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Case Study of a 14-Year-Old Male Patient with Scrub Typhus Infection and Acute Meningitis

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Abstract

Scrub Typhus is a zoonotic disease that is accidentally transmitted to humans by the bite of larval trombiculid mite or chigger. It is an important cause of acute febrile illness in India and is responsible for high morbidity and mortality. In this study, we present a brief medical case report of a 14-year-old male patient who was admitted to the emergency ward of R.G. Kar Medical College and Hospital on early November last year. He was reported to be suffering from fever for 5 days along with convulsion and syncopal attack. He had hyponatremia, altered sensorium, neck rigidity and

was diagnosed with acute meningitis. Enzyme linked immunosorbent assay (ELISA) detected IgM antibodies to scrub typhus in the serum of the patient confirming infection with the bacterial disease. The patient recovered on treatment with antimicrobials, GI prophylaxis agents and antiepileptic drug. The current study highlights a case of acute meningitis in scrub typhus infection and its subsequent treatment. The study thus provides further information on the complications of scrub typhus infection.

Keywords: Scrub Typhus, Meningitis, Antimicrobials, Antiepileptic Drug, GI prophylaxis Agent

1. Introduction

Scrub Typhus, or tsutsugamushi fever, is a zoonotic disease that is accidentally transmitted to humans. It is frequently found in people with outdoor exposure in tropical and subtropical Asian regions^[1]. The causative organism, *Orientia tsutsugamushi*, belongs to family Rickettsiaceae and is transmitted to humans by the bite of larval trombiculid mite or chigger. The pathophysiological hallmark of scrub typhus is disseminated vasculitis^[2] with subsequent vascular injury that involves organs such as skin, liver, brain, kidney, meninges and the lung. The organism multiplies at the site of inoculation that progresses on to necrosis and evolves into an eschar with regional lymphadenopathy^[2]. Within a few days, patients develop rickettsemia with infection of the vascular endothelium resulting in vascular injury in several organs. The injury causes disseminated intravascular coagulation (DIC) with platelet consumption, vascular leak, pulmonary edema, shock, hepatic dysfunction and meningoencephalitis^[3-6].

Scrub typhus presents as an acute undifferentiated fever. The incubation period for symptoms is between six and twenty-one days from exposure^[7]. The clinical picture is characterized by sudden onset fever with chills, headache, backache and myalgia, profuse sweating, vomiting and enlarged lymph nodes^[7]. In some patients, an eschar may develop at the site of chigger feeding, usually at sites where the skin surfaces meet, such as axilla, groin and inguinal areas^[8].

Five to eight days after the onset of fever, a macular or maculopapular rash may appear on the trunk and later extend to the arms and the legs in a small proportion of patients^[8]. Complications of scrub typhus infection include pneumonia^[9], acute respiratory distress syndrome (ARDS) like picture^[10, 11], myocarditis^[12], encephalitis^[13], hepatitis^[14], DIC^[15], hemophagocytic syndrome^[16], acute kidney injury^[17], acute pancreatitis^[18], transient adrenal insufficiency^[19], subacute painful thyroiditis^[20] and presentation as an acute abdomen^[21].

Currently most diagnostic laboratories use the enzyme-linked immunosorbent assay (ELISA) for the detection of IgM antibodies in scrub typhus as it provides an objective result and has sensitivity similar to that of immunofluorescence assay (IFA)^[22]. Detection of IgM antibody is considered to be diagnostic of an acute infection when compared to IgG antibodies which suggest a previous infection especially in endemic areas^[23]. Rapid tests to detect IgM antibodies to scrub typhus have sensitivity ranging from 34.7% to 96.7% and specificity between 93.3% and 99.7%^[23-25].

In this study, we present a brief medical case report of a 14-year-old male patient diagnosed with scrub typhus infection associated with CNS dysfunction and acute meningitis. The clinical symptoms of the patient included fever, convulsion, hyponatremia, neck rigidity and altered sensorium. The patient showed recovery following treatment with antimicrobials, GI prophylaxis agents and antiepileptic drug.

