TITLE
Guillain-Barre Syndrome in a patient with Tuberculosis: A case report from Pakistan

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ABSTRACT

Background: Gullain-Barre Syndrome (GBS) is an important cause of acute muscle weakness in adults which is usually associated with peripheral neuropathy. It is considered to be the post infectious immune mediated disease and Campylobacter jejuni being the most common organism. It is characterized by progressive, symmetrical, proximal and distal tingling sensation and weakness. This case shows an association of GBS with pulmonary tuberculosis.

Case presentation: We report the case of a 65-year-old man with 1 month history of low grade fever, weight loss and anorexia along with productive cough, admitted to our hospital with acute development of rapidly progressive, symmetrical ascending weakness of all 4 limbs. The weakness started in the lower limbs and then spread to the upper limbs within 5 days. He had marked flaccid weakness of all 4 limbs, the weakness being more marked in the distal muscle groups. Within 2 days of presentation, the weakness ascended to involve the proximal and bulbar muscles as well. Chest X-ray was abnormal with three sputum samples positive for acid-fast bacilli. Electrodiagnostic studies revealed markedly prolonged distal latencies and absent H and F reflexes. The patient received intravenous immunoglobulin (I/V IG) along with antituberculosis therapy, to which he responded well and his weakness started improving after 1 week with able to ambulate in 2 months with support.

Conclusion: Gullain-Barre Syndrome is not just associated with respiratory or gastrointestinal diseases but it can also occur in association with other B-cell mediated disorders.

KEY WORDS: Guillain-Barre Syndrome, Tuberculosis, intravenous immunoglobulin, antituberculosis therapy.
BACKGROUND

Gullain-Barre Syndrome (GBS) is an acute post infectious immune mediated disease which affects the peripheral nervous system and is usually triggered by infectious process.\textsuperscript{1,2} Different predisposing factors are known, of which respiratory and gastrointestinal infections predominate.\textsuperscript{3,4} Campylobacter jejuni is the most frequently identified organism.\textsuperscript{4} The underlying pathological mechanism is not clearly known and is still debated. However, an infection-induced aberrant immune response following T-cell activation with production of antibodies and complement seems to be crucial.\textsuperscript{5}

The reason for reporting this interesting case is that there have been very few cases which have been reported so far showing an association of GBS with pulmonary Tuberculosis. Secondly, the old belief that GBS is the result of a T-cell mediated response does not correlate with acquiring Tuberculosis in this case as it is a B-cell mediated response.\textsuperscript{6} Thirdly, as there’s a very high rate of incidence and prevalence of Tuberculosis in Pakistan, one should consider TB in patients presenting with GBS.
CASE PRESENTATION

65-year-old gentleman with no known comorbidities, non-smoker, was admitted with 3 months history of low grade fever, weight loss and anorexia along with productive cough. He came to our hospital with 20 days history of weakness of all 4 limbs. The weakness had started in the lower limbs and then spread to the upper limbs within 5 days, along with urinary symptoms. He was experiencing severe pain and numbness in both of his lower limbs. He became bed bound because of his pain and weakness. On further inquiring he reported that he has been suffering from low grade fever and cough since 3 months along with scanty expectoration. His past medical and surgical history was unremarkable and he had no family history of tuberculosis, polio or other familial neurological disorders.

On examination, he was afebrile, grossly emaciated and bed bound. Neurological examination revealed that the patient was awake, alert and oriented to time, place and person. Higher mental function, extraocular movements, fundoscopy and gag reflex were intact. There was facial diplegia. Motor examination showed bulk & tone was decreased in all four limbs, weakness in all 4 limbs and his power was graded as II/V on Medical Research Council (MRC) scale. Tendon reflexes were diminished in the upper limbs and were absent in the lower limbs. Plantar responses were flexors. Sensory examination was unremarkable. In the chest, bilateral crepitations were found in the upper and mid-zones of the lungs. Rest of the systemic examination was unremarkable.

