



Clinical Manifestations & Complications of Scrub Typhus

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Introduction

Scrub typhus, also known as tsutsugamushi disease, is an acute febrile illness caused by infection with *Orientia tsutsugamushi* and characterized by focal or disseminated vasculitis and perivasculitis, which may involve the lungs, heart, liver, spleen, and central nervous system (1,2,3). The symptoms are usually mild and the clinical course self-limited, with spontaneous recovery after a few days; however, some cases are more severe and protracted, and the disease may be fatal (1). The diagnosis of scrub typhus is based on the patient's history of exposure, the clinical features, and the results of serologic testing (1,4,5). The article provides a review of the clinical features and the complications of scrub typhus.

Clinical Course

The disease in humans results after the introduction of *O tsutsugamushi* through the skin by the bite of a larval-stage (chigger) trombiculid mite (1,5,6). It occurs in persons who engage in occupational or recreational behavior that brings them into contact with mite-infested habitats such as brush and grass. After a blood meal, the chigger detaches and matures into a nymph and subsequently into an adult. Person-to-person transmission of infection has not been reported (5). Periods of epidemics are influenced by the activities of the infected mite. After an incubation period that ranges from 6 to 21 days (usually, 10-12 days), the onset of disease is characterized by fever, headache, myalgia, cough, and gastrointestinal symptoms (1). The severity of the symptoms varies widely, depending on the susceptibility of the host, the virulence of the bacterial strain, or both.

Physical

The illness begins rather suddenly with shaking chills, high fever (104-105°F), myalgia, infection of the conjunctiva and eschar (resembling a cigarette burn) with tender regional lymphadenopathy. Less frequently, ocular pain, wet cough, malaise, and injected conjunctiva are present. A spotted rash on the trunk may be present. Patients experience abrupt onset of severe headache, loss of appetite.

The classic case description includes an eschar at the site of chigger feeding, regional lymphadenopathy, and a maculopapular rash (1,4,5). The chigger bite is painless

and may become noticed as a transient localized itch. Bites are often found at sites where skin surfaces meet or clothes bind, such as the axilla, groin, neck, waist, and inguinal area. Toward the end of the first week, approximately 35% of patients develop a centrifugal macular or maculopapular rash on the trunk, which may become papular. Later it may extend to the arms and the legs. There is usually tenderness from lymphadenopathy in the region of the bite wound or eschar. An eschar at the wound site is the single most useful diagnostic clue (4). An eschar is usually found on Caucasian and East Asian patients but is seen less frequently on South Asians, especially those who are dark skinned (7,8,9). The eschar begins as a small papule that



Fig 1. Showing Eschar

enlarges, undergoes central necrosis, and eventually acquires a blackened crust with an erythematous halo that resembles a cigarette burn (4). The skin surrounding the ulcer is moderately red. Generalized lymphadenopathy and hepatosplenomegaly are common at physical examination (1,5). In a small proportion of patients, tremors, delirium, nervousness, or nuchal rigidity may develop in the 2nd week of illness (1,10).

In children liver dysfunction is very common with elevated CRP, Aspartate aminotransferase and alanine transferase elevated in children ranging from 77 to 100% of cases. The clinical course can be very fast and severe complication may develop, which can result in mortality if appropriate treatment is not given in time.

Complications

Pulmonary Manifestations

Pulmonary involvement is a well-documented complication of scrub typhus infection. The basic pathologic

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process in pulmonary involvement of scrub typhus is Interstitial Pneumonia with or without vasculitis (11). In autopsy series, interstitial pneumonia has been found in almost all patients with scrub typhus (12). At microscopy, blood vessels, in specimens from the interlobular septa and alveolar walls appear congested and surrounded by a mononuclear cellular infiltrate (12).

Acute respiratory distress syndrome may develop in scrub typhus. This is a rarely reported but serious complication (13). Older age, thrombocytopenia, and the presence of early pneumonitis have been suggested as risk factors for the development of acute respiratory distress syndrome (13). With appropriate antibiotic therapy, patients usually recover without serious sequelae.

Cardiac Manifestations

Myocardial lesions were observed in 80% of patients in one autopsy series (2). Cellular infiltration frequently has been observed in the endocardium and pericardium (2,13). Vasculitis and perivasculitis in the myocardium induce cellular infiltration along with hemorrhage and edema of interstitial tissues. Cardiomegaly, which may be due to myocardial or pericardial involvement in the infection (14,15), is usually reversible (11). Cardiovascular complications of scrub typhus were frequently reported before the antibiotic era; However, complications such as palpitations and PVCs were rare during the acute phase of scrub typhus and developed usually during the second or third week of illness in untreated patients.

