Analysis of Two Outbreaks of Scrub Typhus in Rajasthan: A Clinico-epidemiological Study

Raman Sharma1, VP Krishna2, Manjunath2, Hema Singh2, Swati Shrivastava4, Virender Singh1, SS Dariya2, Mukesh Soni2, Shrikant Sharma3

Abstract

Aims and Objectives: To describe the diversity of clinical manifestations, laboratory findings and outcome of scrub typhus in hospitalised patients of SMS Hospital, Jaipur during 2012 and 2013.

Material and Methods: All the cases of febrile illness with thrombocytopenia diagnosed as scrub typhus were analysed. Diagnosis was made by ELISA based IgM serology.

Observations and Results: A total of 125 patients were studied. All of them presented with fever; the other major symptoms were headache, cough, dyspnoea and myalgias. On examination, patients had hepatosplenomegaly, lymphadenopathy and eschar. On investigation elevated SGOT, SGPT with normal or elevated bilirubin levels were the most common findings. Other laboratory findings were thrombocytopenia and deranged renal function tests. Most common X-ray finding observed in these patients was bilateral lung infiltrates. Other complications were MODS, ARDS, hypotension and meningoencephalitis. Majority responded to doxycycline.

Conclusion: Scrub typhus though prevalent is under-reported in our country. It should be considered as an important differential diagnosis in a febrile patient with thrombocytopenia, deranged liver or renal functions, and B/L chest opacities. Early diagnosis and appropriate treatment is rewarding and prevents morbidity and mortality.

Introduction

Scrub typhus is a rickettsial infection caused by Orientia Tsutsugamushi transmitted through bite of Chiggers (larval stage of trombiculid mite). Scrub typhus is an acute febrile illness which generally causes non-specific symptoms and signs. The clinical manifestations of this disease range from sub-clinical disease to organ failure and death.

Deaths are attributable to late presentation, delayed diagnosis, and drug resistance. The public health importance of this disease is underestimated because of difficulties with clinical diagnosis and lack of laboratory methods in many geographical areas.

Scrub typhus has been reported to cause diminution of viral load in HIV-I infected patients, and to help restore immune status of patients but its actual association has to be established yet.1

Scrub typhus, though endemic in India; yet is under reported. During the months of September-November of 2012 and 2013, we encountered a spurt in cases of fever from specific rural areas of Alwar, Dausa, Bharatpur, Karauli (Typhus Islands Figure 1) chiefly presenting with thrombocytopenia, hypoxaemia with B/L chest infiltrates along with impaired liver and renal functions. Dengue serology, malaria parasite in PBF and RT PCR for H1N1 in these patients were negative. On further evaluation, Scrub typhus serology emerged positive in all these patients. Therefore, we decided to study in detail, the clinical features, laboratory parameters and outcome of scrub typhus.

1Sr. Professor, 2 Resident, 3 Assistant Professor, 4 Associate Professor, Deptt. of Medicine, SMS Medical College, Jaipur, Rajasthan
Received: 05.03.2014;
Accepted: 11.06.2014
Material and Methods

All patients admitted with acute febrile illness and thrombocytopenia to SMS Hospital, Jaipur were evaluated. Patients were included in the study group whose Scrub typhus IgM serology was positive. Detailed history and clinical examination followed with a meticulous search for presence of Eschar. Basic laboratory evaluation included complete blood count, peripheral blood smear, blood sugar, liver and renal function tests and chest X-ray. Special investigations like rapid antigen test for malaria parasite, dengue serology (IgM and IgG), Widal test, blood culture, PCR for H1N1 and serology for leptospirosis were done to exclude alternative diagnosis and concurrent infections. Other tests like CSF analysis, MRI brain, and HRCT chest were done as indicated.

Observations and Results

A total number of 125 patients with the confirmed diagnosis of scrub typhus were studied. The mean age of these patients was 38 years. There were 80 (64%) female patients; in which 6 were pregnant and 45 (36%) patients were male. 80% of cases were from rural areas while 20% came from semi-urban areas. Majority of patients were from Jaipur district (30), Dausa (24), Alwar (18), Bharatpur (12), Karauli (10) (Figure 1). 50% of these patients were farmers by occupation.

Fever (100%), headache (81.6%), cough, dyspnoea (58.4%) and myalgias (48%) were most common symptoms. 26 (20.8%) patients had altered sensorium, 6 (4.8%) had GI bleed and 6 (4.8%) had opisthotonus posturing with muscle spasms (Table 1).

Hypoxaemia (57.6%), hepatosplenomegaly (50.4%) and lymphadenopathy (29%) were most common signs. Eschar was seen in 22 (17.6%) patients and the most common sites were axilla, breast and groin (Figure 2). Hypotension was present in 10 (8%) patients of which 3 required inotropic support. 4 (3.2%) patients showed signs of meningoencephalitis (Table 2).

