



ACUTE DISSEMINATED ENCEPHALOMYELITIS AS A COMPLICATION OF SCRUB TYPHUS

Internal Medicine

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ABSTRACT

Scrub typhus is an acute febrile illness usually characterized by eschar, lymphadenopathy, multisystem involvement caused by *Orientia tsutsugamushi*. Scrub typhus as a cause of acute disseminated encephalomyelitis (ADEM) is extremely rare. This is a case report of a 40 years old female presenting with sudden onset altered sensorium, bilateral lower limb weakness with difficulty in walking, irrelevant speech, urinary and bowel retention since two days, high grade intermittent fever associated with headache and multiple episodes of vomiting for past one week. Cerebrospinal fluid study showed lymphocytic pleocytosis with mildly increased protein. MRI brain showed multifocal encephalitis & MRI spine revealed demyelination at spinal cord suggestive of ADEM. Paired CSF & serum scrub typhus IgM ELISA was found to be positive. She was ultimately diagnosed as a case of scrub typhus complicated with ADEM. After treatment with doxycycline and methylprednisolone patient improved dramatically without any residual neurological deficit during discharge. This case report highlights that scrub typhus should be included in the differentials in patients presenting with ADEM for early diagnosis and treatment in order to reduce mortality and morbidity.

KEYWORDS

Scrub typhus, ADEM, *Orientia tsutsugamushi*, Trombiculid

INTRODUCTION

Scrub typhus is an acute febrile illness usually characterized by eschar, lymphadenopathy, multisystem involvement and a rapid response to doxycycline. (1) It is a rickettsial infection caused by *Orientia tsutsugamushi* which spread to humans through the bite of larval stage trombiculid mites. (2) Central nervous system involvement in scrub typhus is a known complication which varies widely. Case fatality rate in scrub typhus may be as high as 30% if left untreated. Due to its nonspecific clinical presentation and limited awareness scrub typhus is grossly underdiagnosed in India. (3) Acute disseminated encephalomyelitis (ADEM) is an acute demyelinating disease of the central nervous system (CNS) which is usually monophasic in nature. (4) It is usually precipitated by an infection or immunization. However scrub typhus as a cause of ADEM is extremely rare. (5) Here we report a case of laboratory-confirmed scrub typhus who developed clinical features and imaging characteristics of ADEM.

CASE REPORT

A 40 years old female presented with sudden onset altered sensorium, bilateral lower limb weakness with difficulty in walking, irrelevant speech, urinary and bowel retention since two days, high grade intermittent fever associated with headache and multiple episodes of vomiting for past one week. There was no previous history of any neurological deficit as well as no significant family history of neurological disorders. There was no recent history of immunization. On general survey, patient was drowsy, hemodynamically stable and normal capillary blood glucose. On neurological examination, neck rigidity was present with positive Kernig's and Brudzinski's sign and there was loss of bilateral lower limb deep tendon reflexes (DTR) with hypotonia and plantar reflexes were bilaterally non-responsive. There were no signs of cranial nerve involvement. No abnormal movements was found. Other system examination revealed no abnormalities.

Complete hemogram, serum electrolytes, renal and liver function tests were normal. Non-contrast computed tomography findings of brain revealed no abnormalities. Serum sample for dengue NS1 antigen and IgM antibody Enzyme linked immunosorbent assay (ELISA), malaria parasite, malaria dual antigen test, typhi dot IgG & IgM, leptospira IgM ELISA and serology panel were negative. Cerebrospinal fluid (CSF) study showed increased cell count (70/mL) (ref: less than 5/ml) with lymphocytic predominance (95%), mildly increased protein (103 mg/dl) (ref: 15-50 mg/dl), normal sugar (56 mg/dl) (ref: 40-70mg/dl) and adenosine deaminase of 7.0 U/L. CSF for Japanese encephalitis IgM ELISA, Herpes Simplex Virus (HSV) 1 & 2 DNA polymerase chain reaction and Cartridge based nucleic acid amplification test (CBNAAT) for *Mycobacterium tuberculosis* were negative. CSF and

serum oligoclonal bands, anti-aquaporin 4 antibody and serum anti-MOG1 were negative.

