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Scrub typhus in paediatric age group: A report from a tertiary care hospital

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Scrub typhus in paediatric age group: A report from a tertiary care hospital

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Abstract:

Background: Scrub typhus is a rickettsial disease endemic in many parts of India. It is a zoonosis spread by the bite of ticks and mites. **Materials & Methods:** The present retrospective study describes the clinical profile of eighteen pediatric scrub typhus cases who were hospitalized in a tertiary care hospital during the period of 21st January 2010 to 20th December 2010. In all the cases diagnosis was confirmed by Weil Felix test. **Results:** All children presented with fever. Eschar was present in 72% cases. 61% had abdominal pain and 44% had vomiting. Splenomegaly, hepatomegaly, lymphadenopathy, conjunctival congestion and cough were present in 88%, 72%, 61%, 34% and 28% respectively. Diarrhea and rash was present in 22% of children. Alanine transaminase, aspartate transaminase and alkaline phosphatase were elevated in 83%, 88% and 72% respectively. 34% had either hematuria or Proteinuria. 55% had thrombocytopenia. Hypoalbuminemia was detected in 72% cases. 88% had hepatic dysfunction, 22% had acute respiratory distress and 28% had hypotension. Chloramphenicol and doxycycline were the antibiotics used for treatment of the cases. All children responded well to antibiotics and there were no mortalities. **Conclusion:** Scrub typhus can lead to life threatening consequences in children if left undiagnosed and untreated. Therefore early detection of the disease and prompt treatment with the antibiotics can be life saving.

Keywords: Scrub typhus; Rickettsial disease; Eschar

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Introduction

Scrub typhus is a re-emerging infectious disease in India. It is a zoonosis caused by the rickettsial bacteria "Orientia tsutsugamushi" and is transmitted from rodents to humans by the larval-stage trombiculid mites [1]. Scrub typhus occurs most frequently in Southeast Asia, but has been reported from India, Australia and from Astrakhan in Central Asia. [2] The disease is distributed throughout the Asia Pacific rim and is endemic in South Korea, China, Taiwan, Japan, Pakistan, India, Thailand, Malaysia, and Northern Australia and continues to be a public health issue in Asia. The disease usually presents itself as an acute febrile illness with a typical primary necrotic lesion (eschar), generalized lymphadenopathy, rash, and non-specific symptoms such as fever, headache, myalgia and cough [3]. The diagnosis is based on the patient's history of exposure, the clinical features, and an increase in antibody titer, antigen detected in

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blood, or genetic material detected by Polymerase Chain Reaction. The radiologic findings of scrub typhus are varied and nonspecific [4]. The disease is usually self-limited and responds well to antibiotics with

spontaneous recovery occurring in a few days; however fatality has been reported in some cases.

Material and methods

The present retrospective study was conducted at a tertiary care hospital (Sri Ramachandra Medical Centre), Chennai, Tamilnadu. Eighteen pediatric cases with confirmed scrub typhus admitted from 21st January 2010 to 20th December 2010 were included in the study. Data regarding demography, clinical manifestations, duration of illness, and history of treatment by primary pediatrician were collected. Laboratory data such as complete blood counts, hemoglobin, serum electrolytes, renal function tests, liver function tests, urine analysis, urine and blood cultures, peripheral blood smear for malarial parasite, widal test, and serology for leptospirosis, serology for dengue and chest radiography were collected. Ultrasound abdomen and computerized tomography scan wherever available was collected. In all the cases scrub typhus was diagnosed by a Weil Felix test.

Results

This study included eighteen children who were diagnosed to have scrub typhus during the during the time period between 21st January 2010 and 20th December 2010. Of the eighteen children 12(67%) were males and 6(33%) were females. Their mean age was 8.7 years (range 1-16 years). The duration of illness before hospitalization ranged from 4-16 days with an average of 10 days. All children had fever while presentation. Eschar was present in 72% of children. 61% children had abdominal pain and 44% had vomiting. 17% had headache. 88%, 72%, 61% had Splenomegaly, hepatomegaly and lymphadenopathy respectively. Conjunctival congestion was present in 34% of children and 28% had cough. Chest examination revealed crackles/ronchi in 28% cases. Diarrhea and rash was present in 22% of children. Table 1 & table 2 shows the characteristics and clinical features of the cases respectively.

