



A case report on Scrub typhus in second trimester of pregnancy leading to multi organ dysfunction

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I. INTRODUCTION:

Scrub typhus caused by Orientia tsutsugamushi, an obligate intracellular gram-negative bacteria, transmitted by larval trombiculid mites (chiggers), is a zoonosis endemic in the rural areas of South-east Asia and remains a leading cause of acute undifferentiated fever (AUF). Contracted during pregnancy, it may lead to adverse maternal and newborn outcomes, including an unknown burden of maternal and newborn mortality. Clinical diagnosis is poor, due to the similarity in presentation with other infections commonly seen in the tropics such as typhoid, leptospirosis, and dengue fever. While it is increasingly being reported as a cause of fever in pregnancy in tropical countries, missing the diagnosis may result in severe maternal morbidity and adverse fetal outcome which is otherwise preventable. Scrub typhus is uncommon during pregnancy, and it is associated with pre-term delivery, increased foetal loss and small for gestational age infants.

Scrub typhus in pregnancy may present with varying clinical spectrum ranging from mild febrile illness to multi-organ dysfunction. Severe form of untreated disease may result in maternal and/or fetal death. We present the case report of a primigravida in her second trimester of pregnancy with scrub typhus that faced “maternal near miss” and fetal demise.

II. CASE REPORT:

An 18 year old primigravida, with gestational age of 29 weeks went to thiruvannamala government medical college with complaints of fever associated with chills and rigor and cough for 3 days on 28/9/2023. No complaints of vomiting, headache, loose stools, abdominal pain, burning micturition, bleeding or leaking per vaginum. When she was admitted in outside hospital, she was hemodynamically stable with baseline investigations done on 28/9/2023, hemoglobin – 10.2g/dl, platelets – 1.54 lakhs/mm³. Renal function tests and liver function tests were in normal limits. Blood culture showed Klebsiella pneumonia which was sensitive to cefepime and

sublactum. Sputum culture sensitivity, CBNAAT was sent in view of cough and came to be negative. Echo done on 4/9/23 showed Right motion wall abnormality with ejection fraction of 61%. Initial clinical improvement was not there and patient is shifted to ICU on 1/10/2023 in view of worsening dyspnea and tachypnea. Antibiotic therapy was modified and Azithromycin and metronidazole were added. Other fever panel work up showed positive for scrub typhus, hence patient was started on inj doxycycline after explaining the risk to fetus. ABG done showed metabolic acidosis with bicarbonate of 10, hence bicarbonate correction started. Patient was requiring non invasive ventilation in view of severe dyspnea. Then she developed increased work of breathing with repeat Echo showing global hypokinesia of left ventricle with ejection fraction of 40%, hence patient was intubated in view of falling saturation and transferred to our hospital.

On arrival to SRMC, patient received in intubated state, and pulse could not be felt with blood pressure of 60/40 mmHg. In view of bradycardia, one cycle of CPR done and patient was given one dose of adrenaline and started on inotropic support with noradrenaline. Vitals improved after that. Per abdomen, uterus corresponds to 28 weeks, ultrasound done showed absence of fetal heart rate. General medicine opinion obtained and orders followed. All baseline investigations done in SRMC showed hemoglobin 11.2g/dl, total counts-26580 cells/mm³, platelet count-1.62 lakhs/mm³, INR-1.34, serum albumin-2.1, RFT & LFT done – normal, serum procalcitonin-44.8. ABG showed severe metabolic acidosis, patient was given IV hydration and bicarbonate correction. Tropical fever panel showed scrub typhus positive IgM 82.24. Patient in view of hemodynamic instability with septic shock was started on broad spectrum antibiotics, Inj Meropenem 2g IV TDS. In view of scrub typhus with severe ARDS, patient was started on Inj Azithromycin 500mg IV BD and Inj Doxycycline 200mg IV BD. Chest x ray showed pleural effusion of left lung, tapping was done for the same, showed transudate picture. For severe



ARDS patient was initially requiring high pressure with PEEP.

Labour was induced with Tab. Mifepristone given on 4/10/2023 along with tab. Misoprostol 50mcg kept pervaginally and patient expelled a dead male fetus of 1.12kgs and placenta and membranes of 250gms. No excessive bleeding noted. No autopsy of neonate or placental pathology done. After delivery patient's condition improved and was gradually weaned off from ventilator to NIV then to no oxygen requirement on Post partum day 6. Now patient maintaining saturation of 98% in room air. Repeat ECHO showed ejection fraction of 60% and repeat chest xray showed decreasing bilateral lung opacities. Repeat hemoglobin was 7.5g/dl hence InjEncifer given. All her clinical and laboratory parameters improved and hence patient got discharged.