2. Materials and methods

A 14-year-old male patient having fever for 5 days along with convulsion and syncopal attack was admitted to the emergency ward of R.G. Kar Medical college and hospital, Kolkata, on early November 2022. He had hyponatremia, altered sensorium, neck rigidity and suspected with meningitis. At the time of admission (05.11.2022), the patient had blood pressure=130/80 mm Hg, capillary blood glucose (CBG) =154 mg/dl, oxygen saturation (SpO₂) =98%, pulse rate= 72 bpm and Glasgow Coma Scale value (GCS) = 4/15 (E2-V1-M1). In addition, the patient's hemoglobin content was 11.0 g/dl, packed cell volume (PCV)= 33.9%, total leucocyte count= 13,600/mm³, neutrophil content 70%, lymphocyte content 18%,

eosinophil content 08%, monocyte content 04%, and platelet count=2.8 lakh/mm³. The patient was diagnosed with microcytic, hypochromic anemia. Further, blood coagulation studies indicated the following results: P-Time =13.1 sec, INR=1.10 and APTT=23.6 sec.

Serum of the patient was tested for scrub typhus infection at the Virus Research & Diagnostic Laboratory (VRDL), Department of Microbiology, RG Kar Medical College and Hospital, Kolkata, after obtaining ethical clearance from the institution and informed consent. Serum IgM antibodies to scrub typhus was detected by ELISA method following standard kit protocol (J. Mitra & Co. Pvt. Ltd.) according to the manufacturer's instructions. Calculations were done as per kit instructions as follows: Sample O.D. ratio = Sample O.D. ÷ Cut off Value [Cut off Value = 0.372 for Scrub Typhus IgM] (Calculation of Scrub Typhus IgM units=sample O.D. ratio×10)

3. Results

The laboratory investigation report of patient sample recorded on 05.11.2022 is shown in Table 1.

Table 1: Laboratory investigation of patient sample recorded on 05.11.2022

Laboratory investigations	Patient history (recorded on 05.11.2022)
(a) Laboratory parameters (with reference values in parenthesis)	
Total Protein (6-8 g/dl)	5.8
Albumin (3.2-5.0 g/dl)	2.7
Total bilirubin (0.1-1.0 mg/dl)	0.6
Direct bilirubin (0-0.3 mg/dl)	0.2
Urea (10-40 mg/dl)	29
Creatinine (0.5-1.5 mg/dl)	0.6
Uric Acid (M 3.1-7.0 mg/dl; F 2.5-5.6 mg/dl)	3.2
Creatine Kinase (24-170 IU/L)	103
Alanine Transaminase (5-35 IU/L)	18
Aspartate Transaminase (5-35 IU/L)	24
Alkaline Phosphatase (adult 110-310 IU/L)	252
Sodium (135-145 mmol/l)	137
Potassium (3.5-5.0 mmol/l)	3.5
Calcium Total (9-11 mg/dl)	8.2
Magnesium (1.5-2.3 mg/dl)	2.2
Phosphate (2.5-4.5 mg/dl)	3.5
Triglyceride (30-150 mg/dl)	115
Total Cholesterol (< 200 mg/dl)	140
HDL Cholesterol (> 40 mg/dl)	39
S Lipase (37°C) (< 60 U/L)	79
S Amylase (IFCC 37°C) (28.0-100.0 IU/L)	85
S Lactate dehydrogenase (180-360 U/L)	670
Ck-MB (upto 25 IU/L)	19
C-Reactive Protein (< 0.6 mg/dl)	4.5
(b) CSF study	
Glucose (40-74 mg/dl)	87
Micro protein (10-50 mg/dl)	45
Chloride (116-122 mmol/l)	117
Adenosine deaminase (< 10 U/L)	2.0
(b) Other investigations	
MPDA	Negative
Dengue NS1	Negative
HBsAG	Non-reactive
Anti-HCV antibody	Non-reactive

*MPDA=Microarray pooled DNA analyzer; Dengue NS1=Dengue non-structural protein 1; HBsAG= Hepatitis B surface antigen; HCV= Hepatitis C virus

ELISA results indicated the patient was positive for scrub typhus infection. Following CSF study, the patient was provisionally diagnosed with meningitis (GCS value 4). He

was intubated and extubated following standard extubating criteria.

On the following day (06.11.2022), clinical investigation study of the patient was as follows: Hemoglobin=11.4 mg/dl, total leucocyte count=14,700/mm³, neutrophil content 69%, lymphocyte content 14%, monocyte content 17%, eosinophil content 17%, platelet count=253000/mm³, uric acid level= 23 mg/dl, creatinine content 0.78 mg/dl and bilirubin (total)= 0.58 mg/dl, sodium= 129 mmol/l, potassium= 4.0 mmol/l, bilirubin (direct)= 0.19 mg/dl, amylase= 54 IU/L and lipase= 39 IU/L. The clinical parameters recorded on 09.11.2022 were as follows: Hemoglobin= 11.6 gm/dl, PCV= 36.9, total leucocyte count=8400/mm³, platelet count= 3.6 lakh/mm³, neutrophil content 41%, lymphocyte content 48%, monocyte content 04% and eosinophil content 07%. Blood coagulation studies indicated the following results: P-Time =11.0 sec and INR=0.88. The laboratory investigation report of patient sample recorded on 09.11.2022 is shown in Table 2.