Table I. Characteristics of the patients

| | n | % |
|--|-------------|-----|
| Age | | |
| 1-3 years | 3 | 17 |
| 3-6 years | 2 | 11 |
| 7-9 years | 7 | 39 |
| 10-14 years | 4 | 22 |
| 14-18 years | 2 | 11 |
| Gender | | |
| Boys | 12 | 67 |
| Girls | 6 | 33 |
| Treatment by a primary pediatrician before hospitalization | 15 | 83 |
| Ventilator use | 1 | 5.5 |
| Needed ICU admission | 7 | 39 |
| Mortality | 0 | 0 |
| Average number of days taken for diagnosis from appearance of symptoms (M±SD) | 10.9 ± 3.98 | |
| Average Length of stay in days (M±SD) | 6.05 ± 1.85 | |

Of eighteen children seven required Intensive Care Unit care and two required ventilator support. 88% children had hepatic dysfunction and 22% children had acute respiratory distress. Hypotension and thrombocytopenia was present in 28% children. 34% had either hematuria or proteinuria. Tachypnea (respiratory rate > 30/min) was present in 44 % children. One child had co-existing dengue. None of the children had meningeal involvement.

Laboratory investigations revealed anemia in 44% children with mean hemoglobin of 10.3 gms%. 28% had leucocytosis (>11000 cells/mm³) and 3% had leucopenia (<4000 cells/mm³). Alanine transaminase was elevated(>40 U/L) in 83% children and aspartate transaminase was elevated (>40 U/L) in 88% children. 55% children had thrombocytopenia

Table II. Clinical Features of the patients

| | n | % |
|--------------------------------|----|----|
| Fever | | |
| <7days | 4 | 22 |
| 7-14 days | 10 | 56 |
| >14days | 4 | 22 |
| Headache | 3 | 17 |
| Nausea/Vomiting | 8 | 44 |
| Abdominal pain | 11 | 61 |
| Cough | 5 | 28 |
| Conjunctival congestion | 6 | 34 |
| Diarrhea | 4 | 22 |
| Rash | 4 | 22 |
| Crackles / Ronchi | 5 | 28 |
| Tachypnea | 8 | 44 |
| Lymphadenopathy | 11 | 61 |
| Hepatomegaly | 13 | 72 |
| Splenomegaly | 16 | 88 |
| Eschar | 13 | 72 |

Table III. Complications of the patients

| | n | % |
|----------------------------------|----|----|
| Hepatic Dysfunction | 16 | 88 |
| ARDS* | 4 | 22 |
| Hypotension | 5 | 28 |
| Multiorgan involvement | 0 | 0 |
| Acute Renal Failure | 0 | 0 |
| Meningial involvement | 0 | 0 |
| Hematuria/ Proteinuria | 6 | 34 |
| Thrombocytopenia | 5 | 28 |
| Needed ICU care | 7 | 40 |
| Gastrointestinal Bleeding | 0 | 0 |

*ARDS- Acute respiratory distress syndrome.

(<150,000/mm³) and 72% had hypoalbuminemia (serum albumin <3.5 g/dl). Creatinine was not elevated any of the children. Bilirubin was also elevated (>1.5mg %) in one child. Hematuria and proteinuria was present in 28% and 17% respectively. Alkaline phosphatase was elevated (>140 U/L) in 72% of cases. Blood cultures and urine cultures were done in all patients and showed no growth. Antibody against Salmonella species (Widal test) and Leptospira species were all negative in all patients. Antibody against Dengue was negative in all but one child. Chest x-ray abnormalities were detected in 22% cases. Table 3 & 4 shows the complications and laboratory investigations respectively.

Discussion

Scrub typhus is prevalent in many parts of India. It is known to occur all over India, including Southern India and Northern India [5]. 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. Recently outbreaks of scrub typhus were also reported in southern India during the cooler months of the year [6]. Scrub typhus in humans results after the introduction of *Orientia tsutsugamushi* through the skin by the bite of a larval-stage (chigger) trombiculid mite. 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 [4]. The disease usually presents as an acute febrile illness with non-specific symptoms like fever, headache, myalgia, cough and gastrointestinal disturbances. In the present study, all children had fever while presentation. An eschar at the wound site is the most characteristic feature of scrub typhus, but may not be present in all patients. Eschar is a black necrotic lesion resembling a cigarette burn usually found in areas where skin is thin, moist or wrinkled and, where the clothing is tight [3].

