Case Report

An Unusual Case of Recurrent Respiratory Failure

Pushpita Mandal[1]

Myasthenic crisis is a complication of myasthenia gravis characterized by worsening of muscle weakness, resulting in respiratory failure that requires intubation and mechanical ventilation. Advances in critical care have improved the mortality rate associated with myasthenic crisis. This article is about the atypical presentation of a case of recurrent respiratory failure which was finally turned out to be a case of myasthenic crisis. Therapeutic options including mechanical ventilation and pharmacological management is also discussed here.

[*J Indian Med Assoc* 2020; **118(12):** 66-8]

***Key words*: Myasthenia gravis, Autoimmune diseases of the nervous system, Myasthenic crisis, Neurocritical care clinical specialty.**

Myasthenia gravis (MG) is an autoimmune disease commonly affecting middle-aged female populations[1]. This disease is mediated by a type-II antibody reaction in which antibodies directed against post-synaptic nicotinic acetylcholine receptors attack the myoneural junction and damage the post-synaptic membrane via complement fixation. This results in the failure of action potential propagation across the neurons, eventually leading to a neuromuscular weakness without stiffness[2]. Classically, the anticholinergic autoantibodies target the extraocular muscles, leading to fluctuating muscular fatigability, predominantly resulting in bilateral diplopia and ptosis, which is typically worse at the end of the day. It constitutes more than half the cases[1]. Bulbar weakness, leading to dysphagia and dysarthria, has been rarely described as the initial complaint, more commonly in the elderly male population[2].

Case Report

A 68 yrs old male was admitted with increased shortness of breath in our ICU in February 2020. He had background history of type 2 DM, hypertension,COPD. He was a prolonged smoker and received chemotherapy and radiotherapy for mucoepidermoid carcinoma of the tongue earlier. He had a history of cough, cold and shortness of breath on exertion for last 3-4 days. Following which he developed Bells' palsy (difficulty in closing left upper eyelid).

On Examination :

He was tachypnoic (RR>30),tachycardic, and suddenly became unresponsive and bradycardic in the CT scan department (while undergoing HRCT thorax) requiring intubation and ventilation.CXR was suggestive of widening of mediastinum with right lower zone opacity. ABG was suggestive of type 2 respiratory failure. But after a couple of hours he became totally conscious alert and wanted to pull out the tubes. On the next morning he got extubated .

Editor's Comment :

- **Myasthenia gravis (MG) is often complicated by respiratory failure, known as a myasthenic crisis. However, most of the patients who develop respiratory symptoms do so during the late course of disease and have other neurological signs and symptoms. However, in some patients respiratory failure is the initial presenting symptom.**
- **In this case of a 68-year-old male with MG who presented with isolated respiratory failure as his first presenting symptom as illustrated by this case, it is important to consider neuromuscular disorders in cases of unexplained respiratory failure.**

Course in the Hospital :

But again by the evening he had drowsiness, ABG was suggestive of type 2 respiratory failure (ABG-pH 7.29, pCO2 82, pO2 53, HCO3 39.4), he was put on BIPAP initially at (14:6), then increased to (16:6),but ultimately required reintubation and ventilation. HRCT scan of thorax was suggestive of suspected lung mass and right whole lung collapse. FOB (fibreoptic bronchoscopy) was suggestive of right lower lobe bronchus totally plugged with thick secretion, which was aspirated and sent for culture and there was no evidence of any endobronchial growth. BAL fluid culture was suggestive of growth of MDR klebsiella which was sensitive to colistin only, so intravenous colistin was started.He gradually improved and got extubated after 2 days.

But again on next morning, on morning round he was found to have difficulty in neck holding, there was increased drooling of saliva, weakness of proximal muscle and left sided ptosis. He reqired reintubation by the evening due to bradycardia,desaturation and one episode of convultion. Neurologist decided to do EEG, lumbar puncture and NCV at bedside. His acetylcholine receptor antibody level was sent also.