The patient was started empirically on intravenous Ceftriaxone @ 4g/day and Acyclovir@1500mg/day in daily divided doses but no response was found within next three days. Paired CSF & serum scrub typhus IgM ELISA was then sent and came to be positive. Injection Doxycycline@200mg/day was added to the empirical regimen. Magnetic resonance imaging (MRI) of Brain with contrast showed altered intensity hyper on T2-weighted imaging. Fluid attenuated inversion recovery sequences (FLAIR) without restriction in diffusion weighted imaging (DWI) & apparent diffusion coefficient (ADC) without contrast enhancement was suggestive of encephalitis at brainstem, bilateral medial temporal region and bilateral insular cortex. Her MRI spine with contrast revealed demyelination at D10 segment to the distal cord and conus suggestive of ADEM. Injection Methylprednisolone intravenously @ 1g once daily for 5 days was started. Her sensorium gradually improved after 4 days with gradual normalization of tone, deep tendon reflexes and regain of power in both lower limbs. Limb physiotherapy was started and she was discharged after 2 weeks of hospital stay without any residual neurodeficit. On follow-up after 1 month she was doing well.



FIG 1: MRI of brain showing demyelination in bilateral medial temporal region



FIG 2: MRI of Brain showing demyelination in bilateral insular cortex

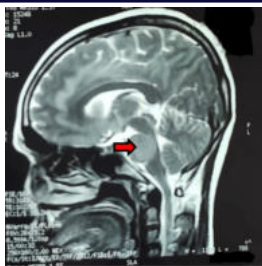


FIG 3: MRI of Brain showing demyelination in brain stem



FIG 4: MRI of brain showing demyelination in the D10 segment to distal cord

DISCUSSION

Scrub typhus is a zoonosis of the western Pacific islands and rural Asia, caused by *Orientia tsutsugamushi*, an obligate intracellular gram-negative bacterium. It is transmitted to humans by the bite of a larval trombiculid mite, commonly known as a chigger. It involves multiple organs including nervous system and is characterized by focal vasculitis or perivasculitis. (6) Common neurological manifestations are meningoencephalitis, cerebrovascular accident, acute transverse myelitis, Guillain Barre Syndrome and encephalomyelitis. ADEM is probably due to molecular mimicry, a cross reactivity between the host's myelin cells or peripheral nerve axons with *O. tsutsugamushi* antibody or antigens presented on infected cells which leads to activation of T and B lymphocytes with production of autoantibodies targeting above mentioned antigens resulting in demyelination. (7) Sudden onset altered sensorium and paraparesis, altered intensity hyper on T2 weighted MRI imaging and FLAIR without restriction in DWI & ADC supports the diagnosis of the ADEM. Lymphocytic pleocytosis with mildly increased protein in CSF also goes in favor of it. Paraparesis and bowel and bladder retention was probably due to myelitis which is comparable to findings on MRI spine with contrast revealing demyelination at cord D10 to the distal cord and conus. No previous history of any neurological symptoms & negative paired CSF and serum oligoclonal bands, anti-aquaporin 4 antibody and serum anti-MOG1 ruled out CNS demyelinating disorders. No recent history of vaccination also rules out post vaccination ADEM. Negative serological testing for common infective causes and positive paired serum & CSF scrub typhus IgM ELISA and good response to Doxycycline and steroid supports the diagnosis of post-infective ADEM due to Scrub typhus. Similar case reports were also mentioned by Wang et al. who reported a middle aged male presenting with fever, dysphagia and loss of speech with multiple lesions in brain & spinal cord in T2MRI and being tested positive for scrub typhus. (8) Roy S et al. reported a 5-year-old boy presented with high fever, altered sensorium, seizure, quadriplegia, and neck rigidity & was ultimately diagnosed as a case of scrub typhus with ADEM. (5) D. Rajesekar et al. published a case of scrub typhus as ADEM where a young male with chorea, meningoencephalitis, pyramidal and extrapyramidal tract lesions, left facial nerve palsy was tested positive for scrub typhus ELISA. (9)

CONCLUSIONS

This case report highlights scrub typhus as an emerging endemic disease in India with life threatening neurological complications such as ADEM. Clinicians should consider scrub typhus as a differential diagnoses in patients presenting with ADEM for early diagnosis and treatment in order to reduce mortality and morbidity.

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