Case Report

DOI: 10.7860/JCDR/2017/28390.10629

Internal Medicine Section

Guillain-Barre Syndrome with Falciparum Malaria and Scrub Typhus Mixed Infection-An Unusual Combination

RAHUL SAI GANGULA[1], WEENA STANLEY[2], ARUNSHESHU VANDANAPU[3], M MUKHYAPRANA PRABHU[4]

ABSTRACT

Guillain-Barre Syndrome is very rare in parasitic and rickettsial infection. Here we report a case of Plasmodium falciparum and scrub typhus mixed infection, presented with quadriparesis. Clinical, Serological, CSF analysis and Nerve Conduction Studies were consistent with Acute Inflammatory Demyelinating Polyneuropathy (variant of GBS). After administration of antimalarials and antibiotics for the mixed infection, patient gradually improved.

Keywords: Areflexia, Cyto-albuminogenic dissociation, Hypotonia, Procalcitonin, Quadriparesis, Vasa-nervosum

CASE REPORT

A 40-year-old male patient daily-wage worker presented to our Emergency Triage with chief complaints of fever since 15 days and difficulty in walking since five days. Fever was sudden in onset, intermittent in nature, high grade associated with chills and rigors, occured once in 2-3 days, subsided with antipyretics or on its own with profuse sweating. After 10 days of commencement of the fever, he had developed motor weakness which progressively increased to a state where he was not able to stand without support. At the time of presentation his weakness had attained a plateau phase with no steady worsening. He presented with quadriparesis with weakness more in the lower limbs. Bowel and bladder functions were intact.

At the time of admission a body temperature of 102ºF, blood pressure of 130/90 mmHg, pulse rate of 84 beats/min and respiratory rate of 18 breaths/min were noted. Physical examination revealed mild icterus and Grade 3 pan-digital clubbing. There was no palpable mass or hepatosplenomegaly. Higher mental functions were intact and cranial nerves were normal. Patient had hypotonia and areflexia of all four limbs and decreased power of lower limb muscles.

History and clinical examination were suggestive of Guillain-Barre Syndrome (GBS). However, other diagnoses like seroconversion of retroviral illness, snake bite were considered.

Laboratory Reports: Lab reports are given in [Table/Fig-1].

Antibodies to *Orienta tsutsugamushi* (scrub typhus-IgM) were detected by ELISA. Malaria Parasite Quantitative Buffy Coat (MPQBC) was positive for *Plasmodium falciparum* (the patient was from a coastal area and from a scrub endemic area, serology was sent for these investigations). Ultrasound of abdomen and pelvis had shown mild hepatomegaly. Baseline ECG was normal.

Lumbar puncture was done and CSF analysis showed cells of 30/cumm and protein slightly elevated (CSF Protein-53 mg/dl). Sensory nerve conduction studies showed mildly reduced SNAP amplitude in bilateral sural nerves. Motor nerve conduction studies had showed markedly reduced CMAP amplitude in right peroneal compared to left peroneal nerve with mildly prolonged Distal Latency (DL): CMAP'S reduced more than 50 percent in right tibial compared to left side with decreased conduction velocities: bilateral median nerve mildly prolonged DL's. F-waves were not recordable in right peroneal nerve; in rest other nerves were normal.

Parameters	Range
ESR	63
Haemoglobin	8.6 gm%
White Cell Count	7200/mcl
Platelet Count	182,000/mcl
Serum Urea	24 mg/dl
Serum Creatinine	0.7 mg/dl
Serum Sodium	125 mmol/l
Serum Potassium	4.8 mmol/l
Serum Total bilirubin	1.9 mg/dl
Serum Direct bilirubin	1.0 mg/dl
Aspartate Transaminase	46 IU/l
Alanine Transaminase	20 IU/l
Alkaline Phosphatase	61 IU/l
Serum Protein	6.30 gm/dl
Serum Albumin	3.03 gm/dl
Serum Globulin	3.30 gm/dl
Random blood sugar	96 mg/dl
Procalcitonin	1.834 mcg/l (positive)
Peripheral smear	Normocytic normochromic to microcytic hypochromic red cells, target cells, polychromasia, anisopoikilocytosis, occasional fragments of RBC, ring forms and gametocytes of *Plasmodium falciparum*

[Table/Fig-1]: Lab parameters.

Nerve conduction studies had confirmed acute inflammatory demyelinating polyneuropathy-variant of GBS. Brighton's criteria were reviewed for the confirmation of GBS [1].

Patient was started on artesunate and antibiotics-ceftriaxone and doxycycline. According to Updated WHO policy recommendation (October 2012) Global Malaria Programme-Single dose primaquine (0.75 mg base/kg) as a gametocytocide in *Plasmodium falciparum* malaria was given after Glucose-6 Phosphate Dehydrogenase levels were found out be in normal range (24 U/gm Hb) [2].

