

Rickettsial Zoonosis with Particular Reference to Scrub Typhus: A Review Paper

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Summary

Rickettsiae comprise a group of microorganisms that phylogenetically occupy a position between bacteria and viruses. They are obligate intracellular gram-negative coccobacillary forms that multiply within eukaryotic cells. A general characteristic of rickettsiae is that mammals and arthropods are natural hosts. Scrub typhus is zoonotic rickettsiosis transmitted to humans through the bite of trombiculid mites. *Orientia tsutsugamushi* is the causative agent for scrub typhus and humans are accidental hosts and become infected when they are bitten by chiggers infected with the agent. The agent multiply at the inoculation site with the formation of a papule that ulcerates and becomes necrotic, evolving into an eschar, with regional lymphadenopathy that progress to generalized lymphadenopathy within a few days. Scrub typhus may be diagnosed in the laboratory by isolation of the organism; serology and molecular diagnosis (PCR). Tetracycline and Chloramphenicol are proven therapy for the rickettsial diseases. The disease can be prevented by the use of personal protective measures including repellents, people entering an exposed area should wear closed in footwear such as boots with socks, and long trousers.

Keywords: Rickettsiae, Scrub typhus

Introduction

Rickettsiae occupy a position between bacteria and viruses (Sanjay, 2012). They require other living cells for growth (like viruses) but (like bacteria) use oxygen, have metabolic enzymes and cell walls, and are susceptible to antibiotics. *Rickettsiae* cause a series of diseases named for the American pathologist Howard Ricketts who discovered that ticks spread Rocky Mountain spotted fever and then isolated the microorganism responsible for Rocky Mountain spotted fever, typhus, trench fever and other similar conditions from the infecting insects (<http://www.medterms.com/script/main/art.asp?articlekey=5368>).

A general characteristic of *rickettsiae* is that mammals and arthropods are natural hosts. Eighteen rickettsioses, caused by organisms within the genus of *rickettsiae*, are recognized and can be divided into the following 3 biogroups (Sanjay, 2012): Typhus group: causing classical epidemic typhus caused by *Rickettsia prowazekii* and *Rickettsia typhi* transmitted by human body louse and rat flea respectively. Spotted fever group: containing a large number of species *Rickettsia rickettsii*, *Rickettsia conorii* etc. transmitted from rodents and other animals by ticks (except *Rickettsia akari*) Rocky Mountain spotted fever is prototype. Scrub typhus: caused by *Orientia tsutsugamushi*.

Scrub typhus is zoonotic rickettsiosis transmitted to humans through the bite of (Kawamura *et al.*, 1995). It has different names called Scrub typhus, tsutsugamushi fever, and mite-borne typhus fever (<http://www.aabb.org/resources/bct/eid/Documents/178s.pdf>).

Humans are accidental hosts and become infected when they are bitten by chiggers infected with *O. tsutsugamushi*. *Trombiculid* mites are the only reservoirs of *O. tsutsugamushi*, which can be transmitted transstadially (from larva to nymph to adult) and trans-ovarially (from the female to next generations); vertebrate hosts provide chiggers with food resources, but are of little importance in the transmission of *O. tsutsugamushi* (Kawamura *et al.*, 1995).

Etiology

The genus *Rickettsia* is included in the bacterial tribe *Rickettsiae*, family *Rickettsiaceae*, and order *Rickettsiales*. They are obligate intracellular gram-negative coccobacillary forms that multiply within eukaryotic cells. *Rickettsiae* do not stain well with Gram stain, but they take on a characteristic red color when stained by the Giemsa stain. They have typical gram-negative cell walls and lack flagella. Their genome is very small, composed of 1-1.5 million bases (Janani, 2012).

Scrub typhus was known in Japanese folklore to be associated with the jungle mite or chigger which was named “dangerous bug” (*tsutsugamushi*) (Sanjay, 2012). *Orientia tsutsugamushi* (ex *Rickettsia tsutsugamushi*) is the causative agent. It is a strictly intracellular bacterium classified in the alpha sub-division of Proteobacteria. Previously classified in the *Rickettsia* genus, it was reclassified due to its specific phylogenetic classification and phenotypic characteristics. Although it has a Gram negative type cell wall, this bacterium is poorly stained with the gram stain. It is stained with the Giemsa stain but not the Giemenez stain (Kawamura *et al.*, 1995).

It differs from the other members in its genetic makeup and in the composition of its cell wall structure since it lacks lipopolysaccharide and peptidoglycan (cd alert) and the most striking difference is in the structure

of the outer envelope; as revealed by electron microscopy, the outer leaflet of the cell wall of *R. tsutsugamushi* is considerably thicker than the inner leaflet, while the opposite is true of the other Rickettsia species (Silverman and Wisseman, 1978).

It is endowed with a major surface protein (56kDa) and some minor surface protein (110, 80, 46, 43, 39, 35, 25 and 25kDa). There are considerable differences in virulence and antigen composition among individual strains of *O.tsutsugamushi*. It has many serotypes: Karp, Gillian, Kato and Kawazaki(NCDC, 2009).

Transmission

Scrub typhus is transmitted by the mite *Leptotrombidium deliense*. The vector mites inhabit sharply demarcated areas in the soil where the microecosystem is favorable (mite islands). Human beings are infected when they trespass into these mite islands and are bitten by the mite larvae (chiggers). The mite feeds on the serum of warm blooded animals only once during its cycle of development, and adult mites do not feed on man. The microbes are transmitted transovarially in mites (NCDC,2009).

