Guillain-Barre' Syndrome Following Scrub Typhus: A Rare Case

Sir,

Guillain-Barre' syndrome (GBS) is an illness characterized by areflexic ascending paralysis with minimal sensory involvement.[1] It has been reported as a sequela of several infections and vaccinations that may elicit an immune cross-reactivity with axonal or Schwann cell membranes.[2] Many patients have had an infection within the previous 6 weeks, most commonly a flu-like illness but also *Campylobacter jejuni* gastroenteritis, Epstein-Barr virus (EBV) or Cytomegalovirus infections (CMV).[3,4] Scrub Typhus caused by *Orientia tsutsugamushi* is a systemic illness that causes generalized vasculitis.[5,6] *O. tsutsugamushi*, an obligate intracellular bacterium, was isolated for the first time in 1930.[5] Scrub Typhus is a public health problem in Asia, where about 1 million new cases are identified annually and 1 billion people may be a risk of this disease.[6] GBS has not been previously reported as a complication of Scrub Typhus, and peripheral nerve system (PNS) involvement following Scrub Typhus has not been investigated systematically either. We report here a case of GBS that occurred following infection with *O. tsutsugamushi*.

A 56-year-old male was referred to our hospital, with progressive weakness (distal to proximal direction), bilateral facial palsy with diplopia in the left lateral gaze. He had a history of travel to Salt Lake area in West Bengal around 3 weeks back, where he had, insect bite in the right lower abdomen followed by the development of ulcer at the same site [Figure 1]. After 3 days, the patient developed mild fever with chills and myalgia. His initial blood tests there revealed normal parameters except for a platelet count of 58,000/cumm, also the levels of SGOT, SGPT and indirect bilirubin were deranged. He was consulted by a local physician who prescribed IV antibiotics and supportive treatment. Fever, chills and myalgia subsided and the patient recovered in 5 days. However, after 1 week, the patient developed inability to wear foot wares, which later progressed to difficulty in getting up from the squatting position over the next 2 days. Symptoms progressively worsened and the patient became bed-bound along with weakness of the upper limbs, bilateral facial involvement and diplopia in the left lateral gaze. The patient presented in our ER with the above complaints.

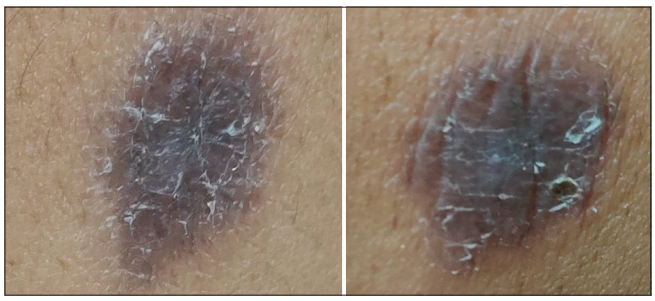

Figure 1: Different stages of healing of the abdominal eschar

On detailed neurological examination, quadriparesis with predominance in the lower extremity (MRC grade III), facial diplegia, left lateral gaze palsy, and areflexia were noted. Sensory system, bladder bowel and other cranial nerves except the facial nerve and sixth nerve were intact. On electrophysiologic studies, demyelinating patterns of motor neuropathies were noted. These findings were compatible with neurophysiologic criteria for acute inflammatory demyelinating polyradiculoneuropathy (AIDP).[1] Mild pleocytosis(10cells/mm^3)withpredominantlymphocytes(80%) and increased protein (227 mg/dl) were found in the cerebrospinal fluid (CSF). A blackish eschar was detected at the right side of the abdomen, which along with background history of insect bite lead us to consider a possibility of Scrub Typhus. Weil-Felix test was done which turned out to be strongly positive for rickettsial infection. The serum antibody titer to *O. tsutsugamushi*, which was measured using an indirect immunofluorescent antibody (IFA) assays, was 1:5120. Further tests revealed that, serum bilirubin was 3.2 mg/dl with a direct bilirubin of 1.0 mg/dl, SGOT level of 362 U/L, and SGPT level of 650 U/L. ELISA for Anti Leptospira IgM was negative, urine qualitative porphobilinogen spot assay was also negative. Serum potassium was 4.7 meq/l and serum TSH was 1.07 uU/mI.

Punch biopsy of eschar followed by histopathology and DNA PCR was performed, it was positive for *O. tsutsugamushi*. For the screening of other infectious etiologies of GBS, stool culture for *C. jejuni* and serological tests for Mycoplasma pneumonia, CMV, HIV, Hepatitis A, B, C, E, and EBV were performed. All results were within the normal range. Antibodies to ganglioside GM1 were not detected. Based on the tests and clinical presentation, the diagnosis of 'GBS following antecedent scrub typhus infection' was made. The patient was put on intravenous Immunoglobulin (IVIg, 2 g/kg, over 5 days), injection Doxycycline 100 mg intravenous BD with symptomatic and supportive treatment. The patient showed remarkable neurological recovery after IVIg therapy.

O. tsutsugamushi infection is characterized by fever, rash, eschar, pneumonitis, meningitis, and disseminated intravascular coagulation, which leads to severe multiorgan failure in untreated cases. Typically, patients with vasculitic neuropathy have painful sensory loss and weakness in the distribution of multiple peripheral nerves, which is referred to as mononeuritis multiplex.[7,8] However, the systematic review of PNS involvement in scrub typhus is rare. Our case showed the pattern of AIDP with symmetrical ascending demyelinating motor neuropathy including both facial nerves, and left abducent nerve which was not compatible with vasculitic neuropathy. To the best of our knowledge,

GBS associated with rickettsial infections is very rare. An association between an infection with Rickettsia conori and GBS was reported in a French study in 1968.[9] Additionally, GBS with Rocky Mountain spotted fever was reported in 1996.[10] Although its pathogenesis has not been completely determined, GBS may be induced by molecular mimicry, toxins, or immune dysregulation.[2] Interestingly, in patients with scrub typhus, both humoral and cellular immunities are activated and play a role in the clearance of *O. tsutsugamushi*.[5] In our case, mild pleocytosis (10 cells/mm^3) was detected. However, CSF antibodies to *O. tsutsugamushi* and other viral markers (antibodies for EBV, CMV, Hepatitis A, B, C, E, and HIV) were not detected. In general, CSF findings in GBS show albuminocytologic dissociations. In other words, a few or no lymphocytes exist.

In conclusion, IVIg was effective in the treatment of our case. Further studies are needed to understand the clinical characteristics of peripheral neuropathy in GBS patients with Scrub Typhus and to elucidate the pathophysiology of GBS in Scrub Typhus.

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.

Shishir Pandey, Dinesh Chaudhari, Pushpendra N. Renjen, Kamal Ahmad[1]

Departments of Neurology, Institute of Neurosciences, and [1]Internal Medicine, Indraprastha Apollo Hospitals, Sarita Vihar, New Delhi, India

Address for correspondence: Dr. Puspendra N. Renjen, C-85, Anand Niketan, New Delhi - 110 021, India.
E-mail: pnrejen@hotmail.com

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