

Case Report

Atypical presentation of scrub typhus encephalitis with cerebral hemorrhage

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ABSTRACT

Scrub typhus, an arthropod borne infection caused by the rickettsial organism *Orientia tsutsugamushi*, is a fairly common disease in north-eastern sub-Himalayan India, particularly the forest areas, and is known to manifest with varied presentations ranging from non-specific fever to severe multi-organ complications. Hemorrhagic manifestations described in the literature are mostly gastrointestinal and genitourinary, secondary to vasculitis and/or thrombocytopenia, but reports of cerebral hemorrhage have been extremely rare. We report a case from sub-Himalayan eastern India where a 23 years old male tea plantation worker presented with recurrent convulsions with magnetic resonance imaging (MRI) brain showing multiple parenchymal hemorrhages with encephalitis involving both the cerebral hemispheres. Although patient developed fever and acute kidney injury later in the course, these were not the presenting complaints despite fever being the most consistent sign of a scrub typhus infection. We suggest consideration of scrub typhus as a differential diagnosis of a cerebral hemorrhage in endemic regions.

Keywords: Scrub typhus, Encephalitis, Cerebral hemorrhage, Atypical scrub typhus, Hemorrhagic manifestation

INTRODUCTION

Scrub typhus is a rickettsial disease caused by *Orientia tsutsugamushi*.^{1,2} It is mostly found in the Asia Pacific region including India, particularly sub-Himalayan forest areas.^{1,2} Manifestation of a scrub typhus mostly is an acute febrile illness, but encompasses severe complications involving renal, hepatic, vascular, gastrointestinal and central nervous system (CNS).³⁻⁵ Hemorrhagic manifestations have been reported as gastrointestinal and genitourinary and are believed to be secondary to vasculitis and/or thrombocytopenia related.^{2,6} Although CNS involvement like encephalitis and meningitis have been reported, cerebral hemorrhage is a very rare complication.^{7,8} Here we report a case of an atypical manifestation of scrub typhus presenting as encephalitis complicated as cerebral hemorrhage. High degree of

suspicion and prompt diagnosis can prevent mortality in a complicated scrub typhus patient.

CASE REPORT

23-year-old male, a tea plantation worker from Jalpaiguri district, West Bengal presented to the emergency department in an unconscious state with the chief complaints of recurrent convulsions since the last evening. The convulsions were sudden in onset, unprovoked, generalized tonic clonic type, and were preceded by vomiting, and associated with frothing from mouth. There was no history of tongue bite or bladder/bowel incontinence. The convulsions were followed by an altered state of sensorium and patient did not regain consciousness in between. There were 3 distinct episodes of convulsions as reported by the parents of the patient before being admitted. The parents denied any history of fever, head

trauma, history of prior seizure episode, substance abuse, or any major illness that required hospitalization prior to this episode.

General examination revealed the patient in an unconscious state, with high degree of irritability. Patient was afebrile at the time of presentation with the stable vitals as follow: pulse: 96/min, blood pressure: 120/80 mmHg, and respiratory rate: 18/min.

There was no pallor, cyanosis, clubbing, jaundice or edema, any visible rash or any other skin manifestation and there was no lymphadenopathy.

In the neurological examination, the Glasgow coma scale (GCS) was 7/13, E2V2M3; tone: exaggerated in all 4 limbs; superficial reflexes: corneal, abdominal, cremasteric, anal all were absent; plantar: extensor bilaterally; deep tendon jerks: exaggerated ankle, knee, biceps, supinator, triceps, all bilaterally; clonus: patellar and ankle clonus were present bilaterally; and other system examinations were unremarkable.

Course in hospital and investigations

Patient was started on anticonvulsants (phenytoin and levetiracetam) with other supporting measures (such as intravenous fluid, pantoprazole, ondansetron, mannitol, Ryle’s tube, Foley’s catheter) to stabilize and sent for MRI brain with routine baseline blood investigations which are described in Table 1.

Fasting lipid profile was within normal limits.

Viral markers with HBsAg, Anti-HCV and HIV were non-reactive.

