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Popular Article

An Overview of Scrub Typhus: A Re-Emerging Zoonotic Threat

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Introduction

Scrub typhus, also known as bush typhus or tsutsugamushi disease is an acute febrile, vector borne zoonotic disease caused by a bacteria called *Orientia tsutsugamushi*. The disease is spread to humans and animals by bites from infected chiggers (larval mites). Fever, headache, body aches, and sometimes a rash are the most common symptoms of scrub typhus. It is a major public health threat in India, other south Asian countries and around the tropics and kills an estimated 10 percent of the approximately one million people infected by it every year. As a result of increased prevalence of the disease in scrub or wasteland, scrub typhus was named. Anyone living in or traveling to areas where scrub typhus is found could get infected. Several factors can help determine the diagnosis of scrub typhus, including the patient's history of exposure, clinical features, and serological results. The use of doxycycline as empirical therapy can be lifesaving when clinical suspicion is high.

Epidemiology

Scrub typhus is endemic across extensive part of south Asia, Australia and the Pacific regions. It is found in India, Pakistan, China, Thailand, Malaysia, Taiwan, Tibet, Japan, Russia, South Korea and Nepal. These regions where scrub typhus is endemic is referred to as “tsutsugamushi triangle.” In India, the presence of scrub typhus has been known for several years. The disease is widely spread all over the country, and was reported in several states - Haryana, Jammu, and Kashmir, Himachal Pradesh, Uttaranchal, West Bengal, Assam, Maharashtra, Kerala and Tamil Nadu (1). During World War II, there was an outbreak of this disease in Assam and West Bengal, in the 1965 Indo-Pak war and in 1990 in a unit of an army deployed at the Pakistan border of India. These reports showed a resurgence of this disease in India. Recently 854 cases of scrub typhus have been reported in the states of Rajasthan between August 4 to September 8 2023. (2)

Etiology Of Scrub Typhus

Orientia tsutsugamushi is the causative agent of scrub typhus. It is a gram negative, obligate intracellular, non-flagellate small pleomorphic coccobacilli. They are 0.5 to 0.8µm wide and 1.2 to 3.0µm long. The organism is highly virulent and should only be handled in a biosafety level-3 laboratory. Their genome is approximately 2 Mb. They are found throughout the body but is present in the greatest number in salivary glands of mites.

Pathogenesis

Trans-ovarian transmission maintains the infection in nature through the larvae of trombiculid mites. The mite has four-stages in its lifecycle: egg, larva, nymph and adult. As only the larval stage (chiggers) can parasitize animals or humans, the mites are dangerous only at this stage. Larvae of this species feed on small rodents, especially wild rats of the subgenus *Rattus*. During the rainy season, man gets infected accidentally by encroaching on the zones of infected mites. In these zones, secondary 'scrub' growth often occurs after clearing of primary forest; hence the term 'scrub typhus'. Once the chiggers have grasped a passing host, they prefer to feed where the skin is thin, tender or wrinkled and clothing is tight. Chiggers do not usually pierce the skin when feeding, preferring to insert their mouthparts down hair follicles or pores. Once attached, they inject a liquid that dissolves the tissue around the feeding site. This liquefied tissue is then sucked up as sustenance for the chigger. As *tsutsugamushi* organisms are abundant in the salivary glands of chiggers, they are injected into their hosts when they feed. As soon as the engorged chigger drops off its host, it burrows into the ground and becomes a nymph (3). Proliferating organisms release cytokines, which damage endothelial integrity, causing fluid leakage, platelet aggregation, polymorphs, and monocyte proliferation, causing focal occlusive end-angiitis and microinfarctions. Skeletal muscles, skin, lungs, kidneys, brains, and cardiac muscles are particularly affected by this process. The condition can also lead to venous thrombosis and peripheral gangrene

Signs And Symptoms

Symptoms of scrub typhus usually begin within 10 days of being bitten. Signs and symptoms may include:

- Fever and chills
- Headache
- Cough, shortness of breath
- Body aches and muscle pain
- Rash
- Regional and generalized lymphadenopathy
- A dark, scab-like region at the site of the chigger bite (also known as eschar) is pathognomonic of scrub typhus.
- Mental changes, ranging from confusion to coma



- Patients become delirious and may develop seizure
- The main pathologic change is focal or disseminated vasculitis caused by the destruction of endothelial cells and the perivascular infiltration of leukocytes. People with severe illness may develop organ failure and bleeding, which can be fatal if left untreated.
- Mortality from this disease is 7-30%.



