Scrub Typhus in a Tertiary Care Hospital in Visakhapatnam

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ABSTRACT

BACKGROUND

Scrub typhus is a serious public health problem in the Asia-Pacific area including, India. It is a zoonotic disease and usually presents with acute febrile illness along with multi-organ involvement caused by *Orientia tsutsugamushi*. It is transmitted to humans by the bite of the larvae of trombiculid mites (Chiggers) which feed on forest and rural rodents. The mites are both vector and natural reservoir. Human infection follows a chigger bite. Incubation period is 6- 21 days. Onset of scrub typhus is characterised by fever, headache, myalgia, cough and gastrointestinal symptoms. A primary lesion which later crusts to form a flat black eschar may be present which is pathognomonic feature of scrub typhus. If the condition is not treated, serious complications may occur involving various organ systems. Owing to potential for severe complications, diagnosis and decision to initiate treatment should be based on clinical suspicion and confirmed by serological tests. The recommended treatment for scrub typhus is doxycycline. Our aim was to study the magnitude of scrub typhus antibodies among febrile patients for a period of one year in a tertiary care hospital and to assess clinical features and outcomes of serologically positive patients.

METHODS

Blood was collected aseptically from 131 patients with request for investigation of scrub typhus from various departments. Screening for scrub typhus was done by rapid Immunochromatographic test to identify antibodies.

RESULTS

During the 1-year study period, a total of 131 serum samples presenting with fever were tested for scrub typhus. Of these, 46 samples were found seropositive. Among these patients, Eschar was found only in 4.3% of cases. In one patient tuberculosis and in 3 patients dengue was found as co-infection. Seasonally the highest number of cases were observed in the cooler months of the year. Male to female ratio was not significant. The percentage of patients positive for scrub typhus was highest (17.6%) in the age group 16-25 years followed by (15.4%) in 26-35 year. None among the age group of 0-15 year was positive.

CONCLUSIONS

Prompt diagnosis, timely antimicrobial therapy and intensive supportive care are important to prevent life-threatening complications. Scrub typhus detected by immunochromatography can be utilized as part of initial investigation to guide the clinicians. In the present study we found that our results highlight that scrub typhus infection is an important cause of fever and active surveillance is necessary to access exact magnitude and distribution of the disease.

KEY WORDS

Scrub Typhus, *Orientia tsutsugamushi*, Trombiculid Mites, Chiggers, Eschar, Zoonosis

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BACKGROUND

This infection is caused by *Orientia tsutsugamushi*, which is transmitted to humans by the bite of infected chiggers (larvae) of trombiculid mites. There are still many unknowns regarding the mechanisms of pathogenesis and the cell biology of the interaction of this bacterium with its host cell, due to the extra research obstacles of studying an obligately intracellular bacterium.⁽¹⁾ The disease is widespread extending from Japan to Australia and from India to Pacific. The scrub Typhus continues to be a public health problem in Asia.⁽²⁾ Scrub typhus in India it has been documented from Jammu and Kashmir, Himachal Pradesh, Uttaranchal, Rajasthan, Assam, West Bengal, Maharashtra, Kerala, and Tamil Nadu. After an incubation period of 6 to 21 days (Mean 10 to 12 days), symptoms of scrub typhus start suddenly and include fever, chills, headache, and generalized lymphadenopathy. At onset of fever, an eschar often develops at the site of the chigger bite. The typical lesion of scrub typhus, common in whites but rare in Asians, which begins as a red, indurated lesion about 1 cm in diameter; it eventually vesiculates, ruptures, and becomes covered with a black scab. Regional lymph nodes enlarge.⁽³⁾ Clinical manifestations range from asymptomatic to severe disease. The mortality rate varies and can be as high 50%.⁽⁴⁾ Misdiagnosis and under diagnosis is known to occur due to lack of availability of diagnostic tests and the specific nature of symptoms, especially when the characteristic eschar is not present.^{(5),(6),(7),(8)} Complications such as pneumonitis, meningoencephalitis, jaundice, renal failure, and myocarditis may also develop. The severity of infection ranges from mild features to multi organ failure and death, which occurs in around 4% of the patients presenting to a hospital. The lung is one of the main target organs for *Orientia*, leading to pulmonary complications of variable severity. Interstitial pneumonia may occur in severe cases.^{(9),(10)} In our study period of one year (July 2017 to July 2018), 131 patients presenting with fever were tested for scrub typhus. Out of these 46 samples were positive. In one patient tuberculosis and in 3 patients, dengue was found as co infection. The present study was conducted to determine the magnitude of scrub typhus antibodies among febrile patients and to determine the seasonality, clinical features and outcome in patients with scrub typhus admitted in a tertiary care hospital in Visakhapatnam (AP). An eschar at the site of chigger feeding is a classic clinical feature of scrub typhus. It begins as a papule at the site of chigger feeding and then ulcerates and forms a black crust like a skin burn from a cigarette. When present, it occurs prior to the onset of fever and other symptoms.^{(11),(12)} The case fatality can be up to 30–70% if no appropriate treatment is received while the median case fatality rate for untreated patients is 6% and for treated patient is 1.4%.^{(13),(14),(15)} Doxycycline is the drug of choice for this illness. Azithromycin has been advocated as an alternative agent.

