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A Rare Case Of Thrombocytopenia In 3rd Trimester Of Pregnancy Due To Scrub Typhus

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Abstract: *Scrub typhus is an important unrecognised cause for undifferentiated acute febrile illness in India. Illness may vary from mild and self-limiting to fatal disease. We report here a case of 27 year old primigravida at 39+ weeks of pregnancy referred to our centre in view of fever since 1 week and thrombocytopenia. She was diagnosed as scrub typhus positive by serum immunofluorescent assay. She was stabilised and taken up for caesarean section for obstetric reasons. Vertical transmission was noticed in this case. She was successfully treated with azithromycin. Scrub typhus should always be listed in differential diagnosis of undifferentiated acute febrile illness with thrombocytopenia.*

Key Words*: Scrub typhus; 3rd trimester; Thrombocytopenia; Azithromycin.*

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I. Introduction:

Scrub typhus is a rare entity causing febrile illness in pregnancy. It is cause by an obligate intracellular gram negative bacterium, *Orientia tsutsugamushi,* and is transmitted by bite of trombiculid mites. It is endemic in rural South East Asia and is leading cause of undifferentiated fever[1]. Bite presents as eschar which mainly clinches clinical diagnosis. It is a painless ulcer that scabs resembling a cigarette burn. Incubation period ranges from 6-21 days. Clinical features vary from mild self-limited febrile illness to severe disease causing MODS and death. Untreated case fatality rate is as high as 30%[2, 3, 4, 5]. In spite of the endemic nature of disease and several epidemics reported from Indian states many cases remain undiagnosed due to lack of suspicion[6]. Clinical diagnosis is poor because it is rare entity and similarity of clinical features with other infections[4, 7]. Also lack of sensitive and specific diagnostic tools at rural clinics where disease is more prevalent leads to under diagnosis[4, 8]. Presence of co-infection further leads to misdiagnosis[4, 9]. Scrub typhus is a rare entity in pregnancy and may present with adverse neonatal outcomes including still birth, low birth weight, preterm labour[2, 4, 11, 12, 13, 14, 15]. Here we present a case of primigravida at 39+ weeks of pregnancy with preterm rupture of membranes referred to us with fever, myalgia and thrombocytopenia.

II. Case report:

A 26 year old primigravida was referred to us at 39+ weeks of gestation with premature rupture of membranes (PROM) with fever and thrombocytopenia (Platelet count-79000/mcL). She was a booked ANC at a periphery hospital where she had regular antenatal check-ups. At 38+ weeks she had history of low grade fever and myalgia. Laboratory investigations were negative for dengue, malaria and typhoid. Her other investigations were normal and hence she was given symptomatic treatment. 1 week later she presented with PROM. There was low grade fever and myalgia. Investigations done were suggestive of thrombocytopenia (Platelet count-79000/mcL) and hence she was referred to our centre for further management.

At arrival she had low grade fever and myalgia. Fever was not associated with chills and rigor. She did not have any history of skin rash, jaundice, diarrhoea, urinary complaints or bleeding manifestations. On examination, she was conscious and coherent. Her pulse rate was 120bpm and BP 120/70. On physical examination there was no rash, eschar, jaundice, hepatomegaly or lymphadenopathy. Foetal growth was appropriate to period of gestation. On per speculum examination there was leakage of amniotic fluid. On per vaginal examination cervix was long, soft minimally effaced, admitting tip of finger, vertex was high up. Laboratory investigations were negative for malaria, dengue and typhoid. Enzyme immunoassay for scrub typhus was positive. Hemogram showed haemoglobin 10.5%, PCV 35%, leucocytosis 16000 and platelet count 74000. Ultrasonography showed single live intrauterine pregnancy with appropriate foetal growth severe oligohydramnios (AFI 1-2). Cardiotocography (CTG) done was suggestive of foetal distress. For obstetric

reasons she was taken up for Emergency LSCS. 2units PRBC and RDP were reserved. Surgery was uneventful. Post operatively she was given injection ceftriaxone 1gram I/V 12-hourly and injection paracetamol I/V 8-hourly and oral azithromycin 500mg once daily. By third day of treatment she was afebrile and myalgia also subsided. Regular monitoring of platelet count was done. On 5th postoperative day, investigations done were normal and platelet count was normal (150000/mcL). Neonate was diagnosed to be scrub typhus positive. Investigations done for neonate were suggestive of thrombocytopenia (Platelet count 72000/mcL). Neonate was also started on azithromycin and platelet count was normalised by day 5 of treatment (platelet count 162000/mcL). Both mother and baby were well at 2 weeks follow-up. Written and informed consent was obtained from the patient for publication of her case report.

