

Scrub Typhus Associated with Central and Peripheral Nervous System Involvement: A Rare Diagnostic Entity

Sir,

Scrub typhus is an acute febrile illness endemic in areas of South East Asia, Japan, Australia, and the Pacific islands. It is caused by *Orientia tsutsugamushi*, an obligate intracellular Gram-negative organism that targets endothelial cells causing vasculitis leading to multisystem involvement.^[1] Meningoencephalitis is the most commonly described neurological manifestation. Peripheral nervous system involvement is relatively rare. Only a few case reports of Guillain–Barre syndrome (GBS) are described in the literature.^[2–4] Here we report a case of scrub typhus in a young male with central and peripheral nervous system involvement.

A 35-year-old farmer presented with 5 days history of high-grade fever, three episodes of seizures, and altered sensorium. There was no history of cough, loose stools, or burning micturition. On examination, subconjunctival hemorrhage was noted along with positive Kernig's sign and Brudzinski's sign and splenomegaly with a Glasgow Coma Scale (GCS) score of E3V3M4. There was no rash, eschar, or lymphadenopathy. Laboratory results showed white blood cell (WBC) of 12,180/mm³ (4000–10,000/mm³), hemoglobin of 10.7 g/dL (12–16 g/dL), platelet count of 36000/mm³ (15000–400000/mm³), aspartate aminotransferase/alanine aminotransferase (AST/ALT) 310/270 IU/L (5–35/5–40 IU/L), and total bilirubin of 3.3 mg/dL (0.2–1.4 mg/dL). Renal function tests showed blood urea of 82 mg/dL (8–20 mg/dL) and creatinine of 8.2 mg/dL (0.5–1.3 mg/dL). Antigen tests for malaria and typhi dot serology were negative. Dengue, hepatitis B, hepatitis C, human immunodeficiency virus 1 and 2, herpes simplex virus, and varicella-zoster virus testing by enzyme-linked immunosorbent assay (ELISA) was negative. *Leptospira* serological test was also negative.

Scrub typhus immunoglobulin IgM antibody was positive by solid-phase immunochromatographic assay in titer of 6.26 (normal-- <0.46).

Magnetic resonance imaging (MRI) Brain was normal. Cerebrospinal fluid (CSF) study showed cells of 80/mm³ (0–5/mm³), protein of 82 mg/dL (15–50 mg/dL), and glucose 58 mg/dL (45–80 mg/dL). Because of acute febrile encephalopathy with multisystem involvement in the form of meningoencephalitis, thrombocytopenia, hepatitis, and acute renal failure with a positive serological study of scrub typhus, the possibility of multiorgan dysfunction syndrome with scrub typhus was kept as a possibility. The patient was treated with doxycycline 100 mg twice daily, three cycles of hemodialysis for acute renal failure, and antiepileptics for seizures. His GCS score after 7 days of treatment was E4V5M6 and renal function tests were completely normalized.

Two weeks into the illness, the patient developed acute flaccid areflexic quadriparesis with bulbar involvement. Nerve conduction studies revealed prolonged distal latencies, reduced conduction velocities, and absent F responses involving motor nerves suggestive of demyelinating polyneuropathy with sparing of sensory nerve action potentials. CSF analysis revealed 8 cells/mm³ with lymphocytic predominance, normal glucose and protein values of 76 mg/dL.

Given the clinical, electrophysiologic profile, and CSF showing albumin cytologic dissociation, a possible diagnosis of post-infectious Guillain–Barre syndrome was made and the patient was treated with intravenous immunoglobulin (IVIG) at a dose of 2 g/kg body weight over 5 days and physiotherapy. The patient improved over the next 2 weeks and was discharged in stable condition when he was able to walk with minimal support.