Table IV. Laboratory Findings of the Patients

| | n | % |
|---|----------|----------|
| Hemoglobin < 10gm% | 8 | 44 |
| Total Leucocyte Count | | |
| <4000 /cu.mm | 3 | 17 |
| 4000- 11,000/ cu.mm | 10 | 55 |
| >11,000/cu.mm | 5 | 28 |
| Platelets | | |
| <1.5 lakhs/cu.mm | 10 | 55 |
| >1.5 lakhs/cu.mm | 8 | 44 |
| Increased ALP* (>140 IU/L) | 13 | 72 |
| Increased ALT** (>40 IU/L) | 15 | 83 |
| Increased AST*** (>40 IU/L) | 16 | 88 |
| Bilirubin level >1.5mg% | 1 | 5.5 |
| Creatinine level >1.4 mg% | 0 | 0 |
| Hypoalbuminemia (<3.5 g/dl) | 13 | 72 |
| Proteinuria (Urine protein \geq 1+) | 3 | 17 |
| Hematuria | 5 | 28 |

*ALP- Alkaline phosphatase, **ALT- Alanine transaminase, *** AST- Aspartate transaminase

In the studies from Thailand [7] and Eastern Taiwan [8] eschar was present in 75 % and 50 % respectively. In the current study 72 % cases had Eschar. Hepatosplenomegaly was present in 94 % of children in our study comparable to the study by Patil et al in which hepatosplenomegaly was present in 85 % cases [9] and the study by Sanjeev Kumar Digra et al where hepatosplenomegaly was reported in 75 % of the cases [10]. Other clinical features that were present in our cases were abdominal pain, nausea/vomiting, rash, conjunctival congestion,

diarrhea which was present in 61%, 44%, 22%, 34% and 22% respectively.

Scrub typhus is still regarded as a life threatening disease in children. Serious complications of scrub typhus include acute respiratory distress, pneumonia, myocarditis, meningoencephalitis, acute renal failure, and gastrointestinal bleeding. A retrospective study from Taiwan [8] reported hepatic dysfunction in 77% of their cases whereas Sanjeev Kumar Digra et al demonstrated hepatic dysfunction in only 14.2% of cases [10]. In contrast in the current study 88% of cases had hepatic dysfunction. Other complications observed in this study were Acute Respiratory Distress Syndrome (ARDS), hypotension, hypoalbuminemia and thrombocytopenia which were observed in 22%, 28%, 72% and 22% respectively.

Routine laboratory investigations does not have much of a diagnostic value in the diagnosis of scrub typhus. However elevated liver enzymes are frequently observed among patients with scrub typhus [11]. Serological methods available for diagnosis of rickettsial diseases include microimmunofluorescence test, immunoperoxidase assay, latex agglutination test, indirect hemagglutination test, enzyme linked immunosorbent assay, dot blot immunoassay (including dipstick test) and Weil-Felix test [10]. Weil Felix test has been used widely in our country for diagnosing scrub typhus. It is highly specific; however it lacks sensitivity. IFA (Indirect immunofluorescence assay) is highly sensitive and considered 'gold standard'. However it is expensive and the test requires fluorescent microscope, trained personnel & cell culture procedures for preparing rickettsial antigen; hence not readily available in our country. Polymerase chain reaction has been used effectively to diagnose acute infection with *Orientia tsutsugamushi* [4]. A rapid immunochromatographic assay which uses recombinant major outer membrane protein Antigen (r56) of *Orientia tsutsugamushi* to detect IgM, IgG and

IgA antibodies has been shown to be reliable and suitable for use in developing countries but is expensive [12].

Doxycycline is the antibiotic of choice for scrub typhus. Chloramphenicol is an alternative and is useful in children. Azithromycin is used in areas where doxycycline-resistant scrub typhus is prevalent and also for children under 8 years old or during pregnancy, where doxycycline is contraindicated [13]. Rifampicin is also effective in treatment of scrub typhus. In this study eleven children were treated with Chloramphenicol and seven were treated with Doxycycline. All children responded well to the treatment and recovered completely. No child in this series had mortality.

Conclusion

In conclusion, this study summarizes the epidemiologic aspects, clinical and laboratory features of scrub typhus in pediatric patients. Scrub typhus is endemic in many parts of India and therefore surveillance should be continued in all these areas. When a child presents with acute fever and hepatic dysfunction diagnosis of scrub typhus must be considered and the presence of an eschar should be looked for, especially when a child resides in a geographical area in which scrub typhus is endemic. No vaccine against scrub typhus is yet available. Therefore, prevention is based mainly on avoiding the arthropod bite [14]. The disease usually responds dramatically to antibiotics therefore early diagnosis and treatment is imperative in reducing morbidity and mortality.

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