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Acute Flaccid Paralysis: A Rare Presentation Following Scrub Typhus

Dr Megha VS, Dr M Ramadevi, Dr C Ramesh Kumar
Third year postgraduate, Department of General Medicine, SVMC, Tirupati
Associate professor, Department of General Medicine, SVMC, Tirupati
Assistant professor, Department of General Medicine, SVMC, Tirupati

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ABSTRACT
Introduction: Scrub typhus, a zoonotic disease prevalent in Southern Asia, particularly in India and China, is caused by *Orientia tsutsugamushi* and transmitted by larval chiggers of Trombiculid mite. It ranges from a nonspecific febrile illness to a multisystem disorder, with neurological manifestations like meningoencephalitis, aseptic meningitis, cerebellitis, and delirium. Guillain-Barré syndrome associated with Scrub typhus is extremely rare such that only four cases reported from India so far.[8-10]
Case report: We report a 47-year-old male with rapidly progressive ascending flaccid quadriparesis, including respiratory muscle paralysis , following high fever and a classic scrub typhus eschar. He tested IgM positive for scrub typhus with cytoalbuminogenic dissociation on CSF analysis and demyelination on electromyogram and nerve conduction studies meeting Brighton's criteria for Guillain-Barré syndrome. He recovered after plasmapheresis and doxycycline treatment.
Conclusion: The antigenic heterogeneity of *O. tsutsugamushi* may lead to Guillain-Barré syndrome through molecular mimicry. This case underscores the importance of early detection of this condition and management with IVIG/ plasmapheresis and Doxycycline.

I. INTRODUCTION

Scrub typhus, a zoonotic disease prevalent in Southern Asia, notably India and China, poses a significant public health challenge.[1]It is caused by the obligate intracellular Gram-negative bacterium *Orientia tsutsugamushi*, transmitted by bite of larval chiggers of trombiculid mites. This disease is the most common cause of acute undifferentiated fever marked by headache, myalgia, lymphadenopathy, rash, and eschar. It can escalate to severe multiorgan dysfunction due to its predilection for endothelial cells, leading to widespread vasculitis and inflammation that affect the lungs, liver, heart, and central nervous system, often resulting in high mortality.[2] Neurological complications such as aseptic meningitis, meningoencephalitis, and cerebellitis are common, but peripheral nervous system involvement, including mononeuritis multiplex, cranial nerve palsies and Guillain-Barré syndrome (GBS), is rare. Particularly, GBS is exceptionally rare and necessitates meticulous diagnosis, with only a few cases documented globally[3-5] and four reported in India[6-8]. Timely diagnosis is crucial to avoid ineffective treatments and facilitate prompt, potentially life-saving interventions, especially in endemic regions. Here, we present a case of scrub typhus in a young male with GBS.

II. CASE REPORT

A 47-year-old male farmer presented to EMD, with buckling of knees while walking and tingling sensation in both legs for 3 days, progressing to difficulty in standing from sitting position over two days. On the second day of hospitalization, he experienced upper limb weakness and difficulty swallowing, leading to intubation due to respiratory paralysis. He had a recent history of high-grade fever for 3days & was prescribed antipyretics & antibiotics which he stopped after 2 days once the fever subsided. No history of yellowish discolouration of eyes and urine, bleeding manifestations, chest pain, breathlessness .Patient had no comorbidities and not on any medications

On examination, patient's GCS was E4VTM5 and his vitals were stable. General physical examination revealed non-tender black escharon the right flank and bilateral nontender inguinal lymphadenopathy was noted. Motor examination shows normal muscle bulk with power of 2/5 in the lower limbs and 3/5 in the upper limbs, accompanied by hypotonia. Reflexes were diminished in the upper limbs (DTR 1+) and absent in the lower limbs (DTR 0) with no response for plantar reflexe bilaterally. Sensory, autonomic, bowel, bladder, and cranial nerve functions were intact. Respiratory and cardiovascular system examination were normal. Abdominal examination revealed no organomegaly.

The patient's comprehensive blood tests, encompassing CBC,RFT,LFT and serum electrolytes, all revealed normal results.Additionally, a full urine examination and ECG exhibited no anomalies.