Scrub typhus, caused by *Orientia tsutsugamushi*, transmitted by trombiculid mites is one of the commonest causes of acute undifferentiated fever constituting almost one-third of all undifferentiated fevers.^[5] The clinical picture is characterized by fever, rash, eschar, pneumonitis, and disseminated intravascular coagulation due to endothelial dysfunction leading to severe multiorgan failure like renal, hepatic, and central nervous system involvement in untreated cases.

Scrub typhus involves the nervous system frequently as a cause of mononuclear meningitis with or without encephalitis. Meningoencephalitis remains the most common neurological involvement throughout India and Asia.^[1,5] Other associated findings described are infarction, cerebral venous thrombosis, transient parkinsonism, and transverse myelitis.^[5] In contrast, peripheral nerve affection has been rarely reported in the literature, mainly as brachial plexopathy,^[6] cranial nerve palsy,^[7] and very few cases of GBS.^[1-4]

There are only three case reports of a GBS-like presentation after scrub typhus reported from India.^[8-10] Two of the reported cases had a GBS-like presentation^[8,10] while only one of them^[9] had meningoencephalitis followed by GBS in the recovery phase.

Pathogenesis of meningitis is ascribed to a possible vasculitis due to endothelial dysfunction, but it does not explain the occurrence of GBS, a post-infectious immune-mediated condition. It is evident from rat models that both T cell-mediated and humoral immunity are generated in scrub typhus and both types are also implicated in GBS pathogenesis. As *O. tsutsugamushi* is antigenically heterogeneous, so some epitopes among many antigens may play a role in the cross-reactivity due to molecular mimicry with axonal or Schwann cell membranes and the development of GBS.^[2] Our case had both central and peripheral nervous system involvement, which is extremely rare and has been described in a single case report from India.^[9]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Authors' contributions

Author 1,2,3 have helped in initial conceptualization and initial draft writing. Author 4 has helped with the final draft editing and submission.

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Conflicts of interest

There are no conflicts of interest.

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REFERENCES

- Ju IN, Lee JW, Cho SY. Two cases of scrub typhus presenting with Guillain-Barré syndrome with respiratory failure. *Korean J Intern Med* 2011;26:474-6.
- Lee SH, Jung SI, Park KH, Choi SM, Park MS, Kim BC, *et al.* Guillain-Barré syndrome associated with scrub typhus. *Scand J Infect Dis* 2007;39:826-33.
- Lee MS, Lee JH, Lee HS, Chang H, Kim YS, Cho KH, *et al.* Scrub typhus as a possible aetiology of Guillain-Barré syndrome: Two cases. *Ir J Med Sci* 2009;178:347-50.
- Lee HS, Lee YJ, Park HY. Guillain-Barre syndrome associated with Tsutsugamushi disease. *J Korean Neurol Assoc* 2007;25:275-7.
- Misra UK, Kalita J, Mani VE. Neurological manifestations of scrub typhus. *J Neurol Neurosurg Psychiatry* 2015;86:761-6.
- Sanjay Kumar Singh SK, Vidyasagar S. Brachial neuritis in association with scrub typhus: A rare presentation. *Int J Sci Res* 2015;4:2629-30.
- Kularatne SA, Fernando R, Selvaratnam S, Narampanawa C, Weerakoon K, Wickramasinghe S, *et al.* Intra-aural tick bite causing unilateral facial nerve palsy in 29 cases over 16 years in Kandy, Sri Lanka: Is rickettsial aetiology possible? *BMC Infect Dis* 2018;18:418. doi: 10.1186/s12879-018-3338-8.
- Sawale VM, Upreti S, Singh TS, Singh NB, Singh TB. A rare case of GuillainBarre syndrome following scrub typhus. *Neurol India* 2014;62:82-3.
- Phillips A, Aggarwal GR, Mittal V, Singh G. Central and peripheral nervous system involvement in a patient with scrub infection. *Ann Indian Acad Neurol* 2018;21:318-21.
- Juneja A, Anand K, Shah M. Guillaine Barre syndrome: A rare occurrence following scrub typhus. *Niger J Med* 2020;29:337.

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