

Tuberculosis and Guillain-Barre syndrome: A chance association?

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Summary

An 18-year-old boy presented with acute-onset quadriparesis that had developed 4 weeks prior. He had an intermittent fever and significant weight loss during this period. After extensive investigations, the patient was diagnosed with an acute motor and sensory axonal neuropathy (AMSAN) variant of Guillain-Barre syndrome (GBS) and disseminated tuberculosis with mediastinal lymphadenopathy, pericarditis, and pleural effusion. Plasmapheresis was performed and first-line anti-tubercular therapy was administered. At the follow-up at 6 months, the patient was asymptomatic, he had no residual weakness and could walk without support, and tuberculosis had completely resolved on X-rays. Many infectious agents have been known to trigger GBS, but only a few cases of GBS and tuberculosis have been reported. This association needs to be evaluated further.

Keywords: Acute motor and sensory axonal neuropathy (AMSAN), disseminated tuberculosis, plasmapheresis

1. Introduction

Guillain-Barre syndrome (GBS) is a rare autoimmune demyelinating polyneuroradiculopathy seen after bacterial or viral infections and sometimes even after vaccinations. The incidence of GBS is about 1-2/100,000 per year (1). Subtypes are described based on electrophysiological patterns, the most common being acute inflammatory demyelinating polyneuropathy (AIDP) and rarer ones being acute motor axonal neuropathy (AMAN) and acute motor and sensory axonal neuropathy (AMSAN).

Tuberculosis is rampant in India and myriad presentations have been reported. Neurological manifestations of tuberculosis include meningitis, tuberculomas, brain abscesses, and radiculomyelitis (2).

Tuberculosis and GBS were first reported to occur together in 1966 and a few cases have been reported since, but the nature of the association between

the two is not yet clear. Reported here is a case involving a young boy who presented with acute onset quadriparesis and who was subsequently found to have GBS and disseminated tuberculosis.

2. Case Report

An 18-year-old boy presented with acute-onset weakness that developed in all 4 limbs 1 month prior. Weakness had started abruptly and progressed from the lower limbs to the upper limbs over a period of 2 days. Weakness in the upper limbs gradually increased for the first 15 days, plateaued, and then started to improve at the point when the boy was seen. During the development of muscle weakness, the boy also had a low-grade intermittent fever and he lost about 6 kg in weight. He had received antibiotics previously and was sent to this Hospital for further management. There was no sensory, bowel, or bladder involvement. He had no history of antecedent diarrhea, upper respiratory tract symptoms, or a history of recent vaccination for influenza or meningococcus.

On examination, he had quadriparesis with a grade of 0 (according to the Medical Research Council (MRC) Scale for Muscle Strength) in the lower limbs and 2 in the upper limbs. The deep tendon reflexes were diminished and the boy had a flexor plantar

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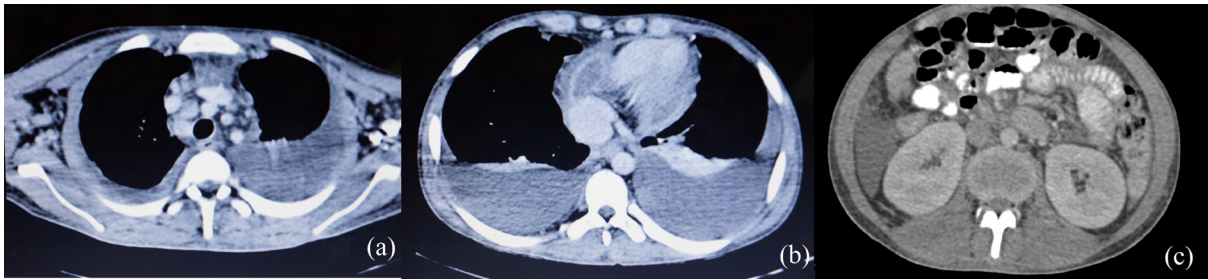


Figure 1. Chest CECT showing (a) multiple enlarged right paratracheal lymph nodes (b) bilateral pleural and pericardial effusion with enhancing pericardium, and (c) retroperitoneal lymph nodes. CECT, contrast enhanced computed tomography.