METHODS

The study was conducted in the department of microbiology in Indus Hospital Visakhapatnam for a period of one year

from July 2017 to July 2018 for test of Scrub typhus specific antibodies. Requisition for testing from treating consultant is taken as IEC clearance and consent from patient. Blood was collected aseptically from 131 in-patients with request for investigation of scrub typhus from various departments. These were the patients having febrile illness of more than 5 days duration. Screening for scrub typhus was done by rapid Immunochromatographic test to identify antibodies. This rapid test (SD Bioline Tsutsugamushi) detects total IgM, IgG or IgA antibodies in human serum against *O. tsutsugamushi*. The test was performed as per recommendation of manufacturer. Briefly, 10 µl serum was applied to sample well and three drops of assay diluent were added. Results were read after 10–15 min. Test had two-coloured lines, a control line “C” and test line “T”. Colour band observed only at “C” was recorded as negative while if observed at both “C” and “T” recorded as positive. Absence of “C” line indicated invalid result.

RESULTS

During the 1-year study period, a total of 131 serum samples were received in the Department of Microbiology with the request to test for scrub typhus specific antibodies. Of these, 46 samples (35.11%) tested positive for the presence of antibodies against *O. tsutsugamushi*. Among the samples tested negative for scrub typhus, two were found to be malaria positive, in seven cases blood cultures were positive for bacteria and remaining were suspected as having viral fevers. The number of adult male and female positive patients were 49% and 51% respectively. No paediatric samples were tested. The month-wise distribution of serologically positive cases is depicted in table 2. A retrospective analysis of the clinical presentation of the serology positive patients found that fever and headache with a mean duration of approximately 5 days was the predominant symptom. The presence of an eschar, though characteristic of scrub typhus was detectable in only 4.3% of patients. Other clinical findings included hepatosplenomegaly and lymph node enlargement. 1/3rd of patients had complications such as acute respiratory distress syndrome, hypotension, acute kidney failure and neurological manifestations such as headache, loss of sensorium and seizures with meningeal signs in varying combinations. Fever was the common symptom. In one patient tuberculosis, and in 3 patients, dengue was associate infection. Out of 46 positive cases, leucocytosis was present in 6 patients, raised blood urea in 13 patients, raised creatinine levels in 8 patients, platelet counts were low in 18 patients and liver enzymes were raised in 90%. During the course of the study, one patient expired due to cardiac arrest and two patients left against medical advice. All the other serologically positive patients were treated with doxycycline and showed remarkable improvement.

