SCRUB TYPHUS EMERGING THREAT

EPIDEMIOLOGY

Epidemiology of Scrub Typhus

Dinesh Kumar, D.J. Raina, Sanjana Gupta, Ana Angurana*

Introduction

Scrub typhus belongs to group of Ricketssial diseases belonging to family Rickettsiaeceae comprising of three genera - Rickettsia, Orientia and Ehrlichia. These organisms are primarily parasites of arthropods such as lice, fleas, ticks and mites. The rickettsial diseases commonly found in India include Scrub typhus, Murine flea borne typhus, Indian tick typhus and Q fever. Q fever and trench fever have been excluded because the former is not arthropod borne and the latter is not an obligate intracellular parasite. Scrub typhus is the commonest and most widespread zoonotic disease among the diseases caused by rickettsial organisms both in India and globally.

Scrub typhus is an acute, febrile, infectious illness that is caused by Orientia (Rickettsia) tsutsugamushi. It is also known as tsutsugamushi disease (from tsutsuga meaning dangerous and mushi meaning insect or mite). Scrub typhus was first described from Japan in 1899 (1) where it was found to be transmitted by mites. Scrub typhus differs from other members in its genetic make up and therefore there are considerable differences in virulence among individual strains of *Orientia tsutsugamushi*. The Rickettsial diseases remain grossly underdiagnosed as routine laboratory tests are unlikely to be diagnostic and presentation non specific. Ricketssial diseases are infact aggravated by sulfonamides, a group of commonly used antibiotics. The widespread use of beta-lactam antimicrobial drugs in some Asian Countries coincides with an increased in the prevalence of scrub typhus (2). One typical feature of the scrub typhus, the punched-out ulcer covered with a blackened eschar indicating the location of the mite bite is usually not looked for because of a preset mind in favour of the bacterial origin.

Problem Statement and distribution

An estimated one billion people are at risk for scrub typhus and an estimated one million cases occur annually (3). Mortality rates in untreated patients range from 0-30% depending on the geographic area and the rickettsial strain and the time of intervention.Deaths usually occur from the primary infection or from secondary complications like pneumonitis, ARDS, encephalitis, circulatory faliure.

The Scrub typhus appears particularly to be distributed in the Tsutsugamushi triangle. The distribution is over a very wide area of 13 million Km square bound by Japan in the east, through China, the Philippines, tropical Australia in thesouth and west through India, Pakistan, possibly to Tibet to Afghanistan and southern parts of USSR in the north. The distribution of the disease closely follows the distribution of Rattus rattus. (4). The vector of scrub typhus is present in most countries of the South-East Asia Region and it is endemic in certain geographical regions of India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka and Thailand.

Indian Situation

Scrub typhus is prevalent in many parts of India but specific data are not available .There have been outbreaks in areas located in the sub-Himalayan belt, from Jammu to Nagaland. There were reports of scrub typhus outbreaks in Himachal Pradesh, Sikkim and Darjeeling (West Bengal) during 2003-2004 and 2007.Scrub typhus is considered a reemerging infectious disease in India (5).

Epidemiological Determinants

Agent Factors

(a) ***Agent***: Rickettsiae are small organisms (0.3 to0.5 x 0.8 to 1.5 micrometer), gram negative bacterium of family Rickettsiacea adapted to obligate intracellular parasitism. They are pleomorphic, appearing either as short rods, or as cocci and occur singly, in pairs, in short chains or filaments. They stain blue with Giemsa's stain and are readily visible under microscope. They grow readily in the yolk sac of the embryonated egg. Rickettsial growth isenhanced by the presence of sulfonamides.The causative agent of scrub typhus is Rickettsia tsutsugamushi (*Orienta tsutsugamushi)*. There are several serologically distinct strains. It is widespread throughout southern and eastern Asia, northern Australia, Indonesia, and the Pacific islands and is transmitted from infected rodents to humans by mites of the family Trombiculidae (6). *O. tsutsugamushi* includes heterogeneous strains classified in five major serotypes: Boryon, Gilliam, Karp, Kato and Kawazaki (7).The causative agent for Scrub Typhus can be cultivated on L929 cells.(8)

From the PG Deptt. of Community Medicine,GMC, Jammu & *Deptt. of Microbiology, School of Biotechnology, Jammu University
Correspondence to : Dr Dinesh Kumar, Assistant Professor, PG Deptt. of Community Medicine, GMC, Jammu J&K- India.

