



PRIMARY NEONATAL SCRUB TYPHUS - A CASE REPORT

SENTHIL KUMAR P PERUMAL

Department of Neonatology,
MADRAS MEDICAL COLLEGE AND GOVERNMENT GENERAL HOSPITAL

Abstract :

Scrub typhus is a rickettsial disease that is endemic to tropical countries. It is extremely rare in the newborn period. To our knowledge, this is the first case report of a primary neonatal scrub typhus presenting with multi-organ dysfunction. We discuss here about the clinical manifestations, diagnosis and life threatening complications of a neonate with primary scrub typhus, who recovered completely with commencement of appropriate therapy. An eschar over the ear clinched the diagnosis. There was a dramatic clinical improvement within 24 hours of treatment. The timely diagnosis and institution of appropriate therapy saved the infant from a life threatening situation.

Keyword : Rickettsia, Scrub typhus, Neonate, Eschar

Introduction:

Scrub typhus is a rickettsial infection caused by *Orientia tsutsugamushi*, which is transmitted either through the bite of the trombiculid mite larvae (Primary) or by vertical transmission from the

mother (Congenital). The disease usually manifests with non specific symptoms such as fever with lymphadenopathy, hepatosplenomegaly and thrombocytopenia. An eschar found on clinical examination is a hallmark for the diagnosis. However atypical and severe presentations [1-4] of scrub typhus have also been reported. Primary infection can be life threatening in neonates if not recognised early and treated appropriately. Neonatal scrub typhus has been reported rarely in the literature. An extensive search of the literature revealed a single case of congenital neonatal scrub typhus reported so far [5].

Case report:

A 27 days old term male neonate born by spontaneous vaginal delivery with a birth weight of 2.7 kg to a 30 year old, third gravida mother with an unremarkable antenatal period was referred to our tertiary care centre with history of continuous, high grade fever of 5 days duration. He had refusal of feeds, lethargy, seizures, respiratory distress one day prior to admission.

He was very sick, highly febrile, lethargic, had severe respiratory distress, poor peripheral perfusion and hypotension. Systemic examination revealed large hepatomegaly and splenomegaly and features of meningo-encephalitis. He was supported with mechanical ventilation, ionotropes and anticonvulsants [Fig.1]. He was started on meropenem and vancomycin with a suspicion of late onset sepsis. After 24 hours of admission, child manifested with oedema, bleeding from GIT and skin. Malaria, dengue and viral encephalitis were the differential diagnosis considered.



Investigations revealed severe thrombocytopenia, prolonged prothrombin time and peripheral smear was suggestive of disseminated intravascular coagulation with no hemoparasites. Features of hepatic dysfunction in the form of conjugated hyperbilirubinemia and elevated transaminases with hypoalbuminemia were noted. USG abdomen revealed hepatosplenomegaly with minimal free fluid. TORCH screening was positive for CMV IgM by ELISA but urine CMV PCR was negative. Blood, CSF, urine cultures were sterile and dengue serology was negative.

After 24 hours of institution of doxycycline therapy baby became afebrile and was weaned off all supportive measures in 72 hours. The anti-rickettsial therapy was continued for 7 days. The infant was subsequently discharged after 2 weeks of admission. On follow up at 4 months of age, he was found to be gaining weight steadily [Fig.3]. There was no hepatosplenomegaly and neurological examination and haematological parameters were normal. However, his long term development needs to be followed up.

Baby had sustained fever spikes and failed to show improvement in spite of intensive care and medications. After 5 days of admission, an erythematous ulcerative lesion (eschar) was noted on the left ear helix which evolved into black scab in 48 hours [Fig.2]. Presumptive diagnosis of scrub typhus was made as the baby presented with unremitting fever, eschar, hepatosplenomegaly, bleeding and thrombocytopenia. Baby was started on doxycycline after sending the blood for scrub typhus. The infant's serum IgM ELISA positivity for scrub typhus confirmed our diagnosis. His mother was asymptomatic and her serum was negative for scrub typhus ruling out vertical transmission.

