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Report of Sporadic Cases of Scrub Typhus - A Threat to Re-Emergence in Assam, India

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A B S T R A C T

China-Burma-India field party of the United States of America Typhus Commission has reported their observations on scrub typhus in Assam and Burma in 1946. Recently, sporadic cases have been reported from areas of Assam covered with scrub forests. Here we report few cases of scrub typhus presented with acute febrile illness associated with typical skin lesion of scrub typhus. Three patients with acute febrile illness reporting to the local hospital of Dima Hasao district (old name North Cachar hills) of Assam were diagnosed as scrub typhus cases on the basis of clinical features and positive Weil-Felix test with OXK titre of 1:320 or more. Clinical features of the cases included fever, headache, body ache, malaise, difficulty in breathing and presence of eschar. None of the cases presented with rash and multisystem complications. All the cases showed a titre of more than 1:320 in Weil-Felix test and responded well to intravenous Cefotaxime and oral Doxycycline. Presence of scrub forests and the vectors in Assam leads to sporadic occurrence of the disease and can be a threat to re-emergence of the disease in Assam.

Introduction

Scrub Typhus is a Rickettsial disease caused by the bite of an infected larva of mite or "chiggers" belonging to the family *Trombiculidae*, genus and subgenus *Leptotrombidium*. *Orientia tsutsugamushi*, the causative agent of scrub typhus is strictly intracellular and prevalent in many parts of Asia including India. Antigenically it is different from other *Rickettsia*. There are at least eight serotypes known and infection with one strain does not provide immunity against infection by others. The disease has occurred amongst troops during World War II in Assam and West Bengal and in 1965 Indo-Pak war in the Jammu - Sialkot sectors. Some cases were also reported during the 1971 Indo-Pak conflict from the northwestern border. There was a resurgence of the disease in 1990 (Singh *et al*., 1992).

Scrub typhus is a public health problem in Asia, where about one million new cases are identified annually and one billion people are at risk of acquiring this disease (Levine, 1946). 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, Acute Respiratory Distress Syndrome (ARDS), encephalitis, circulatory failure (Kumar *et al*., 2010). During the past few years, the number of patients with rickettsial infection and scrub

typhus has increased, especially during the cooler months (Mathai *et al*., 2003). In addition, reports of infection are becoming increasingly common in travelers returning from Asia to their home countries (Silpapojakul, 1997; Watt *et al*., 1994). After the report of American commission for scrub typhus, no reported literature is available from this part of the country describing the magnitude of the problem. Here we report few cases of scrub typhus presenting with acute febrile episode associated with typical skin lesions from Dima Hasao district of Assam.

Case 1

A village women, 40 years old was admitted in the local hospital in the month of June with high fever, generalized body ache, headache and difficulty in breathing of four days duration. On examination, her body temperature was 102^0F and the patient was toxic. There was a black eschar on the left upper arm associated with burning sensation over the area. (Figure 1) Her respiratory, cardiovascular systems were normal.

There was no lymphadenopathy and hepatosplenomegaly. Routine blood, urine and stool examinations were normal. Her X-Ray chest was also normal. Liver function tests were normal. Widal test and tests for malarial parasites were found to be negative. Weil Felix test was done using test kit PROGEN (TULIP Diagnostics (P) Ltd, Verna, Goa) and the OXK titre was found to be 320. The results of the Weil Felix test are depicted in table 1. The patient was treated with intravenous Derriphylline, Cefotaxime (1gm I/V twice daily for 5 days) and Doxycycline (100mg twice daily orally for 6days). The patient recovered from illness after 7 days of treatment and discharged from the hospital.

Case 2

Another female patient, 20 years old also presented in the month of June with high fever, generalized body ache, headache, weakness and a black spot on the inner aspect of the left upper arm of six days duration. On examination, a black eschar was found on the left upper arm (Figure 2). Her respiratory, cardiovascular systems were normal.

There was no lymphadenopathy and hepatosplenomegaly. Routine blood, urine and stool examinations were normal. Her X-Ray chest was also normal. Liver function tests were normal Widal test and tests for malarial parasites were found to be negative. Weil Felix test was found to be positive with OXK titre of 320.The patient was treated with Cefotaxime (1gm I/V twice daily for 5 days) and Doxycycline (100mg twice daily orally for 6days).The patient recovered from illness after 7 days of treatment and discharged from the hospital.

Case 3

A 64 years old women was admitted in the local hospital with complaints of sudden onset fever with chill, malaise, headache, myalgia, difficulty in breathing of 10 days duration. There was no history of vomiting, cough, neck rigidity or rash. Routine blood, urine and stool examinations were normal. Her X-Ray chest was also normal. Liver function tests were normal Widal test and tests for malarial parasites were found to be negative. Weil Felix test was done and the OXK titre was found to be 640. The patient was treated with Cefotaxime (1gm I/V twice daily for 5 days) and Doxycycline (100mg twice daily orally for 6days). The patient recovered from illness after 7 days of treatment and discharged from the hospital.