MRI brain was suggestive of multiple sites of sub-acute hemorrhage with perilesional edema in anterior cranial fossa (46×21 mm) involving both the frontal lobes, right parietal lobe and surrounding edema (Figures 1 and 2) along with a DWI image of diffusion restriction in the splenium and corpus callosum, suggesting an encephalitis (Figure 3). MR angiography was normal.

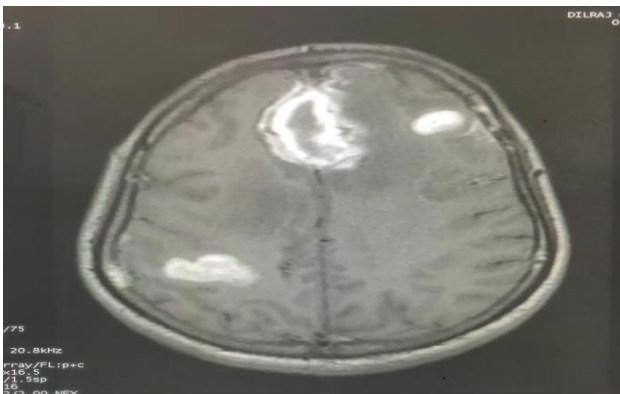


Figure 1: T1 weighted MRI.

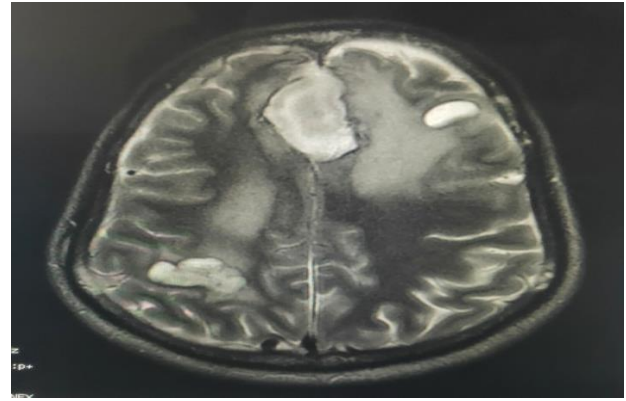


Figure 2: T2 weighted MRI.

Coagulation profile was unremarkable with an international normalized ratio (INR) of 1.2 and activated partial thromboplastin time (aPTT) of 30 seconds.

CSF examination reports are described in Table 2.

Table 1: Baseline blood investigations including blood counts, renal function test, electrolytes, liver function test.

Laboratory investigations	Values
Blood count	
Hemoglobin	16.0
Total leucocyte count (per mm ³)	12120
Neutrophil	78
Lymphocyte	21
MCV	72.5
Platelet (lakh/mm ³)	1.71
Renal function test and electrolytes	
Urea	51
Creatinine	1.1
Na ⁺	133.7
K ⁺	4.83
Liver function test	
Bilirubin (total)	1
Bilirubin (direct)	0.3
Bilirubin (indirect)	0.7
SGOT	91
SGPT	120
ALP	127
Protein (total)	8
Albumin	3.1
Globulin	3.9
LDH	156

Patient was started on ceftriaxone, vancomycin and acyclovir infusions (for encephalitis) but clinical condition was more or less unchanged with an altered sensorium and a high degree of restlessness.

By the 8th day of admission, patient developed fever with acute kidney injury with a urea of 131 and creatinine of

3.7. There was mild proteinuria (1+) with hematuria (RBC 7-8/hpf) with a negative culture report. Patient also had thrombocytopenia with a platelet count of 72,000/dl. Total WBC count dropped a little with 10640 cells/dl. We further tested for dengue serology which was negative, but scrub typhus serum IgM enzyme-linked immunosorbent assay (ELISA) was positive.