The most consistent laboratory finding was elevated SGOT, SGPT; which was observed in 98.4% patients; while only 26.4% of these had raised bilirubin. Thrombocytopenia (platelets < 150,000) was found in 107 (85.6%) patients of which significant thrombocytopenia (platelets < 50,000) was seen in 70 (56%) patients. None of them required platelet transfusions. Leucocytosis (TLC > 10,000) was found in 44.8%. Deranged renal functions was observed in 21.6% patients and urine analysis showed proteinuria in all of these. 72 (57.6%) patients developed hypoxaemia (SpO₂ < 90%) and 17 of these required assisted ventilation (Table 3).

Complications (Table 4) observed were multi-organ dysfunction (28.86%), ARDS (19.2%), hypotension (8%) and meningoencephalitis in 4 (3.2%). Out of 72 (57.6%) who had hypoxaemia, 24 developed ARDS of which 17 required assisted ventilation. Hypotension was documented in 10 (8%) patients of which 7 responded to intravenous fluids while 3 required inotropic support. Out of 27 (21.6%) patients with acute kidney injury, none required dialysis. CSF of patients with meningoencephalitis showed mildly elevated proteins with mild lymphocytic pleocytosis. 2 patients had cerebellar signs with normal MRI brain of which one recovered completely while other one patient had persistent nystagmus with signs of cerebellar involvement, not responding to treatment.

Table 1: Symptomatology in scrub typhus

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>No. of patients (Total=125)</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>125</td>
<td>100</td>
</tr>
<tr>
<td>Headache</td>
<td>102</td>
<td>81.6</td>
</tr>
<tr>
<td>Cough &amp; Dyspnoea</td>
<td>73</td>
<td>58.4</td>
</tr>
<tr>
<td>Myalgias</td>
<td>60</td>
<td>48</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>58</td>
<td>46.5</td>
</tr>
<tr>
<td>Altered sensorium</td>
<td>26</td>
<td>20.8</td>
</tr>
<tr>
<td>GI bleed</td>
<td>6</td>
<td>4.8</td>
</tr>
<tr>
<td>Opisthotonus posturing, Muscle spasms</td>
<td>6</td>
<td>4.8</td>
</tr>
<tr>
<td>Abortion</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
A peculiar feature of opisthotonus posturing was seen in 6 (4.8%) patients (Table 1).

Out of 125 patients, 112 (89.6%) patients recovered, of which 100 patients responded to doxycycline alone with improvement starting within 48 hours. Figure 3 shows complete clearing of lung fields in chest X-ray of one of our patients in response to treatment with doxycycline. 6 patients did not show improvement initially in whom combination therapy with intra venous chloramphenicol and azithromycin was used. Azithromycin was used in 6 pregnant patients. 13 (10.4%) patients succumbed to death in spite of combination therapy and best supportive management. All had MODS and 8 required assisted ventilatory support (Table 5).

**Discussion**

Many reports on scrub typhus from various parts of India especially southern and south-eastern areas have been published (Table 6). This is one of the first
reports on scrub typhus from Rajasthan where this disease has not been reported previously. And to our knowledge this study is one of the largest series of scrub typhus in India, reported till date.

This febrile illness presents in previously healthy active persons and ranges from sub-clinical disease to organ failure to fatal disease. Most of the patients in our series presented with pyrexia, thrombocytopenia, cough and dyspnoea. Unlike malaria and viral illness fever was of longer duration (mean 10 days) and was not associated with chills in majority. Unlike H1N1, dyspnoea was not rapidly progressive. Besides headache, myalgia, cough and dyspnoea, mental changes, GI bleed were other symptoms. Opisthotonus posturing was the peculiar feature seen in our patients, which may suggest possibility of nerve hyper excitability similar to tetany in this disease but further studies need to be done to support this.

Eschar (Figure 2) at the site of attachment of chigger is the most characteristic feature but is not found in all patients. It is a tough black scab surrounded by elevated red areola and is neither painful nor pruritic. In our series eschar was found in 22 (17.6%) patients. Most common sites were axilla, groin, back and breast. This is consistent with the study done in Hyderabad where eschar was found in 12.5% cases. However, in studies from Pondicherry, South Vietnam and Taiwan, eschar was found in 46%, 46% and 60% cases respectively. Eschar was associated with regional or generalised Lymphadenopathy in 29% in our series; while it is 30% in study from Taiwan.

Among the laboratory parameters most consistent abnormality noticed was transaminitis which was observed in 98.4% cases followed by thrombocytopenia (85.6%).

Scrub typhus is known to produce severe complications and has a mortality of 7-30%. Deaths are attributed to late presentation, delayed diagnosis and drug resistance. Pandey et al from Himachal Pradesh reported 3 cases of ARDS, T say et al from Taiwan reported 8 cases of ARDS, 3 cases of AKI, and one case each of myocarditis and septic shock.
In our study, MODS was found in 36 (28.86%) patients. All of them had breathlessness with hypoxaemia and 24 (19.2%) developed ARDS; 17 of these required assisted ventilation of which 8 succumbed to death. Hypotension was seen in 10 (8%), of which 7 responded to IV fluids while 3 required inotropic support. AKI was seen in 27 (21.6%) patients but none required dialysis. 72 (57.6%) patients developed hypoxaemia and 24 (19.2%) developed ARDS. Of the 72 patients with hypoxaemia, 64 had chest X-ray findings in the form of bilateral reticulonodular opacities. Remaining 8 had normal chest X-ray but HRCT of these revealed findings consistent with interstitial pneumonitis (crazy pave appearance) (Figure 4).