(b) ***Reservior***: The true reservoir of infection is the trombiculid mite (Leptotrombidium delinese and L. akamushi). Chigger mites act as the primary reservoirs for O.tsutsugamushi. Once they are infected in nature by feeding on the body fluid of small mammals, including the rodents, they maintain the infection throughout their life stages and, as adults, pass the infection on to their eggs in a process called transovarial transmission. Similarly, the infection passes from the egg to the larva or adult in a process called transtadial transmission. Thus the mite populations can autonomously maintain their infectivity over long periods of time. It is the larva (chigger) that feed on vertebrate hosts and picks up the rickettsiae. The larval stage serves both as a reservoir, through ovarian transmission, and as a vector for infecting humans and rodents.

(c) **Mode of Transmision:** Scrub typhus is transmitted to humans and rodents by some species of trombiculid mites. The mite is very small (0.2 - 0.4mm) and can only be seen through a microscope or magnifying glass. Humans acquire the disease from the bite of an infected chigger (9,10). The bite of the mite leaves a characteristic black eschar that is useful to the physicians for making the diagnosis.The adult mites have a four-stage lifecycle: egg, larva, nymph and adult. The larva (chigger) is the only stage that can transmit the disease to humans and other vertebrates, since the other life stages (nymph and adult) do not feed on vertebrate animals. Both the nymph and the adult are free-living in the soil. The disease is transmitted from mites to 'rats and mice' and the mites in their larval stage contract the disease organism by biting these rodents. Man is an accidental host. The disease is not directly transmitted from person to person.

Host Factors

Usually it is an occupational disease in rural workers and can occur in all the age groups, particularly adults involved in agriculture and forest occupations and males coming in contact with the chiggers. Soldiers living in temporary camps are also predisposed.

Environmental Factors

This is found in areas with a suitable climate, plenty of moisture and scrub vegetation. Wars predispose to the scrub typhus. Soldiers are exposed to chigger bites in forest areas during the military operation. It caused thousands of cases in the far east, Myanmar and Sri Lanka during IInd world war. It is estimated that 36,000 soldiers were either incapacitated or died during World War II (11,12). The overall mortality varied from 7%to 9%, second only to malaria among infectious diseases. Areas like forest clearings, riverbanks, and grassy regions provide optimal conditions for the infected mites to thrive.

Season : It occurs more frequently during the rainy season. However Outbreaks of scrub typhus are reported in southern India during the cooler months of the year (13)

Incubation Period: Usually 10 to 12 days; varies from 6 to 21 days

Race: all races are affected by scrub typhus

Sex: Both men and women ar eequally affected by scrub typhus

Age: People of all ages are affected by it.

Control measures

(a) ***Chemoprophylaxis***

It has been shown that a single oral dose of chloramphenicol or tetracycline given every five days for a total of 35 days, actually prevents against scrub typhus. This procedure is recommended under special circumstances in certain areas where the disease is endemic (14).

(b) ***Vaccine***

There are no effective vaccines for scrub typhus. It is now known that there isenormous antigenic variation in Orientia tsutsugamushi strains, and immunity to one strain does not confer immunity to another (15). Any scrub typhus vaccine should give protection to all the strains present locally, in order to give an acceptable level of protection. A vaccine developed for one locality may not be protective in another locality, because of antigenic variation. This complexity continues to hamper efforts to produce a viable vaccine (16). The first known batch of scrub typhus vaccine actually used to inoculate human subjects was dispatched to India for use by the Allied Land Forces, South-East Asia Command, in June 1945 (17).

(c) ***Case Identification and Treatment***

Case detection and management by health care personnel is important. Tetracycline is the drug of choice. With proper therapy the mortality is nil. A Cochrane review of therapy for scrub typhus involving four trials, which demonstrated no difference between the use of doxycycline and tetracycline, or between tetracycline and chloramphenicol in the management of scrub typhus (18)

(d) ***Vector Control***

Clearing the vegetation where rats and mice live; application of insecticides such as lindane or chlordane to ground and vegetation. The resistance of rodents to various rodenticides needs also to be monitored.

(e) ***Personal Prophylaxis***

Application of mite repellents (diethyltoluamide) to exposed skin surfaces and impregnating clothes and blankets with miticial chemicals (benzyl benzoate) are helpful. One should avoid sitting or lying on the grass or ground without a sheet or cover.Clearing of vegetation and chemical treatment of the soil may help .Digging out a few

inches of soil before laying a temporary camp can also prevent the contraction of disease from the chigger bites.

(e) ***Health Education***

Health education of the people regarding the modes of transmission and personal prophylaxis is of paramount importance and can go a long way in prevention of the disease.