Investigations

Chest X-Ray showed multiple confluent, ill-defined and ring shadows in both upper and mid-zones of lungs which are suggestive of pulmonary tuberculosis. Magnetic resonance imaging
(MRI–dorsal) Spine was done to rule out Pott’s disease which was normal. Three sputum samples were positive for acid-fast-bacilli.

Electrodiagnostic studies showed non recordable median, ulnar and sural nerves while radial sensory was preserved. Motor nerve conduction studies showed prolonged latencies of median, ulnar, posterior tibial and peroneal (TA) nerves of the right side while peroneal nerve from extensor digitorum brevis (EDB) was not recordable. There were low compound muscle action potential (CMAP) amplitudes and conduction velocities. F and H reflexes were not recordable. History of acute weakness along with above mentioned findings on electrodiagnostic studies correlate with the diagnosis of demyelinating neuropathy i.e GBS.

**Differential Diagnosis**

1. Dorsal myelopathy
2. Lumbosacral radiculopathy
3. Drug induced neuropathy
4. Vasculitic neuropathy

**Treatment**

The patient was started on standard dose of human Immunoglobulins in a dose of I/V 0.4g/kg/d for 5 days. He was also given chemotherapy with Isoniazid, 300mg, Rifampicin, 600mg, Ethambutol, 1200mg, Pyrazinamide, 1500mg, Pyridoxine, 50mg.

**Outcome and follow up**

He responded well to I/V IG, with improvement in his forced vital capacity along with no further progression in weakness. His weakness started improving in 1 week and was able to ambulate in
2 months with support. His cough improved and his sputum became negative for AFB in 2 months period. However, he was continued on ATT for a total of 8 months.
DISCUSSION

This case is worth mentioning and contains an immense importance as the patient presented with signs of peripheral neuropathy despite of the evidence of pulmonary tuberculosis. GBS is associated with infections such as viral, mycoplasmal or chlamydial and might follow after vaccinations, operations or stressful events. There have been few case reports from India where rabies vaccination was the reason for acquiring GBS. Worldwide, it is the most frequent cause of acute flaccid paralysis (AFP), with an incidence of 1.2 to 2.3 per 100,000 persons per year. Despite medical treatment, GBS often remains a severe disease; 3–10% of patients die, while 85% patients recover spontaneously, however 10% patients need hospitalization and 20% are still unable to walk after 6 months. Its prevalence has been reported to vary from region to region.

During the period from 1997 to 2002, a study from Hong Kong reported a prevalence rate of GBS to be 42% while Oman and Australia reported it to be 45% and 47%. Similarly in a study conducted in Hazara division of Pakistan, GBS was found in 47% of the study population which comprised of patients with acute flaccid paralysis. The prevalence rate for GBS in Pakistan as reported by WHO is 1,591/159,196,336 of the estimated population.

Pulmonary tuberculosis is a world wide problem and WHO has declared Tuberculosis emergency. According to the 2007 report of WHO, the incidence of pulmonary tuberculosis in Pakistan is 181 cases/100,000/year whereas prevalence is 223/100,000 cases with a high incidence of mortality; 28/100,000 cases with a dramatic increase in multidrug resistant tuberculosis.
With this high prevalence rate of pulmonary tuberculosis, it is likely that GBS may also be prevalent but is unrecognized or treated as possible tuberculous radiculitis and therefore it is imperative to know the likely association of this communicable disease with this highly treatable immune condition. The clinical and radiological features in this case were sufficiently characteristic on the basis of which a diagnosis of pulmonary tuberculosis could be made easily and this was confirmed by samples of sputum positive acid fast bacilli (AFB) smears that were taken on 3 different occasions. This case is interesting in the sense that apart from pulmonary tuberculosis which was evident, the patient presented with a neurological picture of peripheral neuropathy with nerve conduction studies showing a demyelinating picture, supporting the diagnosis of acute inflammatory demyelinating polyneuropathy (AIDP) rather than tuberculous polyradiculitis.

