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Case Report

Non-invasive Ventilation for Acute Respiratory Failure in Myasthenia Gravis Crisis. Case Report and Review of Literature

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Abstract

Background: Myasthenic crisis (MC), which occurs in 15% to 20% of myasthenia gravis (MG) patients, is defined as an exacerbation of muscular hyposthenia and is characterized by the onset of bulbar compromise (dysphagia, dysphonia) and strength deficit of the 4 limbs, including acute respiratory failure (ARF).

In the past, the use of non-invasive ventilation during neuromuscular pathologies with ARF such as MG and Guillain-Barre' Syndrome was not popular, but, recent data, have demonstrated its importance, above all phases of the illness, in particular it can be very effective during MC. It reduces morbidity and mortality compared with invasive ventilation.

Case Report: This case report describes a patient, who developed ARF with respiratory acidosis following MC due to pneumonia and was treated successfully with non-invasive ventilation highlighting this first-line therapeutic approach for the management of acute hypercapnic respiratory failure.

A.S, a 68 -year-old female, non smoker, with a diagnosis of MG, was hospitalized for progressive fever, mental fog, dysphagia and dysphonia, worsening of bulbar weakness and progressive dyspnea. She presented with pneumonia and a severe hypercapnic respiratory failure; non-invasive mechanical ventilation was started on Bilevel positive airway pressure (BiPAP). She also began antibiotic therapy, intravenous immunoglobulin (2 gm/kg), and prednisolone. A nasogastric tube was inserted for enteral feeding. The patient experienced subjective (fatigue, respiratory rate, dyspnea, mental fog) and objective (arterial blood gases) improvements with NIV. Bulbar weakness also improved and her ventilatory support was discontinued after 3 days with on removal of the nasogastric tube. The patient had no complications during the hospitalization and, at discharge, nightly monitoring of arterial saturation performed with 24% FiO2 support did not show any significant desaturation events.

Conclusion: In conclusion, this case report highlights the use of non-invasive ventilation during MC with ARF. By avoiding endotracheal intubation, it can prevent lung infections, barotrauma, atelectasis and other complications. that are related to stays in the intensive care, reducing the costs of hospitalization.

Keywords: *Myasthenic Crisis; Acute Respiratory Failure; Non-Invasive Ventilation*

Introduction

Myasthenia gravis (MG) is an uncommon autoimmune disease, affecting the neuromuscular junction and manifesting as a muscle compromising, to generalized or local weakness, characterized by fatigue with chronic course with remission and exacerbation [1]. Three forms of MG exist: with antibodies against acetylcysteine receptors (AChR) in the post-synaptic motor end plate: with antibodies against muscle-specific tyrosin kinase (MuSK) usually in young women and seronegative, without AChR or MuSK [2-4].

Myasthenic crisis (MC) defined as exacerbation of myasthenic weakness, causing respiratory failure, occurs in at least 15% to 20% of patient with MG and can involve the respiratory and upper airway muscles [5-7]. Inspiratory (diaphragm, external intercostal, sternocleidomastoid and scalene muscles) and expiratory respiratory muscles (abdominal, internal intercostal muscles) can be affected, with consequent respiratory dysfunction, manifestating as weakness and dyspnea [8]. Such patients also experience upper airway and bulbar weakness. Upper airway weakness can lead to respiratory failure by increasing the load of already fatigued respiratory muscles, or through oropharyngeal collapse or obstruction. Signs of bulbar weakness are present such as dysphagia, dysphonia, bifacial paresis and nasal regurgitation. Table 1 are lists the principle symptoms of MC.

1. Localized or generalized muscle weakness a. Ptosis b. Dysphonia c. Bilateral asymmetric extra-ocular d. Bifacial weakness e. Dyspnea
2. Fasciculations
3. Nausea
4. Diaphoresis
5. Excessive tearing
6. Increased oral and pulmonary secretions
7. Diarrhea
8. Bradycardia

Table 1: *Symptoms of MC.*

Traditionally, patients with MC are managed by endotracheal intubation and mechanical ventilation [7-9]. But recently the use of non-invasive ventilation (NIV) is increasing in particularly in MC and in other neurological diseases (Duchenne muscular dystrophy, amyotrophic lateral sclerosis): the use can improve the quality of survival and can avoid intubation [10-13]. The treatment of MC includes specific therapy in the form of immunotherapy (steroids, plasmapheresis or intravenous immunoglobulin). In recent years there has been greater use of NIV in patients with acute neuromuscular respiratory failure, exspecially in diseases for which other specific supportive therapies are available [10,13-16]. Common precipitans of MC are listed in table 2 infectious complications include pneumonia, bronchitis, urinary tract infections, colitis, bacteremia and sepsis and several drugs are the most common precipitating factors MG [16-23]. Although corticosteroids can be used to treat of MG and MC in some patients initial treatment with prednisone leads to exacerbation: the incidence of MC due to steroids ranges from 9% to 18% MG [24].

