



## Pediatric Scrub Typhus

Ira Shah, Vigyan Bang, Vishank Shah, Vaibhav Vaidya

### Introduction

Scrub typhus, also called Tsutsugamushi disease, is an acute infectious disease of variable severity that is transmitted to humans by certain mites (chiggers) of the Trombiculidae family. It affects people of all ages and pediatric scrub typhus is commonly reported in past.

### Review of Pediatric Scrub Typhus

In rural eastern Taiwan, twenty-eight pediatric cases were confirmed to be scrub typhus (either by immunofluorescence assay or polymerase chain reaction) from 2000 to 2005 (1). The majority of the children (60.7%) diagnosed with scrub typhus were male. Approximately half the patients were < 5 years old and the mean age (SD) was 6.1 (3.66) years & were more from rural rather than urban areas. The greatest number of cases was seen in the spring and summer (1).

In another record based study (2) of children under the age of 18 with a confirmed diagnosis were selected for retrospective analysis, hospitalized between 1992 and 2002 at the Taitung branch of Mackay Memorial Hospital, Taiwan. 145 patients fulfilled the diagnostic criteria for scrub typhus, of whom 106 (73%) were adults and 39 (27%) were children. The mean age of the children was 7.6 +/- 4.6 years (2).

A report (3) has been published in past about pediatric Scrub Typhus from Himalayan region of India also. In a retrospective study from India confirmation of the suspected rickettsial disease was done using a gold standard diagnostic test i.e. microimmunofluorescence in pediatric patients with acute febrile illness of unknown etiology. Two serological tests, Weil-Felix and Microimmunofluorescence were used to confirm infection. Five children had fever, vomiting and generalized lymphadenopathy, but none had eschar or rash. One was cured with doxycycline, remaining four patients treated with azithromycin and one died despite treatment. Single case report was also published by us in past from Mumbai (4).

### Epidemiology and Transmission

Because of the prolonged persistence of *O. tsutsugamushi* in the human host, fetal infection acquired transplacentally is a possibility. One examination pairing mother-cord sera in an endemic area found no serologic evidence of transplacental infection (5). Twenty-nine

percent of the mothers demonstrated serologic evidence of past infection; however, no mother was acutely infected at the time of the study. Isolation of *O. tsutsugamushi* from the placenta has not been reported in humans.

### Clinical Manifestations In Pediatric Population

The chigger bite results in a papule, enlarging to a bulla that rapidly sloughs, leaving a shallow ulcer. A black crust surrounded by a 1-2 cm erythematous raised circle then forms (Fig 1) (4). Because mites are frequently acquired when children play in bushes, the initial lesion is commonly on a lower limb. At this time, other systemic symptoms begin, at first insidiously with a low grade fever, headache, chills & anorexia. Within 5 days, an unremitting fever to 40 degrees C (104° F) accompanied by a severe headache is seen in virtually all patients. Generalized lymphadenopathy is the most consistent physical finding, occurring in 80 to 90 % of patients & is especially prominent in the axilla, neck, and inguinal areas. The characteristic rash of scrub typhus is maculopapular & generalized & most prominent on non - exposed skin surfaces. After regression of the eschar, a scar often remains and has been shown to persist for up to 25 years (7). Hepatosplenomegaly and conjunctival injection are common; deafness and tinnitus occur less commonly but are helpful diagnostic features when they do appear. Atypical pneumonia and overwhelming pneumonia resembling adult respiratory distress syndrome have been described (8). The reported incidence of chest radiographic abnormalities in patients with scrub typhus varies from 59% to 72%. Bilateral diffuse areas of reticulonodular opacity, hilar lymph node enlargement, and septal lines are the most common findings (8). Myocarditis and disseminated intravascular coagulation also have been reported (7). The severity of the clinical manifestations varies widely because several different strains of *R. tsutsugamushi* exist.

The primary clinical symptoms in a study from Taiwan included fever (100%), cough (50%), eschar (50%), rash (35.7%), poor appetite (42.9%), lymphadenopathy (42.9%), headache (39.3%), and hepatomegaly (35.7%). C-reactive protein (CRP) was elevated in 100%, an aspartate aminotransferase (AST) was elevated in 100%, an alanine aminotransferase (ALT) level was elevated in 91.3%,

From the Department of Pediatrics, B.J.Wadia Hospital for Children, Mumbai-India

Correspondence to : Dr Ira Shah, 1/B Saguna, 271/B St Francis Road, Vile Parle (W), Mumbai 400056. India



**Fig 1. Rickettsial Rash with Eschar (arrow)**

hypoalbuminemia was found in 88.9% and proteinuria in 50%. The mean (SD) duration of antibiotics was 11.0 (2.68) days and the mean (SD) duration for fever resolution after treatment was 2.8 (2.51) days. Meningoencephalitis was noted in 6 patients. No mortalities was recorded (1).

