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Miller Fisher Variant of Guillain-Barre Syndrome Secondary to Pulmonary Tuberculosis: A Case Report with Review of Literature

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Abstract

Guillain-Barre syndrome (GBS) is one of the common causes for acute flaccid paralysis in adults and mostly preceded by infection. Miller Fisher syndrome (MFS) is a rare variant of GBS with incidence of 1 to 2 in 1,000,000. This syndrome has a triad of ataxia, areflexia, and ophthalmoplegia and diagnosed when two out above three features are present. It usually preceded by viral infection, most commonly *Campylobacter jejuni*, cytomegalovirus, and Epstein–Barr virus. However, it is very rarely reported in pulmonary tuberculosis. The pathogenesis involves an aberrant immune response due to molecular mimicry against myelin gangliosides. Hereby we are presenting an unusual case of MFS variant of GBS associated with pulmonary tuberculosis.

Keywords
- intensive care unit
- Miller Fisher syndrome
- plasmapheresis
- tuberculosis
- pulmonary

Introduction

Guillain-Barre syndrome (GBS) is an immune-mediated polyradiculoneuropathy affecting peripheral nerves and nerve roots with an incidence of one to two cases/per 100,000 persons.[1] The diagnostic criteria include clinical evidence of bilateral symmetric ascending areflexic weakness, with albumin-cytologic dissociation in cerebrospinal fluid (CSF) supported by neurophysiological studies. Miller Fisher syndrome (MFS) is one of the rare variants of GBS.[2] MFS manifests as ophthalmoplegia, ataxia, and areflexia. Two-thirds of cases of GBS are associated with antecedent gastrointestinal or respiratory tract infections.

Tuberculosis (TB) is rampant in the Indian subcontinent. The literature is replete with reports describing an association between GBS and TB. However, an association between the MFS variant of GBS with TB is rarely reported. We show a rare MFS form of GBS with pulmonary TB (PTB).

Case Report

A 58-year-old male presented to the emergency room with complaints of dysphagia, cough with shortness of breath, and slurring of speech for 4 days. He had a history of chronic cough and weight loss of more than 10% in the last 3 months. There was no history of gastrointestinal symptoms or flu-like symptoms in the recent past. He was hemodynamically stable, having a temperature of 38.40C and right-sided bronchial breath sounds with course crepitation in the infraclavicular area. Neurological examination revealed diminished deep tendon reflexes in both lower limbs and ascending motor weakness with Medical Research Council grade 3) in all four limbs. He also had dysarthria and bilateral lower limb ataxia. There was also palsy of bilateral cranial nerves.[3–7]

Exhaustive tests were advised to determine the triggers/etiology of GBS. A routine stool examination was negative for *Campylobacter jejuni*. Blood and urine cultures were sterile. Serology was negative for human

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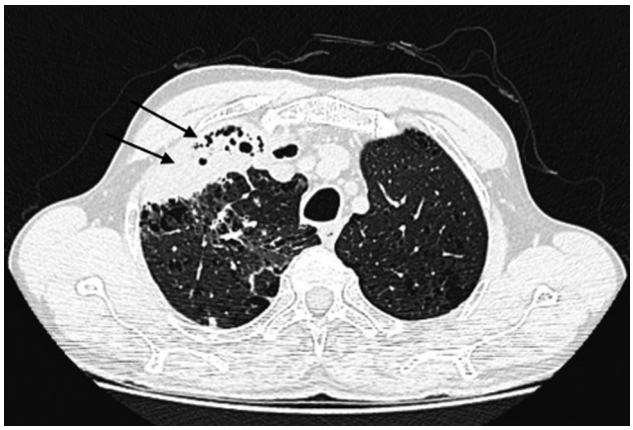

Fig. 1 Consolidation and fibrosis of the right upper zone (black arrowhead).

immunodeficiency virus (HIV), hepatitis B and C, scrub typhus, malaria, *Leptospira*, cytomegalovirus, and Epstein–Barr virus. Hematological and biochemical profiles were average. Antinuclear antibody titer and antineutrophil cytoplasmic antibodies were negative. Brain magnetic resonance imaging with angiography revealed the regular study. Sputum was positive for acid-fast bacilli, and a cartridge-based nucleic acid amplification test detected *Mycobacterium tuberculous*. Chest radiograph revealed a nonhomogenous opacity of the right upper lobe, and high-resolution computerized tomography showed consolidation and fibrosis of the correct upper zone (►**Fig. 1**), confirming the diagnosis of PTB. He was intubated for airway protection, given poor cough reflex. On the 8th day of illness, CSF analysis revealed glucose of 83 mg/dL (blood glucose of 110 mg/dL), protein 86 mg/dL, and cell count of 2 cell/mL suggestive of albumin-cytological dissociation. Nerve conduction studies (NCS) revealed slow motor conduction velocities with reduced amplitude of sensory nerve action potential in bilateral ulnar and peroneal nerves and absent F-wave responses in ulnar, peroneal, and tibial nerves consistent with MFS.