Stressing Conditions	Drugs
Infection	Alfa interferon
Perimenstrual state	Some antibiotics
Surgery	Antiepileptics (gabapentin)
Phsycal stressors	Beta-adrenergic antagonists
Emotional stress	Quinidine
Pain	Contrast media
Fever	Calcium channel antagonists
Environmental state (smoke)	Magnesium
Sleep deprivation	Methimazole
Tapering of immune-modulating medications	Phenytoin

Table 2: *Principal precipitating factors for MC.*

This article reviews the therapeutic approaches and pharmacological treatments for ARF with respiratory acidosis secondary to MC including NIV.

Case Report

A.S, a 68 -year-old female, (non smoker body mass index: 22 Kg/m^2), with a diagnosis of MG from 10 years ago, was admitted to our Respiratory Medicine Care Unit for high fever, which developed 5 days earlier, accompanied by 3 days of mental fog, dysphagia and dysphonia, worsening of bulbar weakness and progressive dyspnea. At admission she had Myasthenic Muscle Score (MMS) of 15/100, Kelly 4. On physical examination, the general condition of the patient was found to be poor, she was in moderate respiratory distress and unable to talk. Her blood pressure was 170/100 and her temperature was 38.7°C. Her cardiovascular exam noted tachycardia, but without murmurs, rubs or gallops. Pulse oximetry revealed a saturation of 87% breathing room air. The neurological examination showed ptosis, bilateral asymmetric extra-ocular muscle weakness and bifacial weakness.

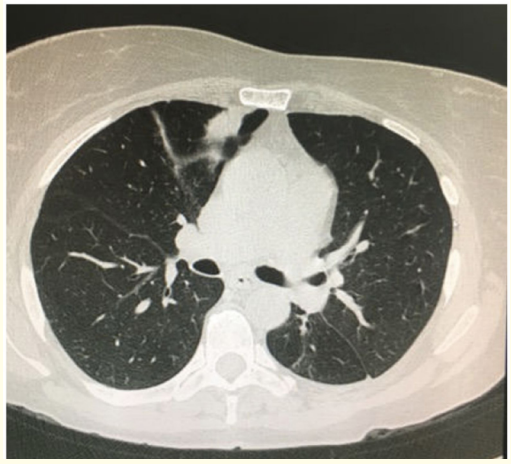

Figure 1: *Images of high-resolution computed axial tomography (HRCT).*

A respiratory examination revealed mild tachypnea with dullness to percussion over the upper-right lung. Auscultation showed decreased breath sounds in the same area, with crackles no wheezing.

The remainder of the physical examination was normal. There was no jugular venous distention or pedal edema.

The laboratories tests revealed leukocytosis at 25000/µL (4000 - 10000) and C-reactive protein 50 mg/dL (0 - 5), erythrocyte sedimentation rate of 90/h (0 - 15). Serum electrolytes and renal and liver function test were normal.

Chest-x-ray in first day was negative, but high-resolution computed axial tomography (HRCT) documented the presence of consolidation in the upper right lung that were identified as pneumonia (Figure 1). Arterial blood gas analysis showed: PaO_2 58 mmHg, $PaCO_2$ 86 mmHg, pH 7.18, serum bicarbonate concentration was 32 mmoli/L, NIV treatment -Bilevel positive airway pressure (BiPAP) - with FiO_2 35% was started: PS 12 cmH_2O, PEEP 5 cmH_2O, with tidal volume of 450 mL (predicted body weight 50 Kg) and backup rate of 16/min. A nasogastric tube was inserted for enteral feeding. After the patient's allergies and potential antibiotic triggers were reviewed, the decision was made to treat with ceftaroline fosamil 600 mg bid: for exacerbation of the myasthenia with intravenous immunoglobulin (2 gm/Kg), prednisolone 40 mg/day were initiated with benefit for tre days. Prophylaxis for deep vein thrombosis and cardiac monitoraing were made.