Results and Discussion

Scrub typhus occurs over a wide area of eastern Asia and the western Pacific region (Saah, 2000). Rickettsial infections are re-emerging and amongst them, scrub typhus is prevalent throughout the world. It appears that the disease is active over a very wide area bound by Japan in the east, through China, the Philippines, tropical Australia in the south and west through India, Pakistan, possibly to Tibet, Afghanistan, and southern parts of Russia in the north (WHO, 1981; Traub *et al*., 1974). During the decades 1970-90, scrub typhus was reported in many countries including China, Japan, India, Indonesia, Malaysia, Thailand and Vietnam. The seropositivity in the general population varied from 2% in India to 40% in Malaysia (WHO, 1979). Recent reports from India and other neighboring countries suggest that there is a resurgence of scrub typhus infection caused by *Orientia tsutsugamushi* in these parts of the world and that the resurgence is associated with considerable morbidity and mortality. In view of low index of suspicion, nonspecific signs and symptoms, and absence of widely available sensitive and specific diagnostic test, these infections are difficult to diagnose.

The disease in humans results after the introduction of *O. tsutsugamushi* through the skin by the bite of a larval-stage (chigger) trombiculid mite (Joklik *et al*., 1992). 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. These mites have a four-stage life cycle (egg, larva, nymph, and adult). The larva feeds only once on a vertebrate. After a blood meal, the chigger detaches and matures into a nymph and subsequently into an adult. Both the nymph and the adult are free living in the soil. Normally, the chiggers feed on small mammals or ground-feeding birds. Humans accidentally enter the natural cycle of infection. Person-to-person transmission of infection has not been reported. Periods of epidemics are influenced by the activities of the infected mite. Therefore, they may be influenced by temperature and humidity. Transmission occurs throughout the year in tropical areas. However, in more temperate zones this is not the case (Watt *et al*., 2003). The severity of the symptoms varies widely, depending on the susceptibility of the host, the virulence of the bacterial strain, or both (Saah, 2000).

The cases with typical clinical presentation of scrub typhus were seen only in pre antibiotic era (Doherty, 1956). With early usage of antibiotics all features of the disease are not likely to be encountered. Serious complications of scrub typhus are not uncommon and may be fatal. Scrub typhus is grossly under-diagnosed in India due to its non specific clinical presentation, limited awareness and low index of suspicion among clinicians, and lack of diagnostic facilities. Hence, it is necessary to maintain a high index of clinical suspicion. In India, the rash is generally not seen (Mehta *et al*., 1993). In the present report also the cases presented with acute febrile episodes along with eschar without any rash or lymphadenopathy or any other signs and symptoms. The sites of the eschars were the inner aspect of the left upper arm where the skin surfaces meet or the cloths bind. But more commonly eschars are found in the lower parts of the bodies of the patients as the mites are also found close to the ground. Another interesting feature is that all the patients were female and is undoubtedly due to similar occupational exposure of both sexes in fields and farms where vectors are numerous. In the hilly areas of Assam, people of both sexes are involved in agriculture and forest occupation and hence frequently come in contact with the chiggers. The diagnosis of a rickettsial illness has most often been confirmed by serological tests. The facility for

specific gold standard techniques like the immunofluorescence antibody test (IFA), the indirect imunoperoxidase (IP) test, ELISA are not available in our laboratory and the isolation of the organisms in animals or cell culture is also limited by the lack of containment facility as well as the lack of expertise in handling these high risk group pathogens (Batra, 2007).

Table.1 Results of the Weil Felix test of the cases

Serial No	OX 2 titre	OX 19 titre	OX K titre
Case 1	1:< 20	1:< 20	1:320
Case 2	1:< 20	1:20	1:320
Case 3	1:< 20	1:< 20	1:640

Fig.1 Showing eschar on the left upper arm

Hence, diagnosis of our cases was done on the basis of Weil Felix test. Weil-Felix test has shown reasonably high specificity but a low sensitivity for the diagnosis of Rocky mountain spotted fever, Mediterranean boutonneuse fever, murine typhus, epidemic typhus and scrub typhus (Batra, 2007). A four-fold rise in agglutinin titres in paired sera is diagnostic for infection with these febrile agents. However, with a single serum sample available, the test is suggestive of infection only at a high cut-off titre (> 1: 320) at which the positive predictive value and the specificity is reliable. In the present report, as only single serum sample was available, the above criteria were followed for diagnosis of the cases. The present sporadic cases of scrub typhus when viewed with the earlier occurrence of cases in 1946 may serve as a warning to us that the people of the scrub typhus prone areas need to take preventive measures. Climate of Assam is sub tropical with mean annual rainfall varying from 1,500 mm to 3,750 mm and the mean annual temperature is between 5°C to 32°C with plenty of moisture. According to the report of Forest Survey of India 2009, the extent of scrub vegetation is 176 sq.km (Forest Survey of India, 2009). Hence, Assam has an environment very much suitable for scrub typhus. In view of these epidemiological determinants, a comprehensives preventive and therapeutic approach at all health care level is essential to reduce morality and

related morbidity of scrub typhus. The reported literatures show that, scrub typhus is a re-emerging infectious disease in India and this emphasizes the need for prospective studies to design effective control measures.

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