Intravenous Immunoglobulins (IVIG) and plasmapheresis was considered in the patient but was not started as patient started improving symptomatically after fifth day of antimalarials and antibiotics. Only antimalarial's, antibiotics and physiotherapy were given to the patient, and he started improving symptomatically and gradually started walking without support.

DISCUSSION

Guillain-Barré Syndrome (GBS) is a well known condition that most often presents as acute monophasic paralysing illness, associated with antecedent infection especially viral [3]. Other triggering bacterial infections (e.g., *Mycoplasma* [4], *Campylobacter jejuni* [5], *Haemophilus influenza* [6]) are also well recognised. Association with protozoal infection has been documented in case reports with *Leishmania donovani* [7], *Plasmodium falciparum* [8] *and Plasmodium vivax* [9] malaria in a limited number of patients. Association with rickettsial infections has been documented in case reports with *Orienta tsutsugamushi* [10], *Rickettsia rickettsi* [11] in very few cases. Association with non-infectious, inflammatory conditions was reported in sarcoidosis [12] in a single case report. There are some case reports suggesting antecedent drugs [13] usage associated with occurrence of GBS.

GBS is an immunologically mediated, acute inflammatory demyelinating polyneuropathy occurring in all parts of the world at all ages. In more than two thirds of cases, a history of a preceding respiratory or gastrointestinal tract infection is obtained [3]. Following an infection there will be development of antibodies which cross react with antigens over the nerves leading to GBS [3].

It has been previously reported following polio immunisation, surgical operations, sarcoidosis, drug induced, upper respiratory tract infections, psittacosis, mycoplasma pneumonia, viral infections such as Epstein-Barr virus, cytomegalovirus, varicella, measles, mumps and hepatitis [14].

Neurological involvement in scrub typhus infection is approximately 12.5 percent according to previous studies [15]. However, peripheral nervous system involvement is rarely reported [16]. Neuropathy associated with scrub typhus is extremely rare and the few reported manifestations include seizures, delirium, cerebral haemorrhage, hearing loss, isolated cranial nerve palsies, transient parkinsonism, peripheral mononeuropathy, polyneuropathy and GBS [17].

According to previous studies atypical neurological manifestations in malaria are cerebral malaria, psychiatric manifestations, cerebellar ataxia, post malaria neurological syndrome, isolated hemiparesis, neurological sequelae and GBS [18]. GBS in vivax and falciparum malaria had been previously reported in very few cases [8,9].

Immune mediated damage is believed to be the cause of GBS [3]. In malaria, asexual stage infection is accompanied by the release of cytokines and other immunological mediators. These immunological mediators might have triggered an inflammation affecting the axons causing demyelination. Other probable explanation might be due to the occlusion of the vasa-nervosum by the parasites or the inflammatory mediators or immune complex antibodies [8,9].

The neurological signs in this patient suggested lower motor neuron paralysis with areflexia. CSF study showed cyto-albuminogenic dissociation. Electrophysiological studies were suggestive of axonal demyelinating polyneuropathy involving lower limbs more than upper limbs. According to Brighton's diagnostic criteria, a diagnosis of GBS was made [1].

This clinical picture had developed after an attack of *Plasmodium falciparum* and *Orienta tsutsugamushi*. Since the patient had no other preceding infections that could account for GBS or drug usage which could have led to this episode, the mixed infection was thought to be the triggering factor for the development of GBS. Though mixed infection was present in the patient, which infection had caused the neuropathy is not known.

Further elaborate epidemiologic and immunopathologic studies are needed to understand the clinical characteristics, establish the association and the mechanisms of GBS with infectious diseases.

CONCLUSION

Here by we conclude that it is worth testing GBS patients for the common endemic infections as it may not be just a single infection, sometimes mixed infections might be the triggering factor for the occurrence of GBS, as presented in our case report.

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PARTICULARS OF CONTRIBUTORS:

1. Junior Resident, Department of Medicine, Kasturba Hospital, Manipal University, Manipal, Karnataka, India.
2. Associate Professor, Department of Medicine, Kasturba Hospital, Manipal University, Manipal, Karnataka, India.
3. Senior Resident, Department of Medicine, Kasturba Hospital, Manipal University, Manipal, Karnataka, India.
4. Professor, Department of Medicine, Kasturba Hospital, Manipal University, Manipal, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Weena Stanley,
214 Valley Flats KMC Manipal, Udupi District, Manipal-576104, Karnataka, India.
E-mail: weenastanley1@gmail.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Mar 16, 2017**
Date of Peer Review: **Apr 24, 2017**
Date of Acceptance: **Jun 13, 2017**
Date of Publishing: **Sep 01, 2017**