Long-Segment Myelitis, Meningoencephalitis, and Axonal Polyneuropathy in a Case of Scrub Typhus

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Abstract

Scrub typhus, a mite-borne zoonotic disease, is endemic in several parts of India. It may cause multisystemic disease involving lungs, heart, spleen, liver, hematological system, and nervous system. Neurological involvement may include meningoencephalitis, cerebellitis, cranial nerve palsies, plexopathy, transverse myelitis, muscle dysfunction, neuroleptic malignant syndrome, parkinsonian syndrome, and Guillain–Barre syndrome. Here, we report a rare patient of scrub typhus, who developed meningoencephalitis followed by long-segment myelitis and axonal polyneuropathy, with hepatic, renal, hematological, and pulmonary involvement, following acute febrile illness with associated neurocysticercosis. He gained consciousness with a resolution of almost all of his complaints, with the exception of muscular power, which showed partial improvement following treatment with doxycycline, azithromycin, and steroids. What needs to be explored is whether the existence of neurological scrub typhus with neurocysticercosis is the coincidental price paid for living in the tropics or there is something more to it as in case of Japanese encephalitis and neurocysticercosis co-infection.

Keywords: Axonal polyneuropathy, long-segment myelitis, meningoencephalitis, scrub typhus, zoonosis

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Introduction

Scrub typhus is a vector-borne zoonosis caused by *Orientia tsutsugamushi*, which is transmitted by the bite of larvae of trombiculid mites.[1]

It is widely distributed worldwide and occurs from Japan, through China to the Philippines, till Australia in the south and

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west through India, Pakistan, Tibet, Afghanistan, and southern parts of the USSR in the north.[2]

In India, this disease has become endemic in various parts of the country like in whole of the Shivalik ranges from Kashmir to Assam, the Eastern and Western Ghats, and the Vindhyachal and Satpura ranges in the central part of India.[2,3]

The disease is characterized by an early phase, which comprises chills and fever, occurring by the 3rd–4th day of bite, and rash and lymphadenopathy appear at the end of the 1st week.[4] The incubation period ranges from 6 to 20 days.[5] The late phase occurs by the 2nd week of illness and comprises of systemic manifestations, such as pneumonitis, pleural effusion, hepatomegaly, edema, acute kidney injury, acute respiratory distress syndrome, and meningitis.[6]

The disease may affect various organs of the body such as lungs, heart, spleen, liver, hematological system, and central nervous system due to inflammation of the blood vessels.[7]

Its neurological manifestations include acute meningoencephalitis and rarely cerebellitis, cranial nerve palsies, plexopathy, transverse myelitis, muscle dysfunction, neuroleptic malignant syndrome, parkinsonian syndrome, and Guillain–Barre syndrome.[8-12]

This report describes a case of scrub typhus with unusual neurological manifestations with co-infection with neurocysticercosis, probably for the first time.

Case Report

A 17-year-old adolescent presented to the casualty department with a history of 15 days of moderate-grade fever and headache. After 4 days, he developed jaundice and generalized convulsive status epilepticus. In the next 4 days, his clinical condition deteriorated and he was referred to our institute.

On admission, he was in shock, pallor and icterus were present, and he had a labored respiration. There were bilateral crepitation in the chest and mild hepatosplenomegaly, and cardiac auscultation was within normal limits. Neurologically, his Glasgow Coma Scale was E3V3M4, plantars were not elicitable, pupils were of normal size and were normally reacting to light, and neck rigidity was present. He was admitted to the Intensive Care Unit and, in view of respiratory failure, he was put on ventilatory support.

He had mild anemia and thrombocytopenia. On biochemistry, there was evidence of hepatic and renal dysfunction. Cerebrospinal fluid (CSF) showed 15 cells/mm^3, all of which were lymphocytes; protein was 113.8 mg/dl, sugar was 107.1 mg/dl, and the smear was negative for acid-fast bacilli, *Cryptococcus*, and Grams staining. The CSF bacterial, tubercular, and fungal cultures and HIV ELISA were negative. His magnetic resonance imaging (MRI) of the head showed gyriform swelling with signal intensity alteration in the form of patchy restriction of diffusion in bilateral parieto-occipital region, left frontal region, and bilateral thalami. Patchy leptomeningeal enhancement was noted over bilateral cerebral convexities, Sylvian fissure, and basal cisterns. Few peripherally cystic lesions were noted in the fourth ventricle. Few areas of T1 hyperintensity showing blooming on gradient echo imaging were noted in few of the cysts. Magnetic resonance (MR) angiography and MR venography showed no significant abnormality. The impression was that of meningoencephalitis with racemose neurocysticercosis of the fourth ventricle [Figure 1].

His serum immunoglobulin (Ig) M and IgG for Leptospira and Toxoplasma and CSF viral markers for dengue, herpes simplex, varicella zoster, Japanese encephalitis, Epstein–Barr virus, *Cytomegalovirus*, Japanese encephalitis, and West Nile virus were negative. His serology in duplicate was positive for antiscrub typhus IgM antibody using InBios International, Inc., USA, ELISA test.