Figure 1. Eschar at site of chigger bite

Diagnosis And Testing

Serological tests still remain an indispensable tool in the diagnosis. Micro immunofluorescence is considered the test of choice. Latex agglutination, indirect haemagglutination, immunoperoxidase assay, ELISA and polymerase chain reaction (PCR) are other tests available. Weil-Felix test (W-F) using *Proteus OXK* strain is commercially available sero-diagnostic test and is in use for many years. A new dipstick test using a dot blot immunoassay format has been developed for the serodiagnosis of scrub typhus. The dot blot immunoassay dipstick is accurate, rapid, easy to use, and relatively inexpensive. It appears to be the best currently available test for diagnosing scrub typhus in rural areas where this disease predominates.

Differential diagnosis can be done from typhoid, malaria, dengue, leptospirosis and meningococcal disease and HIV.

Treatment

Early treatment shows better outcomes and faster resolution than delayed treatment.

The recommended treatment regimen for scrub typhus is doxycycline (2.2 mg/kg/dose bid PO or IV, maximum 200 mg/day for 7-15 days) (4). For prophylaxis, 200 mg may be taken as a single dose. Doxycycline can be used in persons of any age. Some studies found that when both azithromycin and doxycycline were administered together to patients with severe scrub typhus, the bacteria were cleared away quicker and patients improved faster

Alternative regimens include tetracycline (25-50 mg/kg/day divided every 6 h PO, maximum 2 g/day) or chloramphenicol (50-100 mg/kg/day divided every 6 h IV, maximum 3 g/24 h, or 500 mg qid orally for 7-15 days for adults). If used, chloramphenicol should be monitored to maintain serum concentrations of 10-30 µg/ml. Therapy should be continued for a minimum of 5 days and until the patient has been afebrile for at least 3-4 days to avoid relapse. Chloramphenicol is best avoided during pregnancy and reduced doses should be given in hepatic impairment. Azithromycin can be given in



case of pregnant women as doxycycline is associated with foetal risk and contraindicated in them. Jaundice, renal failure, pneumonitis, acute respiratory distress syndrome (ARDS), septic shock, myocarditis and meningoencephalitis are various complications known with this disease. Rapid defervescence after antibiotic is so characteristic that it is used as a diagnostic test for *R. tsutsugamushi*. Treatment with oral antibiotics can be undertaken in mild cases however injectable treatment is recommended for seriously ill patients.

Prevention

- No effective vaccine is available to prevent scrub typhus.
- Reduce the risk of getting scrub typhus infection by avoiding contact with infected chiggers. When traveling to areas where scrub typhus is common, avoid areas with lots of vegetation and bush where chiggers may be found.
- The disease is best prevented by the use of personal protective measures including repellents, people entering an exposed area wear closed footwear such as boots with socks, long sleeved shirts and trousers. Exposed areas of skin and clothing itself should be treated with mite repellents.
- Repellents containing DEET, dusting sulphur, dimethyl phthalate or benzyl benzoate have been suggested as suitable agents.
- When sitting around or camping, groundcovers and tents with closed floors should be used.
- Control of the rodent and marsupial reservoirs may also assist to prevent chiggers coming into areas where humans are living and working.
- Prompt removal of clothing and thorough cleaning of skin and clothes with detergent after work or travel and at the end of the day can reduce the risk of infection.
- Treat clothing and gear with 0.5% permethrin or purchase permethrin-treated items. Permethrin kills chiggers and can be used to treat boots, clothing, and camping gear. Do NOT use permethrin products directly on skin.

Conclusion

Scrub typhus is a growing and re-emerging disease, which is grossly under-diagnosed in under developed/ developing countries due to its non-specific clinical presentation, limited awareness, and low index of suspicion among clinicians and lack of diagnostic facilities, it should be differentially diagnosed from typhoid, malaria, dengue, leptospirosis and meningococcal disease and HIV. Early diagnosis and prompt treatment is essential to prevent severe complications. Diagnostic tools such as blood tests and immunological techniques can be used to confirm the disease. Antibiotics are most effective in the early stages of the disease. Scrub typhus should be treated with the antibiotic doxycycline which may be lifesaving when clinical suspicion is high. It is important to inform the public about the risk factors and preventive measures associated with the disease.



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