Clinical and laboratory manifestations of scrub typhus: A study from a tertiary care hospital in Manipur

Smeeta Huidrom[1,*], L. Kokindro Singh[2]

[1]Demonstrator, [2]Assistant Professor, Dept. of Microbiology, Jawaharlal Nehru Institute of Medical Sciences, Imphal, Manipur

***Corresponding Author:**
Email: srl.manipur.jnmc@gmail.com

Abstract

Introduction: *Orientia tsutsugamushi*, are obligate intracellular Gram-negative coccobacilli belonging to the *rickettsial* family. Transmitted by the bite of infected mites, they cause Scrub typhus - a zoonotic febrile illness, which if not diagnosed is associated with a fatal outcome. It is often under-diagnosed in India and has been attributed to its non-specific clinical presentation, relative lack of awareness of the disease among clinicians and the lack of diagnostic facilities. As in other parts of India, seasonal outbreaks have been reported since 2006 in Manipur too.

Materials and Method: Patients presenting with febrile illness and diagnosed as scrub typhus over a period of 18 months (January 2016 to May 2017) were studied to study their clinical features and laboratory investigations. A single step solid phase immunochromatographic assay which detects IgM, IgG and IgA antibodies against *O. tsutsugamushi* was used to make the diagnosis. All relevant data of the patients were retrieved from the case files.

Results: 24 (23.7%) patients of the 118 clinically suspected patients tested positive for Scrub typhus by serology. Fever, headache and myalgia were the most common symptoms followed by diarrhoea and vomiting. Elevated liver enzymes and serum bilirubin was observed in most of the patients. Eschar was seen in 6 (5%) cases. The cases were however observed to be not confined to the district of Bishenpur, from where previous seasonal outbreaks had been reported. All the patients responded quickly to Doxycycline.

Conclusion: Scrub typhus is being seen with regularity in the recent past and has often been described as a re-emerging rickettsial infection. Increased awareness coupled with high index of suspicion amongst treating doctors with good knowledge of epidemiology and laboratory investigations is needed for an early diagnosis. Cases can be diagnosed using a one step immune-chromatographic assay, a relatively sensitive method and specific test.

Keywords: Pyrexia, Rickettsia, Eschar, Immune-chromatographic, Doxycycline.

Introduction

Scrub typhus presents as a febrile illness. It is a rickettsial infection caused by caused by *Orientia tsutsugamushi*. Epidemiologically, it is endemic to eastern Asia and the western Pacific regions. Scrub typhus is a zoonosis and is a widespread disease in Asia and the Pacific Islands. It also occurs in Japan, South Korea, Nepal, Northern Pakistan, South China, Papua New Guinea, and the Australian states of Queensland and Northern New South Wales. Many cases surface in Europe and other parts of World, where this disease is not endemic, causing a serious problem in their diagnosis and treatment. The traditional belief was that Scrub typhus as a disease had disappeared from India but this has been changed by the many outbreaks which have been reported in the recent past from many parts of the country.[1,2,3]

In Manipur, seasonal outbreaks have been reported, especially in the months of May to October, with regularity in the past few years, since 2006, when the first such outbreak came into the news, when it was described as a mysterious fatal febrile illness. It was also reported that skin lesions were associated.[4,5]

The non-specific clinical presentation of Scrub typhus makes it usually confusable with other febrile illnesses. The differential diagnosis, based on its clinical presentation includes other febrile illnesses like Typhoid, Malaria, Leptospirosis, and Dengue.[1,3,6] This is perhaps attributable to a relative lack of awareness amongst clinicians and is further compounded by lack of diagnostic facilities in many centres.[2,6,7]

Failure to make an early diagnosis leads to many complications and even to death in morbid patients if correct therapy is not instituted early. Some of the complications which have been described are septic shock, acute respiratory distress and syndrome and multiple organ dysfunction.[1]

Weil-Felix tests, ELISA and PCR have been used for the diagnosis of Scrub typhus. Limited availability, high costs of the tests and lack of trained manpower have proved to be one of the reasons why tests for Scrub typhus have been relatively less accessible to patients.[1,5] Immune-fluorescence assay (IFA) is one of the relatively new techniques available for a serologic diagnosis of Scrub typhus.[1]

Materials and Method

As sporadic cases had been reported associated with a seasonal character limited to a certain geographic area in Manipur, the present study was undertaken to find out how many cases of febrile patients were clinically suspected and subsequently diagnosed as Scrub typhus in a tertiary care hospital. Clinical

features, laboratory investigations and clinical outcomes of the patients were analysed.