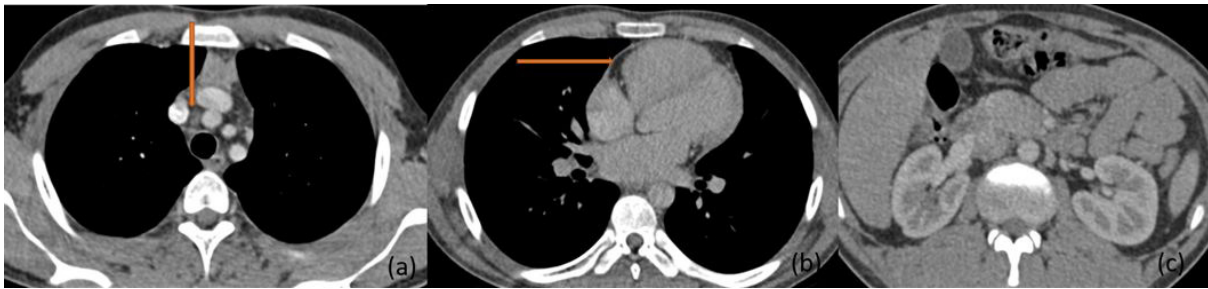


Figure 2. Follow-up CECT images showing (a) reduced size of the mediastinal lymph nodes and (c) retroperitoneal lymph nodes. (b) There is also resolution of pleural and pericardial effusion, with minimal residual pericardial thickening (arrow).

response. He also had bilateral pitting pedal edema, tender hepatomegaly (5 cm below costal margin), and an elevated jugular venous pressure (JVP). Pulsus paradoxus was absent. The rest of the general physical and systemic examination was unremarkable.

Laboratory tests in the form of complete blood counts revealed microcytic hypochromic anemia (Hb8.2 g/dL), while the total leucocyte count and platelet count were within the normal range. The erythrocyte sedimentation rate (ESR) was elevated (115 mm in the first hour). Albumin: globulin reversal was noted with an albumin level of 2.6 g/dL and a globulin level of 5.4 g/dL. The rest of the liver and kidney function tests were normal. A chest X-ray revealed bilateral pleural effusion, with more effusion on the left. Results of a nerve conduction study suggested axonal sensory motor neuropathy in all 4 limbs. Analysis of cerebrospinal fluid revealed elevated protein levels (160 mg/dL) with a normal glucose level and normal cell counts. Magnetic resonance imaging (MRI) of the brain and spine was normal. Overall, neurological findings suggested GBS.

Exhaustive tests were conducted to determine the triggers and etiology of the accompanying fever and weight loss. A routine stool examination was normal. Serology was negative for HIV, hepatitis B and C, cytomegalovirus (CMV), and Epstein-Barr virus (EBV). Serum angiotensin-converting enzyme (ACE) levels, the antinuclear antibody (ANA) test, and serum protein electrophoresis were normal. A 2D echocardiogram revealed pericardial effusion with grade III diastolic dysfunction. Contrast-enhanced computed tomography (CECT) of the chest and abdomen

revealed bilateral pleural effusion, pericardial effusion with pericardial thickening without calcification, and enlarged lymph nodes in the paratracheal region and in the retroperitoneum (Figure 1). Pleural fluid was exudative (protein: 4.4 g/dL, glucose: 3 mmol/L), and lymphocytes were predominant (25×10^6 cells/L, 100% lymphocytes). Elevated adenosine deaminase (ADA) levels (40 IU/L) were noted. In light of the clinical features, enlarged lymph nodes, exudative lymphocyte-rich pleural fluid with high levels of ADA, and pericardial effusion, the patient was diagnosed with disseminated tuberculosis.