Once the chiggers have grasped a passing host, they prefer to feed near vulnerable areas of skin. This is usually where the skin is thin, tender or wrinkled. Chiggers also like areas where 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 large numbers of the *R. tsutsugamushi* organisms are found in the salivary glands of the chigger, they are injected into its host when it feeds (Devine, 2003). After feeding, the engorged chigger will drop off its host, burrow into the ground and transform into the more mature nymphal version of the mite. (Devine, 2003).

Clinical signs

The bacteria multiply at the inoculation site with the formation of a papule that ulcerates and becomes necrotic, evolving into an eschar, with regional lymphadenopathy that progress to generalized lymphadenopathy within a few days. Before symptoms develop, patients are rickettsemic (Sandip, 2010). Other specific clinical signs are: abrupt onset of febrile illness; headache; myalgia; sweats; conjunctival infection; lymphadenopathy; mental changes (cognitive dysfunction to delirium and coma); scar develops at the site of mite bite; hepatomegaly; splenomegaly; cough; leukopenia/lymphopenia and thrombocytopenia. (<http://www.aabb.org/resources/bct/eid/Documents/178s.pdf>).

Diagnosis

Diagnosis of scrub typhus relies on a network of epidemio-clinical data, including fever, headache, skin rash and scar occurring in patients in rural and endemic areas. Scrub typhus may be diagnosed in the laboratory by isolation of the organism, serology and molecular diagnosis (PCR)(NCDC, 2009).

Epidemiology

Scrub typhus is endemic in northern Japan, Southeast Asia, Western Pacific Islands, Eastern Australia, China, Maritime areas and several parts of south-central Russia, India, and Sri Lanka. More than 1 million cases occur annually (Marina and Gregory, 2014).

Localized, rural foci of risk are recognized where the vector (larval stages of *trombiculid* mites, referred to as chiggers) occurs and where natural environments are disturbed, as well as in rice paddies, atolls, and plantations. Disease prevalence is stable in endemic areas(<http://www.aabb.org/resources/bct/eid/Documents/178s.pdf>). Most travel-acquired cases of scrub typhus occur during visits to rural areas in endemic countries for activities such as camping, hiking, or rafting, but urban cases have also been described (NCDC, 2009). It affects people of all ages and even though scrub typhus in pregnancy is uncommon, it is associated with increased foetal loss, preterm delivery, and small for gestational age infants(Amy and Prithwis, 2013). Residents of endemic areas, military personnel, and tourists are at risk populations for the disease(<http://www.aabb.org/resources/bct/eid/Documents/178s.pdf>).

Scrub typhus normally occurs in a range of mammals, particularly field mice and rodents. The *L. deliense* groups of vector mites are widely distributed all over the country coexisting primarily with rodents and other small mammals. On the body of small mammalian hosts, the chiggers attach in clusters on the tragus of the ear, the belly and on the thighs. The *Leptotrombidium* mites, on the rat host, may appear orange or pink. The typical vector *L. deliense* is generally found associated with either established forest vegetation or secondary vegetation after clearance of forest areas. This species is generally abundant on grasses and herbs where bushes are scarce (NCDC,2009).

Treatment

Tetracycline and chloramphenicol are proven therapy for the rickettsial diseases. Doxycycline in a dose of 100

mg twice daily for 7-15 days or Chloramphenicol 500 mg four times a day PO for 7-15 days (for children 150 mg/kg/day for 5 days) is recommended. Tetracycline may cause discoloration of teeth, hypoplasia of the enamel, and depression of skeletal growth in children; the extent of discoloration is directly related to the number of courses of tetracycline therapy received. Therefore, tetracycline should not be used for children under 8 years of age and for pregnant women (NCDC,2009). Azithromycin is the recommended drug in pregnancy and for children. Rifampicin is effective in areas where doxycycline resistant is present (Rajapakse *et al.*, 2011).

Prevention and control

There are no effective vaccines for scrub typhus due to enormous antigenic variation in *Orientia tsutsugamushi* strains and immunity to one strain does not confer immunity to another (Ritesh, 2010). The mite vectors of scrub typhus are especially amenable to control because they are often found in distinct areas (Typhus Island). These foci can be eliminated by treating the ground and vegetation with residual insecticides, reducing rodent populations, and destroying limited amounts of local vegetation (NCDC, 2009).

Other specific protection measures that can be practiced are wearing protective clothes, using insect repellents containing 5% emulsion of dimethylphthalate, dibutylphthalate, benzyl benzoate diethyltoluamide, avoiding sitting or lying on bare ground or grass and clearing of vegetation and chemical treatment of grass (Ritesh, 2010).

Conclusion

Scrub typhus is a zoonotic disease in which humans are infected accidentally by biting chiggers infected by *O.tsutsugamushi*. It is manifested clinically by high fever, intense generalized headache, diffuse myalgias, and in many patients, rash and an eschar at the site of the chigger bite. Since there is no effective vaccine for the disease other preventive measures have to be taken seriously in endemic areas.

The disease can be prevented by the use of personal protective measures including repellents, people entering an exposed area wear closed in footwear such as boots with socks, and long trousers. Exposed areas of skin and clothing itself should be treated with mite repellents.

Awareness creation is the best approach for preventing the disease by educating or informing at risk population to take measures like avoiding unnecessary visits to bush areas, wearing protective clothing such as long-sleeved shirts and pants, and applying insect repellents to exposed skin to prevent chigger bites when visiting bush areas.

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