26 (20.8%) patients had altered sensorium in the form of agitation, delirium or obtundation. Two patients had signs of cerebellar involvement of which one recovered fully with doxycycline while in other, nystagmus with ataxia persisted. 4 (3.2%) patients developed meningoencephalitis. These patients in addition to fever also had headache, vomiting, neck rigidity and altered sensorium. MRI brain was normal in all these cases. CSF of all these patients showed mildly elevated proteins with mild lymphocytic pleocytosis. This is consistent with the result of other studies.3-5 Thus scrub typhus should be considered an important differential diagnosis in patients presenting with fever of more than 5 days, presenting with signs of meningitis, mild lymphocytic pleocytosis in CSF.

Although rickettsiae can be isolated from or detected in clinical specimens, serological tests still remain an indispensable tool in the diagnosis. Micro-immunofluorescence is considered the test of choice. Latex-agglutination, indirect haem-agglutination, immuno-peroxidase assay, ELISA and polymerase chain reaction (PCR) are other available tests. PCR is more sensitive than the serological test for diagnosis of scrub typhus and prolonged persistence of *O. tsutsugamushi* DNA in blood can be demonstrated despite clinical recovery of the patients. No current diagnostic test is sufficiently practical for use by physicians working in rural areas. A new dipstick test using a dot blot immunoassay format has been developed for the sero-diagnosis of scrub typhus. The dot blot immunoassay dipstick is accurate, rapid, easy to use, and relatively inexpensive. It appears to be the best currently available test for diagnosing scrub typhus in rural areas where this disease predominates.10,12,13

In our study we used ELISA to diagnose scrub typhus by In Bios ELISA kit. Its sensitivity is almost 100% and specificity is around 96%.14

Doxycycline 100 mg BD for 7 days is the treatment of choice. Tetracycline 500 mg QID, Chloramphenicol 500 mg QID, Azithromycin 500 mg OD, Rifampicin 900 mg per day for same duration have been found effective in patients who respond poorly to doxycycline. Rapid defervescence after antibiotic is so characteristic that it is used as a diagnostic test for *R. tsutsugamushi*.9-11

In our study, 112 (89.6%) patients recovered fully; of them 100 of them responded to doxycycline alone with improvement starting within 48 hours. Remaining 6 patients unresponsive to doxycycline responded to combination therapy with chloramphenicol or Azithromycin.15 Six pregnant females were also treated with IV azithromycin. 13(10.4%) patients died in spite of combination therapy and best supportive management. Table 6 depicts comparison of our study with various other Indian studies.

### Conclusion

Scrub typhus though prevalent is under-reported in our country. It should be considered as an important differential diagnosis in a febrile patient with thrombocytopenia, deranged liver or renal functions, and B/L chest opacities. Early diagnosis and appropriate treatment is rewarding and prevents morbidity and mortality.

### Table 6: Comparison of our study with other Indian studies

<table>
<thead>
<tr>
<th>Study Origin</th>
<th>Pondicherry (Percentage)</th>
<th>Hyderabad (Percentage)</th>
<th>SMS Hospital Jaipur (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients</td>
<td>50</td>
<td>48</td>
<td>125</td>
</tr>
<tr>
<td>Fever</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Eschar</td>
<td>46</td>
<td>12.5</td>
<td>17.6</td>
</tr>
<tr>
<td>Thrombocytopenia (&lt;150K)</td>
<td>28.1</td>
<td>37.5</td>
<td>85.6</td>
</tr>
<tr>
<td>Elevated SCOT/SCPT</td>
<td>95.9</td>
<td>100</td>
<td>98.4</td>
</tr>
<tr>
<td>Raised Bilirubin</td>
<td>16</td>
<td>NA</td>
<td>26.4</td>
</tr>
<tr>
<td>Deranged RFT</td>
<td>12</td>
<td>33</td>
<td>21.6</td>
</tr>
<tr>
<td>MODS</td>
<td>34</td>
<td>25</td>
<td>28.6</td>
</tr>
<tr>
<td>Hypotension</td>
<td>14</td>
<td>NA</td>
<td>8</td>
</tr>
<tr>
<td>Mortality</td>
<td>2</td>
<td>6.25</td>
<td>10.4</td>
</tr>
<tr>
<td>X RAY Changes</td>
<td>NA</td>
<td>NA</td>
<td>51.2</td>
</tr>
</tbody>
</table>
Acknowledgement

With contributions from Dr. Bharti Malhotra, Dr. Rameshwari (Professors, Department of Microbiology, SMS Medical College) for making available ELISA kit for scrub typhus to us.
Dr. Renu Saigal, Dr. C. L. Nawal, Dr. Hemant Malhotra, Dr. Subrata Banerjee, Dr. Ganpat Devpura (Professors Department of Medicine, SMS Medical College) Dr. Bharat Bhushan Sharma (Associate Professor Department of Medicine, SMS Medical College, Jaipur).

References