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Remarkably, Scrub typhus Ig M was positively detected via ELISA, while tests for leptospirosis and dengue were negative. The Weil-Felix test displayed strong positivity. Serology for various viruses, including CMV,EBV, Hepatitis A,B,C,E, and HIV returned negative results. Stool culture for C.jejuni was also negative. In cerebrospinal fluid(CSF) analysis, cytoalbuminogenic dissociation was observed, with specific values showing a protein level of 1.6 g/dL, albumin at 0.9 g/dl, and glucose at 102 mg/dL. The total cell count in the CSF was 4,with 100% lymphocytes. However, cultures, AFB staining, and gram staining of the CSF were all negative. MRI brain scans with DWl and angiogram displayed normal results. Electromyogram and nerve conduction studies indicated demyelinating polyneuropathy, primarily affecting the lower limbs as prolonged distal motor latencies, absent F wave and slowed motor conduction velocities with abnormal sensory nerve action potentials in the upper extremities compared to the sural nerve.

During the course in hospital, patient was started on Cap Doxycycline 100 mg bd & Intravenous Immunoglobulin at 2g/Kg over 5 days. Gradually patient's muscle power improved and was weaned off the ventilator on day 9. He was discharged in stable condition when he started to walk with minimal aid.

III. DISCUSSION

Infection with O.tsutsugamushi presents a range of symptoms, including fever, rash, eschar, pneumonitis, meningitis, and in severe cases, disseminated intravascular coagulation leading to multiorgan failure if left untreated[2].

Scrub typhus frequently affects the central nervous system, causing Meningoencephalitis which is the most common neurological manifestation in India and Asia. Other reported findings include infarction, cerebral venous thrombosis, transient parkinsonism, and transverse myelitis. However, peripheral nerve involvement is rarely documented, mostly presenting as brachial plexopathy, cranial nerve palsy, and a few cases of Guillain-Barré syndrome. Vasculitic neuropathy, typically manifests as painful sensory loss and weakness affecting multiple peripheral nerves,a condition referred to as mononeuritis multiplex [9,10]

To our knowledge, the association between Guillain-Barré Syndrome (GBS)and rickettsial infections is exceedingly rare.Our case displayed a pattern consistent with Acute Inflammatory Demyelinating Polyradiculoneuropathy (AIDP), characterized by symmetrical ascending demyelinating motor neuropathy, along with bulbar involvement. This pattern was not in line with vasculiticneuropathy. There have been reports of GBS associated with infections like Rickettsia conorii in a French study back in 1968(11) and GBS with Rocky Mountain spotted fever in 1996.(12)The exact mechanism behind how these infections trigger GBS remains incompletely understood but may involve factors like molecular mimicry,toxins, or immune dysregulation.

Interestingly, in scrub typhus patients,both humoral and cellular immune responses are activated and contribute to the clearance of O.tsutsugamushi. Due to the antigenic heterogeneity of *O. tsutsugamushi*, certain epitopes among its various antigens might contribute to cross-reactivity through molecular mimicry with axonal or Schwann cell membranes, potentially leading to the development of GBS.

The immunofluorescent assay (IFA) and indirect immunoperoxidase test (IIP), which utilize cell-culture-derived *O. tsutsugamushi* antigens performed on paired admission and convalescent samplesare considered the 'gold standard' diagnostic tests for scrub typhus[13,14]. They are, however, superior to the old Weil–Felix test (based on detection of antibodies cross-reactive to antigens of the OX-K strain of the unrelated bacteria Proteus mirabilis)[15].

Unless contraindicated, doxycycline is the standard treatment with an adult oral dose of 100 mg twice daily for 7 days. Alternatively Azithromycin (1000–500 mg on the first day followed by 500–250 mg daily for 2 days) is an effective alternative if tetracyclines are contraindicated such as pregnancy.

The diagnosis of Guillain -Barré Syndrome (GBS) is based on Brighton's criteria, which includes clinical, CSF analysis and electrophysiologic profile. Clinically symmetrical ascending flaccid paralysis with hyporeflexia or areflexia and CSF analysis revealing albuminocytological dissociation with ENMG showing demyelinating polyradiculopathy in the absence of identified alternative diagnosis confirms GBS.

Treatment includes Plasmapharesis or administering Intravenous Immunoglobulin at the rate of 0.4mg/kg/day over 5 days. If rapid progression involving respiratory and neck muscles, bulbar involvement, autonomic fluctuations should be admitted to ICU and intubated if needed along with supportive care.

IV. CONCLUSION

Guillain-Barré syndrome (GBS) following scrub typhus infection is rare and often underreported. In endemic areas, it is crucial to promptly rule out scrub typhus in any GBS case of unknown etiology to avoid unnecessary treatment . High suspicion is essential, especially for those at risk of chigger bites, occupational or recreational, as early detection and

treatment can be lifesaving.

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