Complications	No. of Patients	Percentage
Leucocytosis	6	13.0 %
Elevated Blood urea	13	28.2 %
Low Platelet counts	18	39.1 %
Elevated Liver enzymes	41	89.1 %
Elevated Creatinine levels	8	17.4 %
Table 1. Percentage of Associated Complications		

Month	No. of Samples Tested	No. of Positives	Monthly %
July, 2017	06	Nil	Nil
August, 2017	21	07	33.3%
September, 2017	23	06	26%
October, 2017	16	07	43.7%
November, 2017	07	04	57.1%
December, 2017	09	02	22.2%
January, 2018	06	01	16.6%
February, 2018	06	01	16.6%
March, 2018	02	Nil	Nil
April, 2018	05	Nil	Nil
May, 2018	10	01	10%
June, 2018	09	04	44.4%
July, 2018	11	01	9%
Total	131	46	

Table 2. Percentage of Seasonal Occurrence

DISCUSSION

Scrub typhus is an emerging public health problem and an important cause of PUO. Failure of timely diagnosis and treatment can lead to significant morbidity and mortality. This infection is caused by *Orientia tsutsugamushi*, which is transmitted to humans by the bite of infected chiggers (Larvae) of trombiculid mites. There are still many unknowns regarding the mechanisms of pathogenesis and the cell biology of the interaction of this bacterium with its host cell, due to the research obstacles in studying an obligate intracellular bacterium.⁽¹⁶⁾

Classically known as a post monsoon disease, this seasonal occurrence of scrub typhus was a prolonged one, extending well into the month of December.⁽¹⁷⁾ During our study also period of highest incidence was found to be in post monsoon season (August to November). Eschar at the site of attachment of the larval mite/chigger is considered highly suggestive of scrub typhus, but occurs in a variable proportion of patients in different studies.⁽¹⁸⁾ It begins as a papule at the site of chigger feeding and then ulcerates and forms a black crust like a skin burn from a cigarette. When present, it occurs prior to the onset of fever and other symptoms. In our study typical eschar was present only in 2 cases i.e 4.3% of cases, similar rates (4%–12%) also have been reported by some other Indian studies.^{(19),(20),(21)}

The clinical manifestations of this disease vary from minimal to severe fatal illness with multi-organ dysfunction. Lung is one of the main target organs for *Orientia*, leading to pulmonary complications of variable severity. Interstitial pneumonia may occur in severe cases. This has been reported in another study from the Indian subcontinent.⁽²²⁾ In our study 1/3rd of patients had complications such as acute respiratory distress syndrome, hypotension, acute kidney failure and neurological manifestations. Kumar et al found nearly half of their patients (48.5%) had three or more organ systems involved, while 20 patients (30%) had evidence of dysfunction of five organs systems during the course of their hospital stay. The case fatality rate for scrub typhus has been 7%–30%.⁽²³⁾

Mortality for scrub typhus ranges for less than 1% to 50% depending on antibiotic treatment and status of individual infected.⁽²⁴⁾ In our study there was no causality found due to scrub typhus. Thrombocytopenia is an important feature of Scrub Typhus, dengue, malaria and leptospirosis. This was presented by about half of our patients. Leucocytosis was seen in 36 per cent patients. Significantly elevated levels of one or more liver enzymes which is commonly observed in

Scrub Typhus, were also found in our study. The haematological and biochemical parameters were comparable with other reports from India and abroad.^{(25),(26),(27),(28)}

The Weil-Felix test (WFT) is most common and commercially available test for the diagnosis of scrub typhus in developing countries like India. The sensitivity and specificity of the WFT is low and is usually positive during the 2nd week of illness. The gold standard confirmatory tests are the indirect immune peroxidase test and the immune-fluorescent assay (IFA). These tests are costly and not easily available in developing countries like India. Therefore, the diagnosis of scrub typhus is mainly by clinical suspicion and by characteristic clinical finding of, eschar. Therefore, thorough search for eschar over all the areas of body is very important during the clinical examination of all acute febrile illnesses. The current treatment for scrub typhus is Doxycycline and Chloramphenicol. Azithromycin has also been found effective.⁽²⁹⁾

CONCLUSIONS

A high index of clinical suspicion, prompt diagnosis and early institution of appropriate antimicrobials can decrease the morbidity and mortality. Scrub typhus is easily treatable disease. Focus should be on case identification, public education, rodent control and habitat modification to control the impact of Scrub typhus. Vaccines are under trial. Detection of scrub typhus by immunochromatography can be utilized as part of initial investigation to guide the clinicians. In the present study we found that scrub typhus infection is an important cause of fever and active surveillance is necessary to access exact magnitude and distribution of the disease.

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