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TUBERCULOSIS UNMASKS MYASTHENIA: A UNIQUE EXPERIENCE

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Abstract
Myasthenia gravis is an autoimmune disease of the neuromuscular junction where in acetylcholine receptor antibodies binds to and inhibits the action of acetylcholine, thereby presenting as weakness and fatigue on exertion. Myasthenic crisis is a life threatening condition which often mandates emergent life support measures. Tuberculosis is one of the most common causes of precipitation of myasthenic crisis in diagnosed cases of myasthenia. But here we report a case of 25 year old female, diagnosed as sputum positive pulmonary tuberculosis, not a known case of myasthenia who presented to us with generalised weakness and severe type 2 respiratory failure subsequently diagnosed as myasthenic crisis. This case has been a singular experience and posed a challenge to us physicians with regards to successful management as because tuberculosis impeded the use of immunosuppressant to combat the highly fatal disease.

Keywords: Tuberculosis, Myasthenia gravis, Myasthenic crisis

Introduction

Myasthenia gravis is a postsynaptic neuromuscular junction disorder wherein auto-antibodies against acetylcholine receptors bind with the acetylcholine receptors causing impaired neuromuscular transmission manifesting as weakness and fatigability on repeated excursion. [1],[2],[3] Several other auto-antibodies have been implicated as causative agents among which anti-Musk antibody is an important antibody especially when acetylcholine receptor antibody is negative. Myasthenic crisis is a life threatening condition precipitated in diagnosed cases by concurrent infections, noncompliance to medications. Rarely crisis can be presenting manifestation also. Management is primarily based on two principles. One is to increase the local availability of acetylcholine in the synaptic cleft which is achieved by inhibition of acetylcholinesterase. The second principle is immunosuppression to combat the basic pathophysiology which in this scenario is

autoantibody formation. Screening for tuberculosis and other opportunistic infection becomes important in the management of such patients especially before initiation of immunosuppressant drugs especially in an tuberculosis endemic country like India. Previous reports have mentioned tuberculosis as a cause of aggravation of symptoms in diagnosed patients of myasthenia gravis or part of the screening protocol before initiating steroids or other immunosuppressants. But this case provides an unique situation for the internist whereby tuberculosis precipitated myasthenic crisis in a previously undiagnosed patient. Such case is not documented before and posed a challenge for us as physicians to manage as immunosuppressant medications could not be initiated at the outset.

Case history

25 year old female patient was diagnosed as sputum positive pulmonary tuberculosis for which the patient was started on category I anti-tubercular drug therapy 7 days back. During the last seven days the patient started noticing generalised weakness which gradually impaired the working capacity of the patient along with shortness of breath. At the time of presentation the patient also had shortness of breath at rest. The patient also complained of difficulty in opening the eyes. There was no diurnal variation and double vision. The patient also had difficulty in deglutition with nasal intonation of voice and nasal regurgitation of food. On examination, there was anaemia, tachypnea with peripheral oxygen saturation of 70% on nasal oxygen inhalation at 6L/min, cyanosis, tachycardia. There was decreased air entry bilaterally with crepitations and wheeze involving the left lung field. Neurological examination revealed asymmetric ptosis with normal movements of the extra ocular muscles(Figure 1). Pupillary reflexes were normal. Palatal excursion was poor and gag reflex was delayed. Motor examination revealed grade 4 power in all 4 limbs with intact sensations and generalised hyporeflexia. Babinsky response was negative. No signs of cerebellar involvement. Suspecting myasthenia, ice pack test was done with significant improvement in the ptosis. Intravenous administration of 0.5 mg of neostigmine resulted in dramatic response with improvement in the muscle power and also disappearance of nasal intonation of voice and ptosis(Figure 2). Initial investigations revealed a microcytic hypochromic anaemia with haemoglobin of 9.7 g/dl, MCV 78 fl, MCH 26 pg. Liver function test was normal. Sputum for acid fast bacilli(AFB) was positive on presentation. Chest roentgenogram revealed a destroyed left lung field with compensatory right sided emphysematous changes. Arterial blood gas analysis revealed a type II respiratory failure with PH of 7.35, PCO2 67 mmHg, PO2 58 mmHg, HCO3- 36.2 mmol/l. Contrast enhanced CT of brain was ordered to rule out any brainstem pathology such as tuberculoma. Patient was non diabetic and HIV 1 and 2 were also negative. Urgent electrophysiologic testing with repetitive nerve stimulation testing revealed a decremental response with 3 hertz stimulation involving the bulbar muscles, trunk and limbs suggestive of generalised post synaptic neuromuscular junction disorder compatible with generalised myasthenia gravis. Anti-Acetylcholine receptor antibody was positive. Investigation for other possible autoimmune disorderslike ANA in Hep2, rheumatoid factor were negative and the thyroid profile was normal. Contrast enhanced CT imaging of the thorax didnot reveal any evidence of thymic enlargement. Patient was initially given supportive management in the form of high flow moist oxygen inhalation via a non-rebreathing mask, nasogastric tube insertion for feeding purpose, propped up position to prevent aspiration, re initiation of anti-tubercular drugs via Ryles' tube, oral pyridostigmine 60 mg QID along with oral