Standard Diagnostics (SD) Bioline Tsutsugamushi solid phase immunochromatographic assay (SD, Korea) – a one step immune-chromatographic assay which detects IgM, IgG and IgA antibodies against *O. tsutsugamushi*, in the serum, was used to make a diagnosis. Clinical findings and other relevant investigations data were retrieved from the case files of the serologically positive patients and studied.

Inclusion criteria were defined to include all febrile patients, clinically suspicious to be suffering from Scrub typhus, with or without eschar, during the study period January 2016 to May 2017.

Results

Of the 118 febrile patients included in the present study, 24 (20.3%) were serologically positive. The age range of the serologically positive patients were of a wide age range, with youngest being a 6 years old girl and oldest, a 67 years old woman.

Table 1 shows the sex distribution. There were 33.3% (8/24) females and 66.6% (16/24) males. All the patients were of rural background. None of them belonged to villages in and around Bishnupur district.

Table 1: Distribution of serologically positive patients' sex

Sex	Number	Percentage
Males	16/24	66.6
Females	8/24	33.3
Total	24	

Table 2 shows the signs and symptoms in these 24 cases. Patients presented with the chief complaints of fever, myalgia, cough, haemoptysis, breathlessness, and headache. 6 patients showed eschar.

Table 2: Presenting symptoms

Symptoms	Number	Percentage
Fever > 14 days	16	66.6
Cough	22	91.6
Breathlessness	20	83.3
Myalgia	24	100
Headache	24	100
Haemoptysis	8	33.3
Nausea/vomiting	10	41.6
Abdominal pain	10	41.6

Table 3 shows the laboratory investigations results. 66.6% (18/24) of the patients had normal total leucocyte count. 41.6% (10/24) had mild to moderate thrombocytopenia. 91.6% (22/24) of the patients had elevated bilirubin and liver enzyme levels in the serum. 41.6% (10/24) had mildly increased Serum creatinine levels (> 1.5 mg/dl). A single patient with raised protein levels in the CSF was noted.

Table 3: Laboratory investigations

Investigations	Number	Percentage
TC <4000/cu.mm	4/24	16.6
TC>11,000/cu.mm	4/24	41.6
Platelet < 1 lakh/cu.mm	10/24	41.6
Increased SGOT/SGPT	22/24	91.6
Increased Alkaline phosphatase	8/24	33.3
Increased bilirubin	22/24	91.6
Increased creatinine	10/24	41.6

Eschar was seen in 6 of the patients.

Table 4: Complications observed in the patients of Scrub typhus

Complications	Number	Percentage
ARDS	2/12	16.6
Shock	2/12	16.6
Meningitis	1/12	8.3
Renal failure	5/12	41.6
Bilirubin > 1.2 mg/dL	11/12	91.6
Thrombocytopenia	5/12	41.6
Lymphadenopathy	4/12	33.3

Discussion

Rickettsial infections or rickettsioses (also called typhus) are one of the major causes of acute febrile illness in the Asia-Pacific region. They are caused by obligate intracellular coccobacilli and belong to the family Rickettsiaceae. They infect humans through arthropod vectors.

Of the Rickettsioses, including the spotted fever group (SFG) and the typhus group, Scrub typhus is caused by *Orientia tsutsugamushi* (OT) (formerly *Rickettsia tsutsugamushi*). Scrub typhus, a zoonosis, derives its name from its association with the jungle mite or chigger which was named "dangerous bug" (tsutsugamushi) in Japanese folklore.

Scrub typhus has been a relatively hitherto unknown disease in India, although India comes under the described endemic zones in the world. The last few decades has however seen many outbreaks being reported from various places in India, as presenting with acute fever, skin rash, myalgia and other non-specific symptoms. One of the pathognomic features which has been described is a necrotic eschar at the inoculating site of the mite. Occurrence of eschar is however rare. South-East Asian patients and indigenous people of endemic areas commonly have a less severe illness, often without any rash or eschar.

The Standard Diagnostics (SD) BIOLINE Tsutsugamushi test is a solid phase, immunochromatographic assay, developed using the

major surface antigen 56 kDa of representative strains of *O. tsutsugamushi,* for the rapid qualitative detection of IgM, IgG or IgA antibodies to *Orientia tsutsugamushi* in human serum, plasma or blood. A sensitivity of 99%, specificity of 96% and serological agreement of 97.5% with immune-fluorescent assay has been described.

In the present study, patients were observed to most commonly present with fever with myalgia (100%), headache (100%) and cough with respiratory distress (91.6%). Other symptoms were diarrhoea, vomiting and abdominal pain. A few cases also had lymphadenopathy with hepato-splenomegaly. Only six patients had the characteristic eschar with skin rash, which is a diagnostic feature.