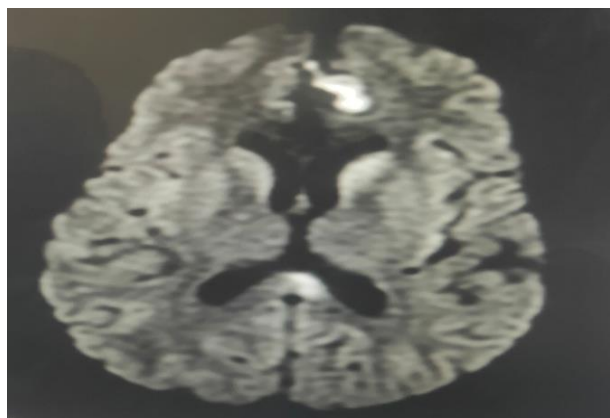


Figure 3: DWI MRI.

Table 2: Cerebrospinal fluid examination.

CSF examination	Values
Opening pressure	Normal
Appearance	Clear
Cell count	4
Cell type	All lymphocytes
Sugar	115
Protein	18
LDH	59
ADA	2.54
IgM for Japanese encephalitis	Negative
HSV 1 and 2 PCR	Negative

Doxycycline was started immediately via Ryle's tube feeding. Course of illness following adding doxycycline was improved dramatically. Patient's high level of irritability was visibly controlled by 12 hours. By 48 hours, patient had an improved sensorium with eye opening on verbal commands. From 3rd day of starting doxycycline, patient could accept oral feeding and we removed Ryle's tube and stepped-up oral feeding gradually over days. We discontinued acyclovir and vancomycin. Intravenous (IV) fluid was maintained along with physiotherapy and rehabilitation and patient kept improving. By 7th day of starting doxycycline, patient could communicate verbally and could sit on the bed after being aided by the healthcare staff. Renal function improved with a follow up creatinine of 1.2 mg/dl and urea 31 mg/dl. A follow up MRI brain the next week revealed a subacute hemorrhage and did not show any sign of encephalitis or edema. Patient continue to improve clinically with further physiotherapy and rehabilitation before he could be referred back to a local hospital to continue the rehabilitation.

DISCUSSION

Scrub typhus is an acute onset febrile illness caused by the rickettsia *Orientia tsutsugamushi*, and has been very commonly found in Asia Pacific region including India, particularly sub-Himalayan and other forest areas.^{1,2} This infection is known for a varied clinical picture ranging from a non-specific febrile illness to a life-threatening multi-organ complication including renal, hepatic, vascular, and central nervous system involvement.³ Common neurological complications have been described as meningitis and/or encephalitis.^{4,5} Bleeding manifestations mostly reported as gastrointestinal and genitourinary, and has been hypothesized as a consequence of vasculitis, coagulopathy or thrombocytopenia.^{2,6} Reports of a scrub typhus encephalitis transforming as a cerebral hemorrhage are extremely rare.^{7,8} Our case presented with recurrent convulsions from multiple brain hemorrhages with extensive perilesional edema and signs of encephalitis in the MRI brain. Moreover, the hemorrhages are not characteristic of a cerebrovascular accident, rather more likely to be explained by vasculitis. Fever has remained the most consistent reported clinical feature of scrub typhus.^{2,3,9}

Despite baseline investigations with leukocytosis, altered albumin to globulin ratio suggested an infective etiology, fever was absent at the early stage, even with encephalitis. The patient developed fever, thrombocytopenia and acute kidney injury only after a week of admission. In the view absence of any high-risk behavior and all the other possible conditions that could be responsible for a brain hemorrhage, along with the dramatic response to the doxycycline, we concluded the case as a scrub typhus infection presenting as an encephalitis, complicated by a cerebral hemorrhage with a delayed acute kidney injury. Other than the initial absence of fever, what further challenged the diagnosis in the beginning was absence of an eschar which is found in about 7% to 97% of patients in endemic areas.¹⁰

To our best knowledge this is the first case being reported where scrub typhus encephalitis complicated with intracerebral hemorrhage presenting in an afebrile state.

CONCLUSION

Scrub typhus can present with a life-threatening complication like cerebral hemorrhage and without the common presentations like fever or eschar. Cerebral hemorrhage should have scrub typhus as a differential diagnosis in endemic regions. Prompt diagnosis with an adequate antibiotic treatment in an early state can significantly reduce mortality in such a case.

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