He was started on antitubercular therapy (ATT) (isoniazid, rifampicin, pyrazinamide, and ethambutol) and underwent five sessions of plasmapheresis. There was an improvement in cough reflex and motor power after the third plasmapheresis session. He got extubated on day 10 of the intensive care unit stay, but after 3 days, he developed hospital-acquired pneumonia (multidrug-resistant *Klebsiella pneumoniae*) and was reintubated again. Antibiotics were upgraded according to the culture sensitivity report. The next day he developed abdominal distension, oozing of blood from the central venous catheter site and hypotension. On further workup, he was found to have a drop in hemoglobin to 5 g/dL; total platelet count was 89000 cells/μL, international normalized ratio was 3.2, and fibrinogen was 77 mg/dL suggestive of disseminated intravascular coagulation (DIC). To exclude the possibility of ATT-induced hepatitis, liver function test was sent, which was expected. Contrast-enhanced computer tomography abdomen showed a large retroperitoneal hematoma over the left iliac fossa. He was transfused with multiple packed blood cells and blood products, including cryoprecipitate, but finally, he succumbed to septic shock and DIC.

Discussion

GBS is a disease of peripheral nerves known for its association with various infections. The mean age of onset is 40 years, and the incidence increases after age 50. Besides acute inflammatory demyelinating polyneuropathy, other clinical variants of GBS are axonal motor and sensorimotor neuropathy (AMAN, AMSAN), MFS, and Bickerstaff brainstem encephalitis. Our patient had ataxia and areflexia with typical MFS NCS and CSF findings. The most frequently identified infection for precipitation of GBS is *Campylobacter jejuni*, and less often by cytomegalovirus, dengue, chikungunya, Zika, and HIV.[2] The causes mentioned above trigger the host immune system and produce antibodies against gangliosides of myelin of peripheral nerves, which in turn lead to neuropathy and muscle weakness.[2]

TB has both pulmonary and extrapulmonary manifestations. Neurological manifestations of TB include tuberculomas, meningitis and brain abscesses. The pathogenesis of GBS in TB is best explained by molecular mimicry involving both cell-mediated and humoral immune responses.[3]

The review of reported cases is mentioned in ►**Table 1**.[3–6,8–10] The most common clinical features of the presentation of GBS are ascending quadriparesis with areflexia or hyporeflexia, and few case reports showed sensory involvement.[4,8]

According to the American Academy of Neurology, intravenous immunoglobulins (IVIG) are as effective as plasmapheresis for treating GBS.[10] Mohta et al described the AMSAN variant of GBS, where the patient underwent five sessions of plasmapheresis and showed improvement during the hospitalization and discharged.[5] Another 40-year-old male patient presented with the AMSAN variant, where IVIG was given for 5 days, but as there was no improvement at day 21, he underwent plasmapheresis, but there was no neurological improvement. He progressed to chronic inflammatory demyelinating polyradiculoneuropathy.[8] Our patient also underwent plasmapheresis and showed neurological improvement. To our knowledge, only one case of MFS due to PTB has been reported in a 70-year-old male who recovered after treatment with IVIG and ATT.[6] Our patient also showed clinical improvement in motor power and cough reflex after treatment and to the best of our knowledge, this is probably the first reported case report of MFS secondary to PTB from the Indian subcontinent.

From the pattern of disease progression and clinical response after starting ATT, TB was considered the cause of MFS in this case. However, the possibility of both occurring by chance could not be ruled out.

