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PULMONARY TUBERCULOSIS AND GUILLAIN-BARRÉ SYNDROME (GBS): A CHANCE ASSOCIATION OR A Causal?

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ABSTRACT

Introduction & Objectives: Although there are many case reports on GBS in patients with Tuberculosis since the incidence of the disease is rare, the association between them could not be tested. We attempt to compare all such cases along with a new case of Multi-drug resistant Tuberculosis (MDR TB) with GBS syndrome presented to us. **Materials and methods:** All the previously published cases on GBS in association with Tuberculosis and the present case were studied for common associations and comorbidities. Association between the time of onset of symptoms of Tuberculosis and that of GBS, prognosis, and recovery were compared. **Conclusions:** There is a temporal association between GBS and Tuberculosis. The symptoms of Tuberculosis preceded GBS by an average of 13 weeks. The etiology of GBS is immune mediated with molecular mimicry between epitopes of pathogens and host tissues being likely explanation.

INTRODUCTION

GBS is an Acute, frequently severe, fulminant polyradiculopathy that is autoimmune in nature. Its incidence is 1-4 cases /1,00,000 annually. Clinical features include areflexia, ascending paralysis with or without sensory involvement like tingling dysesthesias in extremities. Bulbar weakness may be present and lower cranial nerves involvement is frequent.1

Most evidence suggests the GBS to be of autoimmune etiology. 70% of cases it is preceded by an acute infectious process (1-3 weeks), which includes respiratory and gastrointestinal infections.

Common pathogens implicated include Campylobacter jejuni (20-30%), Human herpes virus (Cytomegalovirus / Epstein-Barr virus 20-30%). Other viruses include HIV, hepatitis E, Zika, Mycoplasma pneumoniae. Immunization has also been thought to be associated with GBS.

Swine influenza, which was widely used in 1976 and older types of rabies vaccine, which are derived from nerve tissue, are notable examples. Other associations that cannot be explained by chance alone include Hodgkin's disease and systemic lupus erythematosus (SLE).

The immunopathogenesis of GBS includes both cellular and humoral immune mechanisms.

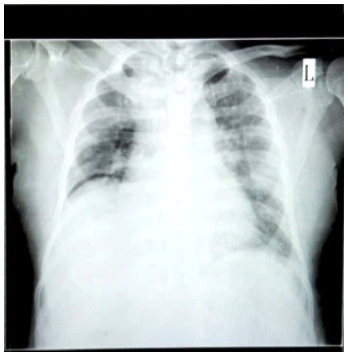
Circumstantial evidence suggests an immune response to non-self antigens that cross react with host nerve tissue. This is due to molecular mimicry (resemblance of epitope) between the host neural gangliosides (GM1, GD1a, GM1b, GaINAc-GD1a, GQ1b, GT1a) and the causative agent.1

Although the above causes were noted in most cases of GBS, in 30% of cases, no cause as found. However, there are many case reports on GBS in patients with Tuberculosis. Tuberculosis involves a cell-mediated, delayed hypersensitivity reaction, which has a resemblance to the pathogenesis of GBS.2 But since the incidence of the GBS is rare and that of Tuberculosis is low, the association between them couldn't be tested. We attempt to compare all such cases along with a new case of Multi-drug resistant Tuberculosis (MDR TB) with GBS syndrome presented to us.

Materials and methods.

A search for all the previously published cases on GBS in association with Tuberculosis was done till 2020. The electronic database searched included MEDLINE (PubMed), EMBASE, Scopus, Web of Science, and Index Copernicus. These cases, along with the present case, were studied for common associations and comorbidities. Association between the time of onset of symptoms of Tuberculosis and that of GBS, the prognosis and recovery were compared.
Present case:

Fig.1 X-ray chest -Patchy consolidation of Right upper lobe.



A 46 years male presented to the emergency with complaints of altered sensorium, fever, and productive cough for the last two months. Chest radiography revealed patchy consolidation of the right upper lobe. Sputum for CBNAAT showed Multi-drug resistant Tuberculosis. Also, the patient had a flaccid weakness of lower limbs more than upper limbs with Deep tendon reflexes being absent. Nerve conduction studies confirmed demyelinating sensorimotor neuropathy, suggesting GBS.