On the third day of admission her clinical condition and bulbar weakness were improved. Her blood gases had reached normal limits; thus she was disconnected from the ventilator. After 4 days of treatment the nasogastric tube was removed.

Home sleep test demonstrated the absence of desaturation events (mean SpO_2 96%, oxygen desaturation index 1.4/h) and the arterial blood gases (with only oxygen support - FiO_2 24%) normalized (pH 7.42 PaO_2 68 mmHg $PaCO_2$ 42 mmHg $SatO_2$ 94% HCO_3^- 24 mmEq/L). After 7 days from admission into hospital, she was discharged.

Myasthenic Muscle Score (MMS) was of 80/100.

Discussion

Disorders of neuromuscular transmission can be an immunological, toxic or genetic origin. Among these rare disorders, myasthenia gravis is the most frequent. The clinical characteristics of MG are fluctuating pronounced weakness that is limited to the voluntary muscles. It is a generalized disorder that often manifests initially as focal weakness. Eye muscle weakness at the onset of MG is evident in most patients resulting in diplopia and ptosis. Oropharyngeal weakness can cause difficulties in articulation, chewing and swallowing. In generalized myasthenia gravis, limb girdle weakness is typically more pronounced in the proximal distal muscle groups. MC is the life-threating exacerbation of MG due to weakness of respiratory muscles and swallowing difficulties [1-7].

MC is a serious occurrence. In the approach to a patient with MC, the respiratory failure must be evaluated and treated in hospital units with experiences in intensive care. Potential precipitating factors must be identified and managed quickly. According to the literature, in this clinical case the development of pneumonia most likely could have been a cause of the decompensation in myasthenia gravis.

In choosing the antibiotic therapy it should be consideredthatthat that several classes of antibiotics have been associated with exacerbation [21,22]. In the event of an infection that causes clinical deterioration in a myasthenia patient the optimal antibiotic selection becomes paramount. As reported (Table 3) we opted for cephalosporin [24,25]. We initiated treatment with immunomodulatory drugs as soon as possible to reduce the likelihood of complications, as suggested by literature [2]. The use of NIV has increased in the recent years in various neurological diseases (Duchenne muscular, dystrophy amyotrophic, lateral sclerosis) both acute and chronic with acute exacerbation [10-14] such as in MC.

Permissible	Caution	Contraindicated
Cephalosporins	Vancomycin	Aminoglycosides
Rifampicin	Aztreonam	Gentamicin
Chloramphenicol	Co-trimoxazole	Ampicillin
Ethambutol	Daptomycin	Streptomycin
Isioniazid	Piper/tazobactam	Macrolides
Tigecycline		Quinolones
Meropenem		
Teicoplanin		
Linezolid		

Table 3: *Antibiotics permitted and contraindicated in MG or to be used with caution.*

Some previous studies concluded that early intubation for mechanical ventilation is an important step in the management of this condition: the patients with MC were intubated endotracheally and mechanically ventilated for median duration of 11 days [26]. Recently, NIV can be especially useful in the management of ARF in MC, in the absence of hypercapnia and with serum bicarbonate concentration <30 mmoli/L [9,13].

Our clinical case demonstrates the succesfull use of BiPAP in selected patients with neurological disease and acute hypercapnic respiratory failure, especially while they await improvements from other specific therapies as in the case of MC. In our case the patient was treated for 3 days with non-invasive ventilation and she was discharged after 7 days from admission. BiPAP has been used as a valid alternative to invasive ventilation. Repeat clinical evaluation and arterial blood gas measurement in the first hours of admission are generally required to determine the efficacy of NIV and the need for invasive ventilation.

Conclusion

This case report shows the effectiveness of NIV for acute hypercapnic respiratory failure in patients with myasthenia crisis, especially in peculiar situations in which rapid improvement is a waited. In particular, a trial in modality BiPAP can avoid the intubation and prevent prolonged invasive ventilation, reducing all consequent complications, including infections, aspiration, atelectasis, thromboembolic disease and decubitus ulcers and stays in the intensive care unit, with reductions in morbidity, mortality and health costs.

Further prospective, randomized controlled trials that compare non-invasive ventilation versus and endotracheal intubation and mechanical ventilation are needed.

Conflict of Interests

All authors declare that they have no competing interests.

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