He was started on doxycycline 100 mg twice a day, antiepileptics, and empirical hepatic- and renal-safe antibiotics. He gradually started recovering. His liver and renal parameters became normal within 7–10 days. His ventilatory dependency reduced slowly and he regained his sensorium. When he gained sensorium, it was noticed that he had quadriplegia. On neurological examination, there was hypotonia in all the four limbs, and the power was 2/5 in bilateral upper limbs and 0/5 in bilateral lower limbs on Medical Research Council (MRC) scale. Deep tendon reflexes were absent and planter reflexes were not elicitable. We could not find any clear-cut sensory level. MRI of the spine revealed intramedullary T2 hyperintensities from C2 to D1, suggestive of myelitis [Figure 1].

Nerve conduction velocity was done which showed decreased amplitudes and mildly decreased conduction velocities, suggestive of sensory-motor axonal polyneuropathy [Table 1]. His electroencephalogram showed slow waves in bilateral frontal and parieto-occipital regions and visual-evoked potential revealed prolonged latency. His anti-aquaporin-IV antibody and autoimmune profile was negative. He was started on methyl prednisolone, albendazole, and azithromycin. Gradually, his limb power started improving and, at the time of discharge, his upper limb power was 4/5 and lower limb power was 2/5 on MRC scale. However, after 3 months of follow-up, his power had still not recovered completely.

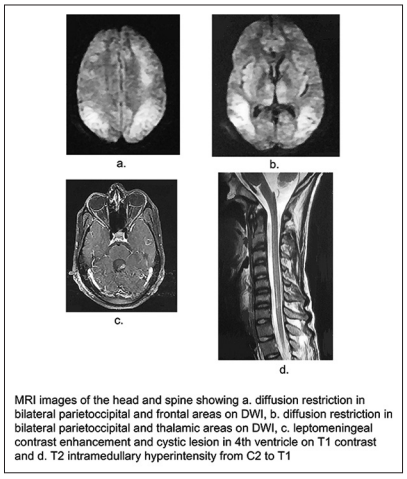
Discussion

The presence of fever with hepatorenal involvement suggested the diagnosis of scrub typhus in this patient, even in the absence of eschar, which was confirmed by IgM ELISA.

The differential diagnosis of hepatic and renal involvement includes leptospirosis, dengue, malaria, and viral hepatitis,[13-16] the laboratory investigations of which were found to be negative in this patient and that of meningoencephalitis with myelitis including dengue fever, herpes simplex,

Table 1: Nerve conduction studies of the patient

Nerve/sites	Latency in ms	Amplitude in mV	Velocity in m/s
Right median motor	Wrist 3.85, elbow 6.65	Wrist 2.4, elbow 1.7	46
Right ulnar motor	Wrist 2.19, below elbow 7.71	Wrist 2.6, below elbow 2.4	43
Right tibial motor	Ankle 4.53, popliteal fossa 17.14	Ankle 1.9, popliteal fossa 1.1	39
Right common peroneal nerve motor	Absent	Absent	Absent
Right median sensory	Onset 2.92, peak 3.39	9.0	38
Right ulnar sensory	Absent	Absent	Absent
Right sural sensory	Absent	Absent	Absent



MRI images of the head and spine showing a. diffusion restriction in bilateral parietoccipital and frontal areas on DWI, b. diffusion restriction in bilateral parietoccipital and thalamic areas on DWI, c. leptomeningeal contrast enhancement and cystic lesion in 4th ventricle on T1 contrast and d. T2 intramedullary hyperintensity from C2 to T1

Figure 1: Magnetic resonance imaging of the head and spine of the patient

varicella zoster, Japanese encephalitis, Epstein–Barr virus, *Cytomegalovirus,* and West Nile virus infections[17-22] were also found to be negative.

Until now, only one case of long-segment myelitis in a person with scrub typhus has been reported.[23]

Inflammation of the blood vessels has been shown to be the probable basis of systemic complications in scrub typhus, and it is possible that either direct or autoimmune vasculitis could be the possible cause of polyneuropathy and long-segment myelitis in this case.[8]

People have shown polyneuropathy with scrub typhus infection, but what has been shown is of demyelinating type in contrast to our patient, whose involvement was of axonal kind.[24]

However, our patient had long-segment myelitis, meningoencephalitis, sensory-motor axonal polyneuropathy as well as co-infection with neurocysticercosis with partial improvement in power and most of the symptoms following treatment with doxycycline and azithromycin, which has probably never been reported earlier. Furthermore, what remains to be explored is whether co-infection with neurocysticercosis and scrub typhus is coincidental price paid for living in the tropics or there is something more to it as in case of Japanese encephalitis and neurocysticercosis co-infection.[25] The surface glycoprotein of the cysticercal cyst may act as an antigen against which the host immune system may respond by forming antibodies, which may worsen the disease in case of scrub typhus as in case of Japanese encephalitis or these two infections may be separate entities.[19]

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.

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Conflicts of interest

There are no conflicts of interest.

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