neostigmine 15 mg BD. Gradually the patient showed improvement and the nasogastric tube was removed with initiation of oral feeds. Steroid could not be started due to sputum being positive for AFB. With proper anti-tubercular drug therapy the sputum became negative in 2 weeks' time and oral prednisolone was started in low dose of 20 mg/day after further one week. There was significant improvement with initiation of steroid and the requirement of pyridostigmine came down. The patient was discharged after 2 weeks in stable condition. Steroid was increased to 40 mg/ day after a period of 3 weeks and then it was maintained at that dose for further one month and then gradually the dose was tapered. The requirement of pyridostigmine also came down and the patient was maintaining well on 60 mg TID orally. The patient was planned for thymectomy operation after completion of 6 months of anti-tubercular drug therapy. But it could not be done due to pulmonary function tests revealing poor lung compliance. At present the patient is doing well on 60mg TID of pyridostigmine orally with the steroid tapered off. Presently the patient is stable and is doing well.

Discussion

Myasthenia gravis is an autoimmune disorder characterised by presence of antibodies against acetylcholine receptors which binds to and blocks the acetylcholine receptors thereby preventing the normal neuromuscular junction transmission.[1],[2],[3] Myasthenic crisis is a life threatening condition where the symptoms of weakness and fatiguability are overwhelming and often the patient needs mechanical ventilator support along with immunosuppressive therapy directed to reduce the load of the autoantibodies.[4],[5] Infections and other stress and noncompliance to medications are very important causes of precipitation of a crisis state. Tuberculosis is a very important infection that has to be kept in mind especially in an endemic country like India. It can worsen the clinical features of a myasthenic patient and precipitate crisis as has been documented in few case reports previously.[6] Screening for tuberculosis is mandatory before initiating immunosuppressive agents in the treatment of myasthenia as tuberculosis can flare up in the immune suppressed state.[7],[8] This case presented to us with an unique scenario wherein a patient presented to us with crisis due to sputum positive pulmonary tuberculosis. This posed special problem as immunosuppressive medications could not be initiated due to the infection. Though the patient improved with supportive management in the form of anti-tubercular therapy, acetylcholinesterase inhibitors, the underlying infection prevented from initiating immunosuppressants from the beginning.

To conclude, myasthenia can present as crisis in certain cases. Tuberculosis is an important entity to be kept in mind during the management of myasthenia patients and it can be a precipitating factor for crisis. Myasthenic crisis can be presenting feature of generalised myasthenia in a previously undiagnosed patient. Prompt diagnosis and early treatment can reduce mortality and morbidity of the autoimmune catastrophe.

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Appendix:

Figure 1: Bilateral ptosis before intravenous neostigmine

Figure 2: Improvement in ptosis after intravenous neostigmine