III. DISCUSSION :

The disease is increasingly being seen in the southern and western parts of India. After an incubation period of 6-21 days, onset is characterised by fever, headache, myalgia, cough and gastro-intestinal symptoms.

Prolonged intensive care avoided a second trimester near miss maternal mortality but not fetal loss. With tachypnea, decrease in oxygen saturation, hypotension, thrombocytopenia, our patient was at the extreme end of spectrum of scrub typhus when she was referred to us. Though her illness started with mild disease but it evolved to severe form over a period of 7 days. A primary papular lesion which later crusts to form a flat black eschar may be present at the site of larval bite. It may be absent in some patients. This leads to local lymphogenous and subsequent hematogenous dissemination, involving endothelial cells and macrophages, which release soluble cell-specific adhesion molecules and causes focal or disseminated vasculitis and perivascular inflammatory lesions resulting in significant vascular leakage and end-organ injury involving different organ systems. This results in a wide array of manifestations depending on the organ system involved.

Pathogenesis of lung injury in Scrub typhus has been attributed to diffuse alveolar damage with hyaline membrane formation, interstitial pneumonitis, and damage to capillaries and lung hemorrhage. It is difficult to predict the course of pulmonary involvement. In self-resolving or promptly treated scrub typhus, lung involvement may be limited to mild interstitial pneumonitis. Deterioration of pulmonary parameters in our patient can be attributed to accumulation of protein-

rich edema in the interstitial and alveolar space that causes progressive dyspnea, hypoxemia, and alveolar infiltrates. With septic shock, hypoalbuminemia, our patient had most of the risk factors for ARDS development and event of ICU admission brought her close to fatal outcome. If the treatment been delayed further this would have progressed to atelectasis and death.

The drug of choice in non-pregnant individuals include oral tetracycline (500mg four times daily) or doxycycline (200mg OD) for seven days. As per United States Food and Drug administration categories of drug safety during pregnancy, tetracyclines come under Category D (evidence of human foetal risks exists but benefits may outweigh risks in certain situations) and hence are contraindicated in pregnant women. Chloramphenicol, a category C drug (animal reproduction studies have shown an adverse effect on the foetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks) is also effective against scrub typhus in both pregnant and nonpregnant women. It is prescribed with caution to late trimester pregnant women because of an increased risk to the foetus at the time of delivery.

Azithromycin, a macrolide antibiotic which falls under category B (no evidence of adverse effects on the fetus in animal studies but there is a lack of controlled studies on human pregnancy) has been found to be more effective treatment for Scrub typhus in pregnancy and lactation and in doxycycline resistant strains causing scrub typhus. Azithromycin, penetrates polymorphonuclear leukocytes and macrophages, which are target cells for *O. tsutsugamushi*. Various doses of azithromycin have been suggested, the most common being 500 mg once a day as serum levels of azithromycin are higher if administered as a once-daily dose rather than in divided doses. While azithromycin has been shown to be as effective as doxycycline for mild to moderate scrub typhus, its efficacy for treatment of severe complicated scrub typhus is largely unknown. Not many systematic studies have reported the duration of antibiotic therapy. Although 10 to 14 days of antibiotics are used to treat complicated scrub typhus.

Many authors have described increased risk of preterm delivery, small for gestation infants and perinatal deaths. In one study, fetal loss was as high as 42.4% and preterm birth was observed in 9.1% of 33 pregnancies despite treatment with azithromycin. Duration of illness of more than



seven days has been described as an independent risk factor for a poor fetal outcome.

Disease mostly starts with non-specific symptoms such as fever, malaise, and lymphadenopathy. This may remain mild and get resolved or progress to severe form. Prolonged duration of illness, delay in appropriate antibiotic therapy results in multi-organ dysfunction. Our patient had mild symptoms initially but disease progressed to severe form resulting in “near miss” because diagnosis and treatment were delayed. Pulmonary involvement was severe enough to require oxygen support by NIV and later on intubation.

Since pregnant patient would approach their primary physician for any complaints, primary care providers should be aware of this differential and should investigate the pregnant patient for scrub typhus early in the course of illness, especially in tropical countries.

IV. CONCLUSION:

It is important to consider this differential early in the course of illness especially in tropical countries. Delay in diagnosis and hence, treatment can result in catastrophic outcome.

Strengths and Limitations Of This Case Report :

The strength includes the reporting of such a case is important as tropical illness can lead to sudden progression of disease if unsuspected and can lead to morbidity and mortality in pregnancy. Also our case was timely detected from the time she presented to our centre, and managed, hence mortality was prevented. The limitation is that more reporting of such cases or case series needs to be done, so that emphasis can be laid on prevention of maternal near miss and maternal mortality occurring due to missed diagnosis of this tropical illness.

Conflicts of interest : the authours declare that they have no conflicts of interest

Informed consent : informed consent was taken from the patient and her husband.

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