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Case Report

Oncological Disorder Masquerading as an Atypical NMJ Disorder

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ABSTRACT:
Myasthenic crisis (MC) can affect any age, ethnicity, or sex and can be precipitated with any stressor, infection being the most common. MC is a clinical diagnosis defined by respiratory failure caused by exacerbation of Myasthenia Gravis. Muscle weakness can involve any voluntary muscle. MC can be differentiated from other neuromuscular junction diseases by the presence of normal reflexes, normal sensation, lack of autonomic symptoms, lack of fasciculations, and worsening weakness with repetitive motion. Treatment should target the inciting event and airway support. Establishing timely consequent immunosuppression and treatment of myasthenic patients in specialized outpatient centres help to avoid repetitive exacerbations and crises.
Keywords Myasthenic crisis, Neuromuscular junction disorders, Ptosis, Myasthenia Gravis

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INTRODUCTION

Neuromuscular junction (NMJ) disorders result from destruction, malfunction or absence of one or more key proteins involved in neuromuscular transmission. The most common pathology is antibody mediated damage or down regulation of ion channels or receptors, resulting in myasthenia gravis (MG), Lambert-Eaton myasthenic syndrome (LEMS), and acquired neuromyotonia (Isaac's syndrome). A second important group of disorders are the congenital myasthenic syndromes caused by mutations in NMJ proteins.[1]

Myasthenia gravis (MG) is an uncommon autoimmune disorder affecting the neuromuscular junction and manifesting as muscle weakness. A multitude of stressors can exacerbate MG. When symptoms are exacerbated, muscle weakness can be severe enough to result in respiratory failure, a condition known as myasthenic crisis (MC).[2]

MG is caused by the action of antibodies against proteins in the neuromuscular junction, and the most common autoantibody is the anti-acetylcholine receptor (AChR) antibody. This antibody reduces the number of postsynaptic acetylcholine receptors available on the end plate of the skeletal muscle. The second most prevalent antibody recognizes muscle-specific kinase (MuSK); this autoantibody is found in up to 70% of AChR-negative MG patients.[3]

MC occurs in 10–20% of MG patients over the course of their disease.[4] While associated with mortality rates

as high as 50–80% in the 1960s, MC is now often reported to be fatal in fewer than 5% of cases as a result of the development of intensive care techniques.[5] Exacerbation of myasthenia must always be regarded as a possible prodromal stage of a crisis and requires rapid and consequent treatment. There is a substantial risk of acute worsening with the need for intensive care, particularly during initial manifestation or with concomitant bacterial or viral infection, as well as resulting from half-hearted or discontinued immunosuppression.[6]

Myasthenic crisis can involve the upper airway muscles, respiratory muscles, or a combination of both muscle groups. Both inspiratory and expiratory respiratory muscles can be affected, manifesting as dyspnoea. Inspiration is performed primarily by the diaphragm and external intercostal muscles and secondarily by the sternocleidomastoid and scalene muscles. Although expiration is primarily passive, the abdominal and internal intercostal muscles can be recruited to assist Upper airway weakness can lead to respiratory failure by oropharyngeal collapse or tongue obstruction and by increasing the work of already fatigued respiratory muscles against a closed airway. Signs of bulbar weakness include dysphagia, nasal regurgitation, a nasal quality to speech, staccato speech, jaw weakness (jaw closure weaker than jaw opening), bifacial paresis, and tongue weakness.[7]

CASE REPORT

A 35-year-old male, known case of Acute Myeloid Leukaemia (AML) for 1 year, on chemotherapy, in remission phase presented in the neurology OPD with complaints of difficulty in closing both eyes for 1 month which started in left eye and later progressed to right eye. The symptoms presented after the patient was put on a course of aminoglycosides for an underlying chest infection by the oncologist. Subsequently patient developed drooping of both eyelids which was more on left side than the right.

Systemic examination

Patient was found to have bilateral bell's phenomenon and asymmetrical ptosis; hence the Curtain Sign is positive. No fasciculation was observed. No signs of bowel or bladder involvement were seen. No sensory deficit was found on examination. Deep tendon reflexes are present (2+). Plantar response if flexor bilaterally. No autonomic features are to be seen on examination. Therefore, a preliminary diagnosis of Post-synaptic NMJ disorder was considered.