(f) ***Rodent Control***

Rodent control is a multidimensional activity that requires multisectoral cooperation. Different control strategies such as trapping, poisoning and use of natural predators are in practice. Habitat modification makes areas less attractive to rodents thereby preventing new populations from recolonizing the habitat. Rats and mice may be encouraged if weeds grow around buildings .Good sanitation in and around buildings creates an environment that is less suited for rodent populations. Repeated increase in rodent population even after the use of poisons also indicates that habitat modification is needed.

Research And Training On Scrub Typhus In The South-East Asia Region

The Armed Forces Research Institute of Medical Sciences (AFRIMS) Bangkok, Thailand is the WHO Collaborating Centre (CC) for Emerging Diseases that is providing technical support for outbreak investigation and capacity building for diagnosis and control of scrub typhus. The Department of Entomology, AFRIMS is the only laboratory in the world that has the ability to grow and colonize scrub typhus-infected Leptotrombidium mites, the vector of O. tsutsugamushi, the Scrub Typhus microorganism.

Conclusion

Keeping these epidemiological determinants into mind a comprehensives preventive and therapeutic approach at all health care levels is need of hour to reduce morality and related morbidity of scrub typhus, a reemerging threat.

References

1. Scrub Typhus. Available at: http://www.searo.who.int/LinkFiles/CDS_faq_Scrub_Typhus.pdf.[Cited on 2009, Dec 25]
2. Seong S, Choi M, Kim I. "Orientia tsutsugamushi infection: overview and immune responses". *Microbes & Infection* 2001; 3 (1): 11-21.
2. Scrub Typhus. Available at: http://www.searo.who.int/LinkFiles/CDS_faq_Scrub_Typhus.pdf [Cited on 2009, Dec 25]
3. Silpapojakul K. Scrub typhus in the Western Pacific region. *Ann Acad Med Singapore* 1997; 26:794-800.
4. World Health Organization Technical Report Series No. 553 Ecology and control of Rodents of Public Health Importance. Report of a WHO Scientific Group.
5. Padbidri VS, Gupta NP. Rickettsiosis in India: A review. *J Indian Med Assoc* 1978; 71:104-07.
6. Scrub Typhus. Available at:http://medical-dictionary.thefreedictionary.com/Orientia+tsutsugamushi. [Cited on 2009, Dec 25]
7. Tamura A, Ohashi N, Urakami H, Miyamura S. Classification of Rickettsia tsutsugamushi in a new genus, Orientia gen nov, as Orientia tsutsugamushi comb. *Int J Syst Bacteriol* 1995; 45: 589-91.
8.. Scrub Typhus. Available at: http://ifr48.timone.univ-mrs.fr/Fiches/Anglais/Otsu_en.pdf. [Cited on 2009, Dec 25]
9. Lerdthusnee K, Khlaimanee N, Monkanna T, *et al*. Efficiency of Leptotrombidium Chiggers at Transmitting Orientia tsutsugamushi to Laboratory Mice. *J Med EntomoL* 2002; 39 (3):521-25.
10. Lerdthusnee K, Khuntirat B, Leepitakrat W, *et al*. Scrub Typhus: Vector competence of Leptotrombidium chiangraiensis chiggers and transmission efficacy & isolation of Orientia tsutsugamushi. *Ann NY Acad Sci* 2003; 990:25-35.
11. Beran GW. Scrub typhus in: Handbook of Zoonoses. Second Edition. Section A: Bacterial, Rickettsial, Chlamydial and Mycotic.1994.pp.663-68.
12. McCallum JE. Military Medicine: From Ancient Times to the 21st Century History, 2008.pp.383.
13. Mathai E, Rolain JM, Verghese GM, *et al*. Outbreak of scrub typhus in southern India during the cooler months. *Ann N Y Acad Sci* 2003; 990:359-64.
14. Frequently asked questions, Scrub Typhus. World Health Organization, Regional Office for South East Asi 2010.pp.12.
15. Kang JS, Chang WH. "Antigenic relationship among the eight prototype and new serotype strains of Orientia tsutsugamushi revealed by monoclonal antibodies". *Microbiol Immunol* 1999; 43 (3): 229-34.
16. Kelly DJ, Fuerst PA, Ching W-M, Richards AL. "Scrub typhus: The geographic distribution of phenotypic and genotypic variants of Orientia tsutsugamushi". *Clinical Infectious Diseases* 2009; 48 (s3): S203-S230.
17. Kelly *et al* .The Past & Present Threat of Rickettsial Diseases to Military Medicine & International Public Health. *Clinical Infectious Diseases* 2002; 34 (4):15.
18 WHO Technical Report Series (11 December, 2009).The 17th Expert Committee on The Selection and Useof Essential Medicines, 23 to 27 March, 2009