Abdominopelvic Manifestations

Abdominal involvement is not uncommon in patients with scrub typhus. Reported pathologic findings in the liver at autopsy have included hepatic congestion, periportal inflammation, and peripheral necrosis (2,12). Hepatic congestion is thought to be caused by heart failure due to myocarditis, periportal inflammation, or both (2). Gallbladder wall thickening in patients with scrub typhus may be due to acute vasculitis with perivasculitis similar to that seen in the liver and other organs. Acute inflammation of the spleen with marked acute splenic congestion and enlargement was observed in 96% of patients with scrub typhus in one autopsy series (12). Splenic infarction also was observed occasionally (12).

Scrub typhus also may involve other abdominopelvic organs, including the gastrointestinal tract and kidneys. It may cause gastrointestinal hemorrhage (1,2,16) and acute renal failure (17). Imaging studies have a limited role in the detection of these lesions and in the management of affected patients. The major endoscopic features that can develop in scrub typhus are superficial mucosal hemorrhage, multiple erosions and ulcers without any predilection sites, and unusual vascular gastrointestinal bleeding (16). The endoscopic features are related to cutaneous lesions and severity of the disease. Endoscopy is useful for diagnosis

and management of gastrointestinal vasculitis related to scrub typhus.

Central Nervous System Manifestations

Autopsy studies have revealed involvement of the central nervous system in almost all affected patients. Although its severity varied considerably, central nervous system involvement usually resulted in meningoencephalitis (1,2). Pathologic findings of central nervous system involvement in scrub typhus include diffuse or focal mononuclear cellular infiltration of the leptomeninges, typhus nodules (clusters of microglial cells), and brain hemorrhage (1,2).

Although central nervous system manifestations is common in scrub typhus (18), only one case report of typhus encephalomyelitis diagnosed at brain MR imaging has been published in the literature. A small number of patients have CNS involvement, with tremors, nervousness, slurred speech, nuchal rigidity, or deafness during, the second week of the disease; however, results from the cerebrospinal fluid examination either are normal or indicate a low number of monocytes.

Hematological Manifestations

More virulent strains of *O. tsutsugamushi* can cause haemorrhaging and intravascular coagulation. Patients may present with disseminated intravascular coagulation (DIC). Patients with scrub typhus often exhibit leucopenia. Acute scrub typhus appears to improve viral loads in patients with HIV. This interaction is currently unexplained. The rash may also have a petechial look to it, due to the perivasculitis of small blood vessels that occurs causing endothelial injury - resulting in small hemorrhages under the skin or petechiae.

Mortality/Morbidity

In the pre-antibiotic era, the mortality in scrub typhus with extensive pneumonitis and cyanosis unrelieved by oxygen, was 100% (19). The illness is usually mild and self-limited. Mortality rates in untreated patients range from 0-30%, depending on the virulence of the infecting strain, host factors, and institution of proper treatment. No significant morbidity or mortality occurs in patients who receive appropriate treatment (20,21).

Conclusions

Scrub typhus is an acute febrile illness caused by *Orientia tsutsugamushi*. The main pathologic change is focal or disseminated vasculitis caused by the destruction of endothelial cells and the perivascular infiltration of leukocytes. The diagnosis of scrub typhus is based on the patient's history of exposure, clinical features, and results of serologic testing. Regional and generalized lymphadenopathy is common. The pulmonary manifestations of scrub typhus include interstitial pneumonia, interstitial edema, and hemorrhage caused by vasculitis. Abdominal manifestations include splenomegaly, periportal edema, gallbladder wall thickening, and



lymphadenopathy. Although the severity of scrub typhus varies considerably, involvement of the central nervous system is seen in almost all patients and can result in meningoencephalitis. The possible presence of scrub typhus infection in a patient with fever and respiratory distress should be considered, particularly if an eschar is seen or if the patient has a history of environmental exposure in a geographic area in which scrub typhus is endemic. A high degree of clinical suspicion and familiarity with the various clinical & radiologic manifestations of scrub typhus allow early diagnosis and timely initiation of appropriate therapy, and thereby may help reduce patient morbidity & mortality.

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