Majority of the patients, 16/24 (66.6%), serologically diagnosed with Scrub typhus, in the present study presented with fever of more than 14 days duration and were clinically labeled as cases of pyrexia of unknown origin. 10 (41.6%) patients presented with gastrointestinal symptoms viz. diarrhoea and vomiting. Gastrointestinal symptoms have been reported as a probable differentiating feature of Scrub typhus from similar infections like Leptospirosis and Dengue by Saleem et al.[3]

Many of the patients in the present study group had increased serum SGOT, SGPT and Bilirubin levels.

Majority of the patients in the present study group had deranged liver functions (raised AST, ALT, bilirubin).

Only five cases (41.6%) had increased Serum Creatinine levels.

Widal test showed maximum positivity (13.6%) among the scrub cases. This shows the possibility of production of cross reacting antibodies between the two pathogens.

One patient was Dengue positive (ELISA).

Cases of Scrub typhus have been reported primarily from the district of Bishenpur in Manipur.[4] In the present study none of the cases belonged to villages in and around Bishenpur, thus highlighting the point that the disease is not confined to the district.

The standard treatment of choice described for Scrub typhus is Doxycycline (200 mg/day). Other useful drugs are Chloramphenicol, Azithromycin and Rifampicin. The rapid resolution of fever after administration of Doxycycline is so characteristic that it has been described as a therapeutic test.

It was observed that all of the patients, in the study, subsequent to a serological diagnosis of Scrub typhus were prescribed Doxycycline and all of them responded dramatically with resolution of symptoms within 5 days.

The need for increasing awareness, amongst doctors, that Scrub typhus is an emerging rickettsial febrile illness, often seen in rural areas of Manipur, India, is shown by the current study. Clinician need to be made aware of the requirement of a high index of suspicion with the proper use of diagnostic methods to ensure that cases are not missed during diagnosis. Simple serological tests like the Standard Diagnostics (SD) Bioline Tsutsugamushi solid phase immunochromatographic assay (SD, Korea) are of aid in making a confident and correct diagnosis. Physicians should be sensitized more to the endemic nature of this disease and the utility of empiric treatment with Doxycycline to reduce the high mortality observed with the disease.

Conclusion

Scrub typhus, like in many parts of India, is an emerging endemic rickettsial infectious disease in Manipur, where it is often seen following a seasonal pattern. Patients usually present with unexplained pyrexia and other non-specific symptoms making a correct diagnosis difficult. The observation of deranged liver enzymes and increased serum bilirubin coupled with the presence of gastro-intestinal symptoms may help in the diagnosis. The presence of an eschar is pathognomic for Scrub typhus. The absence of an eschar to rule out Scrub typhus is of limited utility as it may be absent in patients belonging to endemic areas. Early diagnosis and treatment with appropriate antibiotics, especially Doxycycline, will go a long way in preventing complications and fatalities associated with the disease.

References

1. Mahajan SK. Scrub typhus. J Assoc Physicians India 2005;53:954-8.
2. Oberoi A, Varghese SR. Scrub typhus-an emerging entity: A study from a tertiary care hospital in North India. Indian J Public Health 2014;58:281-3.
3. Saleem M., Shivekar S., Gopal R. Clinico laboratory profile of scrub typhus at a rural tertiary care hospital in south India. Int J Cur Res Rev 2005;7(10):75-78.
4. Singh KG, Singh TN, Singh TG, Khuman T, Singh SI, Singh K. An outbreak of scrub typhus in Bishenpur District, Manipur 2006. JMS 2008;22(3):139-142.
5. S K Singh, R Ram2, L Marangmei, G Chakma. Case Series on Scrub Typhus from a tertiary care hospital of North East India. J of Dent & Med Sc 2014;13(11):62-64.
6. Sinha P, Gupta S, Dawra R, Rijhawan P. Recent outbreak of scrub typhus in North Western part of India. Indian J Med Microbiol 2014;32:247-50.
7. Vivekanandan M, Mani A, Priya YS, Singh AP, Jayakumar S, Purty S. Outbreak of scrub typhus in Pondicherry. J Assoc Physicians India 2010;58:24-8.
8. S. A. M. Kularatne, J. S. Edirisingha, I. B. Gawarammana, H. Urakami, M. Chenchittikul. I. Kaiho. Emerging rickettsial infections in Sri Lanka: the pattern in the hilly Central Province. Trop Med and International Health 2003;8(9):803-811.
9. KD Lee, C Moon, WS Oh, KM Sohn, BN Kim. Diagnosis of scrub typhus: introduction of the immunochromatographic test in Korea. Korean J Intern Med 2014;29:253-255.

How to cite this article: Huidrom S, Singh LK. Clinical and laboratory manifestrations of scrub typhus: A study from a tertiary care hospital in Manipur. Indian J Microbiol Res 2017;4(4):434-436.