In 1966, Felix Leneman has reviewed 1100 cases of Guillain Barre Syndrome of which 365 cases occurred de novo while rest of the 735 cases were associated with other illnesses of which tuberculosis (of the lung and brain) was found in 1% of the patients as associated illness. Such association is almost always accidental therefore its considered as a probable or possible etiological factor.\(^7,15\)

Similarly, 2 case reports have been published from Srilanka in 1983 that have shown an association of GBS with chronic pulmonary tuberculosis. Both of the patients had a history of weakness of all 4 limbs which was of acute onset over a background of chronic cough, low grade fever and weight loss. Chest X-ray showed multiple ill-defined confluent shadows in the upper zones which was strongly suggestive of pulmonary tuberculosis. They had marked flaccid paralaysis in all 4 limbs with diminished tendon reflexes and loss of all sensory modalities in a glove and stocking distribution. Both of the patients were treated with anti-tuberculous
chemotherapy along with steroids. Improvement in symptoms was noted in just one patient. Majority is of the opinion that cell-mediated delayed hypersensitivity reaction is the basis as it is also a feature of tuberculosis. The underlying pathology of the GBS is usually an acute inflammatory polyneuropathy. A T cell mediated pathogenesis is likely although a complement dependent antibody targeted attack on schwann cell surface antigens. The accumulating evidence implicates an immune response to glycolipids resembling ganglioside GM1 in the pathogenesis of GBS. The activation of T cells in GBS is evident from the presence of increased numbers of circulating T cells bearing activation markers and of increased concentrations of soluble IL-2 receptor. In a nutshell pathologic findings in GBS include lymphocytic infiltration of spinal roots and peripheral nerves (cranial nerves may be involved as well), followed by macrophage-mediated, multifocal stripping of myelin. In GBS up to two thirds of patients report an antecedent bacterial or viral illness prior to the onset of neurologic symptoms and more studies are required to document whether it may occur after a chronic B cell mediated disorder.

**Conclusion:** Guillain-Barre syndrome is a neurological disorder which can lead to muscle paralysis. Not all cases associated with complicated tuberculosis presenting with limb weakness and bladder and bowel dysfunction are due to Pott’s disease, because these conditions if not recognized early can result in significant morbidity. Timely appropriate investigations are required to recognize the possible treatable but rare complications of this communicable infection as there’s high prevalence of Tuberculosis in South Asia. Differential diagnosis is of paramount importance.
Consent:

Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Abbreviations

I/V IG: Intravenous immunoglobulin
GBS: Gullain-Barre Syndrome
TB: Tuberculosis
MRC: Medical Research Council
CMAP: Compound muscle action potential
EDB: Extensor Digitorum Muscle
AFB: Acid Fast Bacilli
AFP: Acute Flaccid Paralysis
AIDP: Acute Inflammatory Demyelinating Neuropathy

Competing interest

The authors declare that they have no conflict of interests.

Author’s contribution

JA contributed to the study design, acquisition of data and in drafting the manuscript. FM has been involved in drafting the manuscript. JR has also contributed in drafting the manuscript and revising it critically. MW has been involved in interpretation of the data and in critically analyzing the manuscript. All authors read and approved the final manuscript.


## Table 1: Sensory Nerve Conduction Studies

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<th>S.No</th>
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<th>Recording site</th>
<th>Stimulation Site</th>
<th>Latency (ms)</th>
<th>Distance (cm)</th>
<th>Amplitude (µV)</th>
<th>NCV (m/s)</th>
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<tr>
<td>6</td>
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Table 2: Motor Nerve Conduction Studies

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<th>Distance (cm)</th>
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* RMAPB (Right Median- APB), RUADQ (Right Ulnar ADQ), R.POST T (Right Posterior Tibial), R.PERONEAL (Right Peroneal), R. PER T.A (Right Peroneal Tibialis Anterior), R.H.REFLEX (Right H reflex), L.H.REFLEX (Left H reflex), PFH (Proximal fibular head), DFH (Distal fibular head).