, lung, brain, liver, kidney, pancreas and skin leading to multiple organ failures (Rajakpse et al., 2012). It is associated with increased pre term delivery, foetal loss and small for gestation infants. It leads to vasculopathy of placental vessels due to inflammation; this explains the mechanism of oligohydramnios in our patient (Paris et al., 2012). Vertical transmission of scrub typhus is rarely found and previously only two cases of neonatal scrub typhus have been reported (Suntharasaj et al., 1997; Wang et al., 1992).

In our case the patient presented with acute febrile illness with nonspecific generalised body symptoms. Presence of fever with maculopapular petechiae rashes pointed towards dengue, chikungunya, scarlet fever and measles as differential diagnosis (Thomas et al., 2010). Presence of unnoticed atypical eschar pointed towards Rickettsiosis (scrub typhus fever), anthrax, disseminated fungal infection or an insect bite as differential diagnosis (Sundriyal et al., 2013). Routine laboratory investigations revealed thrombocytopenia and mildly elevated liver enzymes. Blood pressure monitoring revealed normal values in serial readings and urine proteins were nil. Hence pre-eclampsia and HELLP were ruled out as differential diagnosis.

A provisional diagnosis of dengue and scrub typhus co infection was made based on the presence of rash, eschar, thrombocytopenia and hepatic dysfunction (Subedi et al., 2021). Considering the diagnostic dilemma patient was started on broad spectrum antibiotic ceftriaxone in injectable form along with oral azithromycin. Later the provisional diagnosis was confirmed with serological tests results. Serological tests showed the presence of IgM antibodies for both dengue and scrub typhus infection suggestive of an acute infection. Broad spectrum antibiotic ceftriaxone was started to treat acute febrile illness without any underlying cause when the serology reports were awaited. The antibiotics recommended for the treatment of scrub typhus are as described (Table 2).

Table 2 Antibiotics recommendations for scrub typhus treatment (Poolmalar and Rekha, 2014; Mahajan et al., 2009)

Drug	Dosage	Category of drug (According to us-FDA)	Pregnancy use
Doxycycline	100mg BD 7-15 days	Category D	Contraindicated
Chloramphenicol	500mg QID 7-15 days	Category C	Potential risks outweighs the potential benefits
Azithromycin	500mg BD	Category B	Drug of choice

Our patient was given azithromycin 500mg bd due to the severity of disease and delay in diagnosis. Additional supportive and symptomatic treatment prevented the patient to go in DIC and septic shock. Mild respiratory discomfort and mild pleural effusion on chest X-ray was due to third space fluid accumulation in dengue infection and endothelial cell invasion of lungs vessels due to scrub typhus infection (Watthanaworawit et al., 2016; Phongsamart et al., 2008).

4. CONCLUSION

In endemic areas scrub typhus co infection along with dengue infection should be considered as a differential diagnosis for acute undifferentiated fever with during pregnancy. Presence of rash and atypical eschar could lead to easy diagnosis of dengue and scrub typhus infections. Early diagnosis and prompt treatment of this rare combination of infection leads to favourable maternal and foetal outcomes.

Financial relationships

All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

Other relationships

All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Author contributions

All authors have contributed equally to the case report.

Ethical approval

Not applicable

Informed consent

Written consent was obtained from participant in this study.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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