- His CSF showed cell count of 2(all lymphocytes), protein 40mg/dl, sugar 150mg/dl.
- His NCV report showed (normal distal latencies,

[1]MD (Medicine), FCCCM (Mumbai) Senior Consultant, Critical Care and Internal Medicine, Woodlands Multispeciality Hospital, Kolkata 700027 and Corresponding Author

Received on : 10/12/2020
Accepted on : 14/12/2020

reduced CMAP amplitudes and reduced conduction velocity of bilateral median, ulnar, tibial & common peroneal nerve, All F responses of both upper and lower limbs were absent, bilateral soleus H reflexes were absent, bilateral median, ulnar, sural SNAPS were absent…final impression was **bilateral axonal type sensory motor polyneuropathy involving all four limbs.**

As it was 3rd time intubation it was decided that tracheostomy will be done, but later on it was decided to give him a trial of IVIG infusion 400mg/kg/day for next 5 days. Gradually his neurological status improved, neck holding got better, he was put on oral steroids in high dose. Got extubated after 5 days. He was put on appropriate antibiotic as per culture sensitivity report. His BAL galactomannan was also very high (value 2.71, normal reference range was negative <.50, positive>=.50). So he was put on voriconazole intravenously 400 mg twice daily for 1 day then 200 mg twice daily for next 14 days. By this time his acetyl choline receptor antibody report came which showed positive result in **high titre(59.8). (**Reference value for positive was>0.50).

So our diagnosis **was an atypical variety of myasthenia presenting with myasthenic crisis with sensory motor axonal polyradiculoneuropathy.** He was put on pyridostigmine 60 mg tds, oral steroid and mycophenolatemofetil.

But unfortunately again after 2 days he had started showing weakness of respiratory muscles, so again required reintubation, this time it was decided to put him on plasmapheresis. Nephrologists gave the regimen for plasmapheresis.

He received plasmapheresis for total 5 days,and then gradually over a period of another 2-3 days his respiratory parameters got improved and he got extubated and discharged subsequently.

Discussion

Myasthenia gravis is an autoimmune disorder causing skeletal muscle weakness, most commonly in the eyes, bulbar muscles, limbs, and respiratory muscles[1]. Whilst it usually presents with ocular symptoms or dysarthria, dysphagia and fatigable chewing, our patient presented with difficulty in breathing, needing recurrent ventilatory support[3]. This case illustrates importance of considering uncommon causes for common presentations, when it does not fit in with the diagnosis.

This patient had myasthenia gravis presenting with respiratory failure due to respiratory muscle weakness. Several studies have reported respiratory muscle weakness in patients with generalised myasthenia gravis[9,10]. **This case is unusual in that :**

• The respiratory muscles were affected predominantly and patient had no prior history of progressive neuromuscular weakness or increasing fatiguability symptom at the end of the day.

• There was associated sensory-motor-axonal polyradiculoneuropathy.

• Acetyl choline receptor antibody was present in high titre and patient required both IVIg and plasmapheresis

Epidemiology :

• Although data are limited, the proportion of patients with myasthenia gravis who experience at least one myasthenic crisis may be as high as **10 to 20 percent** and the annual risk of myasthenic crisis among patients with myasthenia gravis is approximately **2 to 3 percent**. In 13 to 20 percent of patients who present with myasthenic crisis, it is the first manifestation of myasthenia gravis. Most myasthenic crises occur in the first few years after the diagnosis of myasthenia gravis, when the disease is often in its most active phase.

• Clinical features:Patients who develop myasthenic crisis typically experience increasing generalized or bulbar weakness as a warning. Occasionally, patient presents with respiratory insufficiency out of proportion to limb or bulbar weakness. In a report of 44 patients who developed 63 episodes of myasthenic crises, the crisis began with generalized weakness, bulbar symptoms, or weakness of respiratory muscles Myasthenia gravis is most frequently associated with antibodies against acetylcholine receptors (AChR) in the post-synaptic motor end plate. A second form of myasthenia gravis, usually seen in young women, involves antibodies against muscle-specific tyrosine kinase (MuSK). A third group of patients has antibodies to neither AChR nor MuSK, and these patients are considered seronegative. Clinically, these patients are similar to patients with AChR antibodies. Overall, women are twice as likely as men to be affected. A bimodal distribution of myasthenic crisis is seen[11,12]. An early peak prior to age 55 affects women 4:1, whereas a later peak after age 55 affects women and men equally[4].

Advances in mechanical ventilation and critical care have been paramount in improving mortality associated with myasthenic crisis.

Precipitants of Myasthenic Crisis :

The most common precipitant is infection. One series documented infection in 38% of patients presenting with myasthenic crisis; most commonly, the infection was bacterial pneumonia followed by a bacterial or viral upper respiratory infection[8].

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[4].

