

Scrub Meningoencephalitis – A Case Series

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Abstract: Scrub typhus caused by *Orientia tsutsugamushi* is a common zoonotic disease with high incidence in hilly areas of Manipur. Clinical presentation is variable with high mortality rate. We studied series of scrub cases who presented with features of meningoencephalitis. **AIM:** To study the clinical and laboratorial presentation of scrub typhus complicated by meningoencephalitis. **CASE SERIES:** We have collected 7 cases of scrub typhus admitted in medicine ward who presented with clinical features suggestive of meningoencephalitis over a period of one year (August 2017 to August 2018). It included 4 males and 3 females. Patients presented with 5-8 days of fever with 1-2 days of altered sensorium, convulsion, ataxia. Neurological examination showed fall in sensorium with neck stiffness. Eschar was present in 3 cases. All routine investigations and fever work up was done. Scrub typhus antibody was positive in all patients. CSF study was done in all cases showed raised protein with low normal sugar and lymphocytosis. Patients were treated with doxycycline or azithromycin along with other supportive measures. Two patients expired others improved without any neurological sequelae. **CONCLUSION:** All cases of fever with altered sensorium scrub typhus should be considered as a differential diagnosis and empirical therapy should be initiated in those patients comes from high endemic regions.

Date of Submission: 08-12-2018

Date of acceptance: 24-12-2018

I. Introduction

Scrub typhus or bush typhus is a zoonotic disease caused by *Orientia tsutsugamushi*, endemic in South East Asia, Northern Australia. Transmitted by bite of trombiculid mites commonly found in areas of heavy scrub vegetation during wet season.^[1,2] Commonly presents with fever, myalgia, cough and gastrointestinal symptoms after an incubation period of 6-21 days patients may develop complications like thrombocytopenia, acute kidney injury, pneumonitis and ARDS. Encephalitis is a rare complication of scrub typhus.^[1,2] neurological complications include seizure, cranial nerve deficits, vasculitic cerebral infarct, brain hemorrhages, polyneuropathy, sensorineural hearing loss, meningitis or meningoencephalitis.^[3,4] These manifestations may be due to direct invasion of CNS by the organism as has been shown by polymerase chain reaction (PCR) of cerebrospinal fluid (CSF)^[4] or may be due to the unique propensity of the organism to infect vascular endothelial cells, thereby causing microinfarct.^[5] Scrub typhus meningitis/meningoencephalitis remains an unclear entity and diagnosis have to be based on clinical features, especially on the presence of an "eschar" and positive serological test for scrub typhus. Although the organism can be detected in clinical specimens, serological tests are still an indispensable tool for diagnosis. Microimmunofluorescence is considered as the test of choice. However, this is not readily available, and its complexity limits its use. The Weil-Felix test using the Proteus OXK strain is a commercially available sero-diagnostic test. A minimum positive titer is 1:80 or a four-fold rise over previous levels is significant. Several studies have shown that Weil-Felix test has a high specificity.^[6] Another test that helps in rapid diagnosis with the good sensitivity is lateral flow format immunochromatographic test (ICT) for the detection of *O. tsutsugamushi* IgM, IgG antibodies.^[7] This study is done to know the clinical profile of scrub meningoencephalitis in Manipur.

II. Materials and Methods

Aim of the study was to know clinical presentation and laboratory findings in a scrub typhus patients complicated by scrub meningoencephalitis.

This is a hospital based prospective observational study undertaken in Department of Medicine, in a tertiary care center, Imphal, from the period August 2017 to August 2018.

Inclusion criteria

All patients above 12 years of age admitted in the Department of General Medicine with diagnosis of scrub typhus and having features of meningitis/meningoencephalitis.

Exclusion criteria

Patients having associated CNS diseases not related to scrub typhus (i.e., CVA, tumor, neurocysticercosis, epilepsy, etc.).

Cases where CSF analysis was not done.

Diagnosis of scrub typhus complicated with meningoencephalitis has been made if a patient presented with: Acute febrile illness with altered sensorium supported by eschar specific for scrub typhus plus serological test positive for scrub typhus (Weil–Felix test titer for OXK \geq 1:160 or positive immunochromatographic card test for detection of IgM antibodies to *O. tsutsugamushi*).

III. Results

Total seven scrub typhus cases complicated with encephalitis, admitted in medicine ward during August 2017 to August 2018 period of one year, 5 cases were male and 2 females. Mean age of the patients 35 ± 15.23 yrs.