III. Discussion:

Scrub typhus is a rare entity causing febrile illness in pregnancy. It is cause by obligate intracellular gram negative bacteria, *Orientia tsutsugamushi,* and is transmitted by bite of trombiculid mites. It is endemic in rural South East Asia and is leading cause of undifferentiated fever. It is an emerging zoonosis with increasing urbanisation of rural areas[1].

Clinical features in pregnancy are similar to those of non-pregnant adults. It includes fever with chills, myalgia and headache. Characteristic eschar is found in less than 60% cases and often missed in dark skinned individuals. Also site of eschar which is usually where mite bites is often located in covered areas and can be easily missed unless actively searched for[14]. Also eschar occurrence is rare in South East Asian patients[14, 15]. Our patient presented with low grade fever and myalgia. There was no eschar on examination. Thrombocytopenia was observed after 1 week of fever onset. Infection causes disseminate vasculitis and perivascular inflammatory lesions resulting in vascular leak and end organ injury[14, 16]. All organs including lungs, liver, kidney and brain are susceptible to damage. Laboratory studies usually reveal leukopenia, thrombocytopenia, deranged liver and kidney function tests, proteinuria and reticulonodular infiltrate on chest X-ray[16]. In pregnancy it may be associated with adverse neonatal outcomes including still birth, low birth weight, preterm labour[14, 16]. However, the exact impact of this infection on foetal outcome is still unclear[11]. Mortality rate in untreated individuals can be as high as 30%[2, 3, 4, 5, 16, 17], but we were able to achieve good foetomaternal outcome in our patient. In spite of the endemic nature of disease and several epidemics reported from Indian states many cases remain undiagnosed due to lack of suspicion[6]. Clinical diagnosis is poor because it is rare entity and similarity of clinical features with other infections[4, 7]. Also lack of sensitive and specific diagnostic tools at rural clinics where disease is more prevalent leads to under diagnosis[4, 8]. Presence of co-infection further leads to misdiagnosis[4, 9]. In our case also diagnosis was missed as she did not have any characteristic signs or symptoms. She presented with low grade fever and myalgia. Malaria, Dengue and typhoid tests done were negative. Lack of awareness and lack of specific diagnostic tools in rural areas lead to delayed diagnosis. The recommended standard treatment of scrub typhus in non-pregnant adults is doxycycline[18]. However, it is classified as a category D drug, and is contraindicated in pregnancy due to the associated foetal risks. Chloramphenicol, a category C drug, may be given in late trimesters of pregnancy with caution[14]. Azithromycin, a macrolide antibiotic, is a category B drug and has emerged as the drug of choice during pregnancy and lactation[17, 18]. Various doses of azithromycin have been recommended, the most common being 500 mg OD for 3-5 days[17]. Some studies have reported successful treatment with 500 mg single dose[11, 14, 17]. Azithromycin had comparable efficacy when compared to doxycycline[19]. Azithromycin penetrates polymorphonuclear leukocytes and macrophages, which are target cells for O. Tsutsugamushi[2, 11, 14, 15]. In our case also patient improved on initiation of azithromycin. Case series by Kim YS et al, Poomalar GK et al, Mahajan SK et al reported good response with azithromycin treatment having no relapses with good maternal and foetal outcome[11, 15, 20].

IV. Conclusion:

High suspicion of scrub typhus is required in patients who present with unexplained fever and thrombocytopenia especially in rural areas. Clinical diagnosis is delayed due to nonspecific symptoms, lack of awareness among clinicians, and poor testing facilities, especially in rural areas. Early diagnosis and treatment with azithromycin is associated with excellent maternal and foetal outcomes.

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