Fig 1:Sick edematous neonate on day 2 of ventilation





Fig 2: Eschar on the left ear

Fig 3: Well baby on 4 months follow up

Discussion:

Scrub typhus is a rickettsial infection caused by *Orientia tsutsugamushi*, a small gram negative cocco-bacillus. It is transmitted to humans, who are accidental hosts, through the bite of the infected larva (chiggers) of a trombiculid mite which serves both as vector and reservoir [6]. The bacteria multiply at the inoculation site with the formation of a papule that ulcerates and become necrotic, evolving into an eschar. The eschar is painless and non pruritic, hence can be missed if located in hidden areas [7]. It can be a shallow ulcer in moist areas such as groin, axilla and popliteal fossa. In older children, regional lymphadenopathy occurs that progresses to generalised lymphadenopathy within a few days. The target cells of *Orientia tsutsugamushi*, in humans, are endothelial cells throughout the body, macrophages and cardiac myocytes. Rickettsial infection occurs, causing focal or disseminated vasculitis [6] and perivasculitis with significant vascular leakage and end-organ injury to the lungs, heart, liver, spleen and central nervous system. It can result in serious life threatening problems like interstitial pneumonitis, non-cardiogenic pulmonary edema, myocarditis, shock, meningoencephalitis, acute renal failure and disseminated intravascular coagulation.

In this neonate, in the setting of high grade fever, hepatosplenomegaly and thrombocytopenia, and DIC, with an eschar on the ear, a diagnosis of Scrub typhus was considered and confirmed by a positive IgM Enzyme Linked Immunosorbent Assay (ELISA). Doxycycline therapy initiated a prompt defervescence of fever within 24 hours with complete resolution of complications. Dramatic response to doxycycline, in itself, is considered to be diagnostic of scrub typhus [1, 8, 9]. Oedema seen during the course was probably due to increased vascular permeability secondary to vasculitis [1]. Seizures may be attributed to meningoencephalitis/ aseptic meningitis due to scrub typhus. The clinical symptoms and signs observed in scrub typhus are usually as a result of the typical pathogenetic process. A recent report [10] implicates the cytokine storm, associated with the immune response, in the pathogenesis of complicated scrub typhus. Once the cytokine cascade is triggered, the infection becomes a life threatening one, as the immune system loses its regulatory role. This occurs when there is a delay in initiating therapy. Immune complexes or immunoglobulin aggregates in blood may also produce cross reactivity to various antigens. This may explain the positive CMV IgM result.

In the previous case report [5], the neonate presented with fever, hepatosplenomegaly, coagulopathy and seizures. A presumptive diagnosis of sepsis with meningitis was made and started on broad spectrum antibiotics. Later, they demonstrated positivity of scrub typhus both in mother and the baby using

quantitative Weil-Felix test suggesting vertical transmission. The neonate was managed with exchange transfusion. The vertical transmission from the mother was ruled out in our neonate. As primary scrub typhus occurs due to the bite of chiggers during outdoor activities, infection in newborn is uncommon as they are mostly indoors, but can occur when chiggers are brought in by others through fomites or during travel

Conclusion:

It is increasingly evident that scrub typhus needs to be considered, though rare, along with bacterial sepsis, viral infections, fungal sepsis, TORCH infections, enteric fever, congenital malaria and IEM in the differential diagnosis of all acute febrile illnesses/ sepsis in the newborn period. Early diagnosis is possible only if there is a high index of suspicion for scrub typhus. Undue delay in administering appropriate antibiotics may lead to increased morbidity and mortality.

Key message:

1 Primary scrub typhus can occur even in neonates.

2 Scrub typhus though rare should be considered in the differential diagnosis of any neonate presenting with unremitting fever, organomegaly and lymphadenopathy.

3 Morbidity can be very high, especially in neonates, in cases where diagnosis is delayed.

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