Table 1 Summary of reported cases of TB associated with GBS and its variants

Author/year	Patient information	Clinical features of GBS	Clinical and radiological findings of TB	Duration of symptoms of GBS and TB	GBS variant	Treatment received	Outcome
Vyravanathan and Senanayake 1983[4]	Case 1: 18 y/male Case 2: 56 y/female	Case 1: weakness of limbs, areflexia, loss of sensation; CSF: no cell; protein 0.36 g/dL Case 2: Three weeks of weakness of all four limbs, diminished DTR, impaired sensation CSF: no cell; protein 0.80 g/dL	Case 1: loss of appetite and weight, cough, fever CXR: multiple confluents, ring shadows in b/l UZ Case 2: fever, loss of appetite, cough CXR: multiple confluents, ring shadows in b/l UZ, MZ	Case 1: GBS:10 d PTB: 3 mo Case 2: GBS: 3 wk PTB: 2 mo		Case 1: ATT, steroid Case 2: ATT, steroid	Case 1: improved Case 2: expired
Canham and Iseman 2014[8]	25 y/male	Lower limb weakness, absent sensation CSF: no cell, normal protein NCS: slow motor conduction velocities, absent F wave responses, prolonged sensory latencies and decreased amplitudes	Productive cough, hemoptysis, CT chest–bilateral cavitary pneumonia Sputum AFB positive	GBS: 2 wk PTB: 6 wk prior to weakness		IVIG, ATT, steroid	Progressed to CIDP
Mohta et al 2017[5]	18 y/male	Acute onset ascending quadriparesis, ↓ DTR CSF: cell < 05; protein 160 mg/dL NCS-AMSAN	Fever, weight loss CECT: bilateral pleural, pericardial effusion, enlarged paratracheal and retroperitoneum lymph nodes	GBS: 2 d Disseminated TB: 1 mo	AMSAN	Plasmapheresis, ATT	Improved
Lakhotia et al 2017[3]	16 y/female	Acute onset ascending quadriparesis, areflexia NCS: absent H-reflexes bilateral soleus muscles, absent F-wave	Sputum AFB positive CXR-bilateral parahilar lymphadenopathy	GBS: 1 d PTB: 1 wk prior to GBS and was on ATT		IVIG, ATT was continued which was already started 1 wk prior to hospital admission	Improved
Malakar et al 2019[9]	Case1: 46 y/female Case 2: 32 y/male Case 3: 52 y/male Case 4: 39 y/male	Case 1: acute ascending limb weakness; CSF: no cell protein 122 mg/dL NCS-AIDP Case 2: b/l LL weakness, patchy sensory loss and left LMN facial palsy; CSF: 3 cell, protein 158 mg/dL NCS-AIDP Case 3: sudden onset ascending quadriparesis, areflexia; NCS-AMAN. CSF: no cell with high protein Case 4: leg paresthesias and weakness	Case 1: weight loss, cough, anorexia Sputum AFB positive CXR—fibrosis, old healed lesion of past PTB Case 2: cough, hemoptysis sputum gene expert positive Case 3: SOB, cough with sputum AFB +ve CXR: right lung fibrosis Case 4: cough, anorexia, weight loss, sputum AFB +ve	Case1: GBS: 12 d PTB: 1 mo Case 2: GBS: 2 d PTB: 18 d Case 3: GBS: 5 d PTB: 3 mo Case 4: GBS: 15 d PTB: 2 mo	Case 1: Case 2: Case 3: AMAN Case 4:	Case 1: IVIG, ATT Case 2: IVIG, ATT Case 3: ATT Case 4: IVIG, ATT	Case 1: improved Case 2: improved Case 3: improved Case 4: improved
Singh et al 2020[10]	50 y/male	Acute, ascending quadriparesis, areflexia CSF: <5 cell, protein 140 mg/dL NCV-AMSAN	Fever and productive cough CT chest: multiple mediastinal lymphadenopathy, fibro cavitation in B/L upper lobes Endotracheal tube aspirate gene expert positive	GBS: 10 d PTB: 3 wk	AMSAN	IVIG, ATT	Expired
Park et al 2020[6]	70 y/male	Horizontal diplopia and ataxia, CSF: cell-17, protein 66 mg/dL; NCS: slow motor conduction velocities, absent F-wave	Sputum production, cough, and fever; sputum AFB positive CT chest-consolidations and diffuse nodules in both upper lobes	GBS: 1 d PTB: 1 wk	MFS	IVIG, ATT	improved

Abbreviations: AIDP, acute inflammatory demyelinating polyneuropathy; AMAN, axonal motor neuropathy; AMSAN, axonal sensorimotor neuropathy; ATT, antitubercular treatment; AFB, acid fast bacilli; B/L, bilateral; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; CKD, chronic kidney disease; CSF, cerebrospinal fluid; CT, computed tomography; CXR, chest X-ray; DTR, deep tendon reflex; GBS, Guillain-Barre syndrome; IVIG, intravenous immune globulin; LL, lower limb; MZ, middle zone; MFS, Miller Fisher syndrome; NA, not available; NCS, nerve conduction study; PTB, pulmonary tuberculosis; TB, tuberculosis; TBM, tubercular meningitis; UZ, upper zone; VAP, ventilator-associated pneumonia.

Conflict of Interest
None declared.

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