Patients presented with 5-8 days of fever associated with myalgia, head ache, cough, abdominal pain, vomiting in variable extend, later developing altered sensorium and irrelevant talking for 1-2 days. generalized tonic clonic seizure was present in three patients(43%).

Initial neurological examination was showing a fall in sensorium in all patients(100%), neck rigidity in five patients(71%), focal neurological deficit in the form of hemiparesis in one patient(14%),none of patients showed cranial nerve palsies. Eschar(fig.1) was present in three patients (43%).

On investigation CBC showed normal or increased leukocyte count with thrombocytopenia in 4(43%) patients.LFT was showing mild elevation in bilirubin with four to five times elevation in liver enzymes in 6(86%) patients.KFT was deranged in four patients (43%), Urine routine showed mild proteinuria 6(86%) patients.NCCT brain was done in five patients came mild cerebral oedema in 2 patients and normal in 3 patients.Scrub typhus antibody test was positive in all patients done with help of SD bioline test kit. Other causes of meningoencephalitis like bacterial, viral, tubercular encephalitis, cerebral malaria, dengue, Japanese encephalitis work up was negative.

Image.1: Showing typical eschar of scrub typhus.



CSF study was done in all 7cases showed raised protein mean being 135.14 ± 76.83 mg/dl, with low normal sugar of mean 45 ± 5.50 mg/dl, and lymphocytosis in all cases(100%) with mean TLC of 22.14 ± 21 cells/cumm (tab.1)

Table.1 Showing CSF analysis of patients

CSF	Protein(mg%)	Sugar(mg%)	TLC(cells/cumm)
Pt 1	300	45	70(L86N14)
Pt 2	124	52	10(L90N10)
Pt 3	82	46	10(L80N20)
Pt 4	128	42	13(L70N30)
Pt5	102	52	30(L90N10)
Pt 6	140	38	6(L66N34)
Pt 7	74	40	16(L71N29)

Patients were treated with doxycycline 100mg twice daily orally for 10 days or injection azithromycin 500mg once daily for 5 days. Empirical ceftriaxone and other supportive treatments were given. Two patients expired during hospital stay(28%). Five patients recovered without neurological sequelae.

IV. Discussion

Scrub typhus is an acute febrile illness that may affect multiple organs, including the central nervous system (CNS).^[8]The common symptoms are fever, headache, myalgia, nausea, and vomiting, followed by breathlessness, gastrointestinal complaints, rash, and jaundice.^[9] An eschar at the site of larval feeding is the single most important diagnostic clue; however, it is less frequently seen in dark skinned people.^[8]Common neurological features are headache, altered sensorium, seizure, focal weakness, and neck stiffness.^[10] Systemic manifestations are more frequent in patients with CNS involvement. Rarely, immune-mediated CNS involvement may result in optic neuritis, myelitis, acute disseminated encephalomyelitis, and neuropathy.^[9] Pathologic findings of CNS involvement in scrub typhus include diffuse or focal mononuclear cellular infiltration of the leptomeninges, clusters of microglial cells, and brain hemorrhage. Cerebrospinal fluid (CSF) examination may reveal lymphocytic pleocytosis and raised protein levels.^[4]

Diagnosis in our patients was made with help of endemicity, history of fever more than 5 days with altered sensorium and other constitutional symptoms, Typical Escher, positive antibody testing, and CSF analysis. Other differential diagnosis like bacterial, viral, tubercular encephalitis, cerebral malaria, dengue, Japanese encephalitis were considered and excluded.

In this study deranged liver function in the form of raised enzymes and hypoalbuminemia was present in 6(86%), deranged KFT in the form of elevated creatinine 4(43%), leukocytosis in 43%, thrombocytopenia in 4(43%), and mortality was high (28%) cause of death was ARDS and Multi organ dysfunction, Others recovered without neurological sequelae

So timely, diagnosis and immediate treatment can cure scrub typhus patients. Clinician should have a high index of suspicion especially in patients presenting with fever and altered sensorium, associated with deranged liver function and elevated creatinine, and thrombocytopenia. They should be checked for eschar and tested for scrub typhus at the earliest.

V. Conclusion

In all cases of fever with altered sensorium scrub typhus should be considered as a differential diagnosis and empirical therapy should be initiated in those patients comes from high endemic regions.

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Raghavendra Ashok Navi. "Scrub Meningoencephalitis – A Case Series". IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 12, 2018, pp 72-74.