Table 2: Laboratory investigation of patient sample recorded on 09.11.2022

Laboratory investigations	Patient history (recorded on 09.11.2022)
(a) Laboratory parameters (with reference values in parenthesis)	
Total Protein (6-8 g/dl)	7.6
Albumin (3.2-5.0 g/dl)	4.2
Total bilirubin (0.1-1.0 mg/dl)	0.8
Direct bilirubin (0-0.3 mg/dl)	0.3
Urea (10-40 mg/dl)	19
Creatinine (0.5-1.5 mg/dl)	0.7
Creatine Kinase (24-170 IU/L)	103
Alanine Transaminase (5-35 IU/L)	28
Aspartate Transaminase (5-35 IU/L)	20
Alkaline Phosphatase (adult 110-310 IU/L)	240
Sodium (135-145 mmol/l)	136
Potassium (3.5-5.0 mmol/l)	4.0
Triglyceride (30-150 mg/dl)	116
Total Cholesterol (< 200 mg/dl)	150
HDL Cholesterol (> 40 mg/dl)	42
C-Reactive Protein (< 0.6 mg/dl)	2.4

The patient was intravenously injected with the following antimicrobials: Ceftriaxone (dosage-2 gm), Vancomycin (dosage-500 mg), Acyclovir (dosage-500 mg) and Doxycycline (dosage-100 mg). Besides these, Ranitidine (50 mg) and Ondansetron (4 mg) was administered as GI prophylaxis agents. The patient was also treated with the antiepileptic drug Levetiracetam (500 mg) for treatment of seizures.

4. Discussion

Scrub typhus is a seasonal disease with high incidence in the post monsoon season. The incidence of scrub typhus probably increases in this season because of the increase in growth of scrubs which enables the increase in mite populations. Several neurological manifestations have been observed in the setting of scrub typhus infection. These include meningitis, meningoencephalitis, seizures and altered sensorium as observed in previous studies [13, 26]. Central nervous system (CNS) involvement is a known complication of scrub typhus which ranges from aseptic meningitis to frank meningoencephalitis [27]. The causative organism, *Orientia tsutsugamushi*, is an obligate intracellular parasite of professional and nonprofessional

phagocytes that invades the central nervous system as part of systemic infection and is found in endothelial cells of blood vessels and in circulating phagocytes. Cases of acute encephalitis syndrome due to scrub typhus infection has been reported in an earlier study [28]. A case series of scrub typhus from Pondicherry reported meningitis as a common CNS complication [29].

In the current study, we report a case of scrub typhus infection in 14-year-old male patient with CNS dysfunction (GCS score = 4/15) associated with acute meningitis. Cases with meningitis have been reported to be associated with a lower rate of mortality (6.2%), than the higher rates among cases with renal impairment (57%), pulmonary complications (68%), hypotension requiring inotropes (84%), and hepatitis (59%) [11]. Incidence of CNS dysfunction and meningoencephalitis in cases of scrub typhus have been reported to range from 9.5% to 23.3% as reported in earlier studies [11, 29, 30].

As *Orientia tsutsugamushi* lacks a proper cell wall, the cephalosporin group of antibiotics is virtually ineffective against scrub typhus [31, 32]. The treatment of choice for scrub typhus is doxycycline. The antirickettsial drugs, azithromycin and doxycycline have both been shown to be effective in the treatment of scrub typhus, but the resolution of symptoms has shown to be faster in doxycycline compared to azithromycin [33].

5. Conclusion

In the current study, we present a medical case report of a 14-year-old male patient diagnosed with scrub typhus infection having CNS dysfunction and acute meningitis. The patient was reported to have fever for five days along with convulsion, syncopal attack, hyponatremia, neck rigidity and altered sensorium. The patient recovered on treatment with antimicrobials, GI prophylaxis agents and antiepileptic drug. The current study reports a case of neurological disorder in scrub typhus infection and is clinically important for undertaking future detailed surveillance, patient management, developing effective public health responses and public awareness to scrub typhus infection.

6. Acknowledgement

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7. Disclosure of conflict of interest

The author has no potential conflicts of interest to disclose.

8. Statement of ethical approval

The studies on patient samples were carried out after obtaining ethical clearance from the institution and informed consent.

9. Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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