In another retrospective study, the most common clinical manifestations of pediatric scrub typhus were fever (n=39; 100%), cough (n=28; 72%), anorexia (72%), eschar (69%), chill (67%) and lymphadenopathy (64%). The most common complications were hepatic dysfunction (77%) and pneumonitis (54%). Three children (8%) required intensive care, but the overall survival rate was 97%. One child died with multi-organ failure within 8 hours after admission. Doxycycline was an effective antibiotic for pediatric scrub typhus in Taiwan as per this study (2).

In a report from India five children had fever, vomiting and generalized lymphadenopathy, but none had eschar or rash (3).

However, in our own case (4) presented with remittent fever for 10 days, erythematous hemorrhagic rash which started over face and then spread over the body for past seven days, altered sensorium for two days and two episodes of generalized tonic clonic convulsion prior to admission. He had a bite on left calf 15 days prior to this illness.

There was no vomiting, bleeding from any site or focal neurological deficit. On examination, he was febrile (101°F) with heart rate of 120/min, respiratory rate of 30/min, blood pressure of 106/66 mm of Hg. There were multiple blackish reddish-pigmented lesions over trunk and legs with eschar over left calf (Fig-1)

#### **Diagnosis (3,9,10)**

The Weil-Felix OX-K strain agglutination reaction may be the only serologic test available in less developed countries. It can aid in confirming (in early convalescence) a tentative diagnosis made during the acute phase of the disease when specific therapy can be lifesaving. However, it is not very sensitive; OX-K agglutinins develop in only a little more than 50 percent of scrub typhus patients. Moreover, OX-K agglutinins are also produced by relapsing

fever. However its low cost makes the Weil Felix test a useful test in the diagnosis of scrub typhus. A fourfold rise in agglutinin titres in paired sera, or a high cut-off titre (>1:320) in single samples are diagnostic for infection.

Immunofluorescent tests are much more diagnostic and reliable. Unfortunately, because of the multiplicity of scrub typhus strains, eight or more antigenic strains must be included in the sophisticated immunofluorescent tests for scrub typhus; these tests are available in only a few specialized laboratories. Apparently, a high immunofluorescent titer may represent repeated infections. An indirect immunoperoxidase test is now available and is sensitive, specific, and reproducible. No cross-reactivity occurs when testing against diseases other than scrub typhus. The indirect immunoperoxidase test is superior to the Weil-Felix reaction and comparable to the immunofluorescent test in the serodiagnosis of scrub typhus and seems to be a practical substitute for immunofluorescence.

A dot immunoassay also has been applied to the serodiagnosis of scrub typhus. The results are easily interpreted by untrained personnel because the naked eye readily distinguishes the differences in intensity of color between positive and negative reactions. Scrub typhus can be suspected when a patient gives a history of recent exposure in a geographic area where scrub typhus occurs. If, in addition, a local eschar, evanescent rash, and general and regional lymphadenopathy along with fever, headache, and conjunctival suffusion are present, the physician should be alerted to suspect scrub typhus; however, it cannot be differentiated with certainty from dengue, leptospirosis, malaria, or typhoid fever.

#### **Treatment (1,-4, 11-14)**

Tetracyclines is the drug of choice. In younger children Chloramphenicol or quinolone group of antibiotics is used to avoid staining (10). One study demonstrated that a single 200-mg dose of doxycycline was as effective as a 7-day course of tetracycline in treating patients with scrub typhus. However, in this study, therapy was not instituted until day 10 of the disease. Since serologic confirmation of scrub typhus is difficult and delayed doxycycline therapy is associated with a poorer prognosis, early empirical doxycycline therapy should be initiated if there is clinico-epidemiologic suspicion of scrub typhus (13).

Immunity begins to develop only during the second week of the illness. Because both chloramphenicol and doxycycline are rickettsiostatic, patients with scrub typhus who are treated in the first week of illness may require sporadic short courses of antibiotic therapy for prevention of relapse. Strains with reduced susceptibility to antibiotics have been observed in northern Thailand. Rifampin may offer an alternative for treatment of such infections (9).



### Prognosis

The prognosis varies widely because of significant differences in the severity of disease caused by different strains in different populations and in various geographic areas. Mortality rates in the pre-antibiotic era varied from 1 to 60 percent. With the use of antimicrobials, fatalities rarely occur. When treatment is begun early in the course of scrub typhus, relapses as well as definite second attacks of the disease are common. The wide heterogeneity of scrub typhus strains is believed to account for the frequent reinfections that occur after scrub typhus infection; reinfections are rarely or never seen after other rickettsial diseases.

### Prevention

Vector control involves impregnating clothing and smearing exposed skin surfaces with residual insecticides like dimethyl or dibutyl phthalate. Short-term measures of vector control by cutting, burning, or bulldozing of vegetation along with heavy spraying of camping grounds with insecticides such as dieldrin, lindane or chlordane can be effective. Chemoprophylaxis is feasible for persons with high-risk exposure for short periods. Doxycycline given once a week provides effective chemoprophylaxis against

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