The patient underwent 5 sessions of plasmapheresis on alternate days. Once tuberculosis was considered likely, the patient was started on category I ATT along with steroids. During hospitalization, weakness continued to improve and the fever subsided. The patient was discharged but closely followed. At the follow-up at 6 months, the patient was afebrile, he had regained 4 kg in weight, pedal edema had resolved, and weakness had considerably improved with a muscle strength grade of 5 in all 4 limbs. Steroids had been tapered off by this time. Repeat computed tomography (CT) imaging showed resolution of tuberculosis, and anti-tubercular therapy was halted (Figure 2).

3. Discussion

In the current case, the clinical presentation and test results led to a diagnosis of GBS. Since studies have noted improvement even up to 4 weeks after the onset of weakness (3), the patient was treated with plasmapheresis. A detailed evaluation suggested

Table 1. Summary of reported cases of GBS and tuberculosis

Author and year (ref. No.)	Diagnosis	Treatment	Outcome
Vyrvanathan <i>et al.</i> 1983 (8)	Pulmonary tuberculosis with GBS	ATT and physiotherapy	Recovered completely
Soehardy <i>et al.</i> 2005 (6)	Pulmonary tuberculosis and GBS (AMSAN variant)	ATT and IVIG	Recovered completely
de la Torre <i>et al.</i> 2010 (5)	Extrapulmonary tuberculosis (cervical lymph node) with GBS	ATT and IVIG	Recovered (patient developed IBD 2 months later)
Taha <i>et al.</i> 2012 (7)	Pulmonary tuberculosis with GBS (AIDP)	ATT and IVIG	Recovered completely
Canham <i>et al.</i> 2014 (4)	Pulmonary tuberculosis with pericardial effusion and GBS (AIDP)	ATT and IVIG	Difficulty walking with restricted ankle movement and constrictive pericarditis
Current case	Disseminated tuberculosis (Mediastinal and retroperitoneal lymph nodes, pleural effusion, pericardial effusion with thickening) and GBS(AMSAN)	ATT and plasmapheresis	Constrictive pericarditis without functional disability

AIDP, acute inflammatory demyelinating neuropathy; AMSAN, acute motor sensory axonal neuropathy; ATT, antitubercular therapy; IBD, inflammatory bowel disease; IVIG, intravenous immunoglobulin.

tuberculosis, but the patient's neurological status precluded confirmation of that diagnosis with endobronchial ultrasound (EBUS)-guided lymph node sampling. The diagnosis of tuberculosis was confirmed by the treatment response (complete clinical and radiological response) at the 6-month follow-up.

To the extent known, 5 cases (4-8) involving tuberculosis in association with GBS have been published thus far (Table 1). The association has mostly been reported with pulmonary tuberculosis. All previously reported cases had features suggesting tuberculosis prior to the onset of weakness. This is the second such case with an AMSAN variant of GBS. The subtypes of GBS in India (9) follow the same distribution as in the rest of the world: AIDP is the most common (73.8%), followed by AMAN (13.4%) and AMSAN (4.6%). The AMSAN variant is very rare and has a worse prognosis and delayed recovery. The current patient presented quite late in the course of his illness, but prompt management and treatment of the underlying condition resulted in a satisfactory response. Plasmapheresis had not been used in any of the previously reported cases. In all of the cases, patients responded to treatment but those with pericardial effusion had constrictive pericarditis (including the current patient).

The temporal association between GBS and the patient's other symptoms suggests that this association is unlikely to be due to chance. Hence, the ability of *Mycobacterium tuberculosis* to trigger GBS needs to be investigated. The pathogenesis of GBS is believed to be immune-mediated. A greater delay in cell-mediated immunity in tuberculosis has been suggested as the mechanism responsible. Molecular mimicry

leading to autoimmunity and damage to nerves is also a possibility.

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