He was started on IV Immunoglobulins. He recovered from GBS and was later started on anti-Tuberculosis drugs. The patient was transferred to an isolation centre for treatment of multi-drug resistant Tuberculosis and later was started on home-based therapy. He succumbed to Tuberculosis after one month of illness.

Previous cases.

Table 1 shows the list of previously published cases of GBS associated with Tuberculosis in chronological order.

Table 1. Published cases of GBS associated with Tuberculosis

	Publication		Age & sex		Time Symptoms to GBS	Relation To Treatment	Type of TB	Co-Morbidities	Outcome
	Year	Authors (et al.)							
1	1983	Vyravanathan[2]	18	M	6 m	Before Treatment	PTB		Recovered
2	1983	Vyravanathan	56	F	5 m	Before Treatment	PTB		Death 3 day
3	2005	Soehardy[3]	40	M	-	After starting treatment	PTB	Marfan syndrome	AMSAN-CIDP
4	2007	Chong V H[4]	70	M	Several months	Before Treatment	Intestinal TB		Recovered
5	2008	Canham[5]	25	M	6-8 weeks	Before Treatment	PTB		CIDP
6	2010	de la Torre[6]	74	M	Unknown	Before Treatment	LN TB	IBD	Recovered
7	2012	Aza M Taha[7]	47	M	2 weeks	Before Treatment	PTB		Recovered
8	2017	Mohta[8]	18	M	Simultaneously/ unknown	Before Treatment	PTB		AMSAN
9	2018	Karmel webb[9]	68	M	-	-	Intravesical BCG/ miliary TB	CD, CAD, Ca bladder	Recovered
10	2019	Malakar[10]	46	F	18 days	Before Treatment	PTB		Recovered
11	2019	Malakar[10]	32	M	16 days	Before Treatment	PTB		Recovered
12	2019	Malakar[10]	52	M	85 days	Before Treatment	PTB	Recurrent TB	Recovered
13	2019	Malakar[10]	39	M	45 days	Before Treatment	PTB		Recovered
14	-	Present case	59	M	2-3 months	Before Treatment	PTB	DM	death After 1 month

(Abbreviations: PTB- Pulmonary tuberculosis, LN TB- lymph node tuberculosis, DM- diabetes mellitus, CD- Crohn's disease, CAD- Coronary artery disease

Observations-

Most of the reported cases were in males, except for two cases. The Mean age of the patients was 46 years, but no specific age pattern was observed. Most striking was the temporal association of TB preceding GBS by an average of 2-3 months (about 70 days). In most cases, the treatment was not initiated except for one case. Although pulmonary tuberculosis was reported more often, no form of tuberculosis was exempt from the association of GBS. GBS, when treated, did not seem to be affecting the prognosis of pulmonary Tuberculosis except in advanced disease. Chong, V. H et al., in their paper, clearly documented the temporal association of CIDP. They noted a recovery in weakness with Anti-Tuberculosis drug, and relapse when the patient stopped taking medication.4

DISCUSSION AND CONCLUSIONS:

To date, 14 published cases (including the present one) of GBS in patients with Tuberculosis were found. Hence the data is too small to come to any reliable conclusion. However, there seems to be an increase in the frequency of such cases reported in recent years, especially from India.

The low incidence of GBS cases reported could be due to the weakness being considered as secondary to peripheral neuropathy from anti-TB drugs. Also, most of the people are treated on home-based therapy, away from medical supervision of experts. The general condition and nourishment of the patient are usually poor, thus causing the caregivers to overlook the weakness.

The complexity of diagnosing GBS may be one more reason for lower reporting of such cases.

The etiology of GBS is immune mediated with molecular mimicry between epitopes of pathogens and host tissues being likely explanation. In Tuberculosis, a cell-mediated, delayed hypersensitivity reaction is involved. Hence there is a resemblance between the pathogenesis of GBS and Tuberculosis.2 Although, in GBS campylobacter and cytomegalovirus are commonly implicated, 30% of cases have no antecedents. Thus, it is important to consider mycobacteria as a potential trigger and strengthen the reporting of such cases. To conclude, the physicians should have a high level of suspicion for GBS in patients with tuberculosis presenting with weakness. Reporting of all such cases will help in making optimal statistical studies in the future to prove if such association is by chance or not.

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