Numerous medications may exacerbate MG[15,16], including quinidine, procainamide, α-adrenergic antagonists, calcium channel antagonists (verapamil, nifedipine, felodipine) magnesium,antibiotics (ampicillin, gentamicin, streptomycin, polymyxin, ciprofloxacin, erythromycin), phenytoin, gabapentin, methimazole, α-interferon, and contrast media[5]. These medications should be used cautiously in myasthenic patients, especially after surgery. Any medication suspected of precipitating myasthenic crisis should be discontinued.

Although corticosteroids can be used in the treatment of

MG, initial treatment with prednisone led to an exacerbation of MG in almost half of patients in 1 series. The incidence of myasthenic crisis resulting from corticosteroids ranges from 9%-18%. Thus, commencement of corticosteroids for the treatment of MG should always occur in a hospital setting, where respiratory function can be monitored.

Of the 46 episodes of MC, extubation failure occurred in 20 (44%), including 9 of 35 episodes (26%) of reintubation. Male sex, history of previous crisis, atelectasis, and intubation for more than 10 days were associated with extubation failure[7]. Lower pH and lower forced vital capacity on the time of extubation, atelectasis, and bilevel intermittent positive airway pressure use after extubation predicted the need for reintubation[16]. Atelectasis showed the strongest association with both end points.

Conclusions

Extubation failure is relatively common in patients with MC. Atelectasis is the strongest predictor of this complication[17].

References

1 Bedlack RS, Sanders DB — On the concept of myasthenic crisis. *J Clin Neuromuscul Dis* 2002; **4:** 40.
2 Wendell LC, Levine JM — Myasthenic crisis. *Neurohospitalist* 2011; **1:** 16.
3 Berrouschot J, Baumann I, Kalischewski P, *et al*— Therapy of myasthenic crisis. *Crit Care Med* 1997; **25:** 1228.
4 Rabinstein AA, Mueller-Kronast N — Risk of extubation failure in patients with myasthenic crisis. *Neurocrit Care* 2005; **3:** 213.
5 O'Riordan JI, Miller DH, Mottershead JP, *et al* — The management and outcome of patients with myasthenia gravis treated acutely in a neurological intensive care unit. *Eur J Neurol* 1998; **5:** 137.
6 Mier A, Laroche C, Green M — Unsuspected myasthenia gravis presenting as respiratory failure. *Thorax* 1990; **45:** 422.
7 Dushay KM, Zibrak JD, Jensen WA. Myasthenia gravis presenting as isolated respiratory failure. *Chest* 1990; **97:**232.
8 Gummi RR, Kukulka NA, Deroche CB, Govindarajan R — Factors associated with acute exacerbations of myasthenia gravis. *Muscle Nerve* 2019; **60:** 693.
9 French DM, Bridges EP, Hoskins MC, et al. Myasthenic Crisis In Pregnancy. *ClinPract Cases Emerg Med* 2017; **1:** 291.
10 Sanders DB, Wolfe GI, Benatar M, *et al* — International consensus guidance for management of myasthenia gravis: Executive summary. *Neurology* 2016; **87:** 419.
11 Neumann B, Angstwurm K, Mergenthaler P, *et al* — Myasthenic crisis demanding mechanical ventilation: A multicenter analysis of 250 cases. *Neurology* 2020; **94:** e299.
12 Carr AS, Hoeritzauer AI, Kee R, *et al* — Acute neuromuscular respiratory failure: a population-based study of aetiology and outcome in Northern Ireland. *Postgrad Med J* 2014; **90:** 201.
13 Cabrera Serrano M, Rabinstein AA. Causes and outcomes of acute neuromuscular respiratory failure. *Arch Neurol* 2010; **67:**1089.
14 Juel VC. Myasthenia gravis: management of myasthenic crisis and perioperative care. *Semin Neurol* 2004; **24:** 75.
15 Jani-Acsadi A, Lisak RP — Myasthenic crisis: guidelines for prevention and treatment. *J Neurol Sci* 2007; **261:** 127.
16 Chaudhuri A, Behan PO — Myasthenic crisis. QJM 2009; **102:** 97.
17 Rabinstein AA, Wijdicks EF — Warning signs of imminent respiratory failure in neurological patients. *Semin Neurol* 2003; **23:** 97.

For the birth of something new, there has to be a happening. Newton saw an apple fall; James Watt watched a kettle boil; Roentgen fogged some photographic plates. And these people knew enough to translate ordinary happenings into something new.

— Sir Alexander Fleming