Investigations

Repeated nerve stimulation was performed following the signs observed in examination and a significant decremental response along with post-tetanic exhaustion was seen. All serum electrolytes level (sodium, calcium, magnesium, phosphate) were found to be normal. Creatinine phosphokinase (CPK) levels were found to be normal. Final diagnosis of Myasthenic crisis was made.

Treatment and Follow-up

The patient was started on Methylprednisolone at the dose of 1mg/kg/day for 10 days. During this period patient developed progressive symmetrical weakness of bilateral lower limbs which subsequently progressed to symmetrical weakness of bilateral upper limbs. The patient also developed difficulty in breathing which authenticated our final diagnosis.

Patient was further evaluated for Mediastinal tumour. Contrast enhanced computed tomography (CECT) chest was done which did not show any evidence of thymoma. MRI brain with spine screening was done to rule out brain parenchymal involvement for leukemic infiltrates which came out to be normal.

DISCUSSION

Myasthenic crisis is defined as a constellation of clinical conditions in which within a few days, or more rarely, a few hours, there is severe weakness of bulbar-innervated muscles or the respiratory muscles which restricts breathing or speech ability so severely that supportive feeding, intubation or ventilation are require. Myasthenic crises thus require hospitalization in a monitored intermediate care facility or intensive care unit. Critical incidences are acute respiratory insufficiency, aspiration resulting in aspiration pneumonia, globus caused by restriction of the ability to swallow or cough, or generally the consequences and risks of immobility/bed confinement and intensive care.[8]

Major precipitating factor is infection in almost 38% of patients presenting with myasthenic crisis; most commonly was bacterial pneumonia followed by a bacterial or viral upper respiratory infection. Other precipitants include aspiration pneumonitis, surgery, pregnancy, perimenstrual state, certain medications, and tapering of immune-modulating medications. Other antecedent factors include exposure to temperature extremes, pain, sleep deprivation, and physical or emotional stress. Approximately one-third to one-half of patients may have no obvious cause for their myasthenic crisis.[7]

Numerous medications may exacerbate MG, including quinidine, procainamide, b-adrenergic antagonists, calcium channel antagonists (verapamil, nifedipine, felodipine), magnesium, antibiotics (ampicillin, gentamicin, streptomycin, polymyxin, ciprofloxacin, erythromycin),34- phenytoin, gabapentin, methimazole, a-interferon, and contrast media. These medications should be used cautiously in myasthenic patients, especially after surgery. Any medication suspected of precipitating myasthenic crisis should be discontinued. The 2 primary pharmacologic therapies available for myasthenic crisis are intravenous immunoglobulin (IVIg) and plasma exchange (PE).[9]

Patients in myasthenic crisis develop markedly hypermotoric delirious states; however, exact incidences are not known. Whether specific pathophysiological aspects related to myasthenia are involved, e. g., dysregulation of the cholinergic system after discontinuation and re-introduction of cholinesterase inhibitors, is speculative. Plasmapheresis or equivalent immune adsorption can influence the course of the disease very favourably within a few days. By using these early in the case of exacerbation which does not respond sufficiently to pyridostigmine, intubation and ventilation can be frequently avoided. As an alternative to PLEX/IA, intravenous immunoglobulin therapy can be performed in the case of e. g., manifest infection. In the case of exacerbation with significant bulbar involvement, corticoids are not indicated due to their delayed effect and regular worsening during the first weeks of treatment. After stabilization, consistent immunosuppression with corticoids and azathioprine should be initiated during the further progression of the disease.[6]

CONCLUSION

MC should be in the differential of any patient with muscular weakness and respiratory compromise. Intensive care management of MC should focus on ruling out infection and respiratory support. Strong consideration should be given to beginning with non-invasive positive-pressure ventilation for ventilatory support. Corticosteroids, depolarizing paralytics, and acetylcholinesterase inhibitors should be avoided in patients with MC in the emergency department.

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