Myasthenia Gravis Crisis

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Definition

- **Myasthenic crisis** is a life-threatening manifestation of myasthenia gravis (MG) defined by respiratory insufficiency that requires the use of invasive or noninvasive ventilation.

- **Impending Myasthenic crisis** describes a rapid worsening of MG that could lead to a crisis in days to weeks .

Case 1

- A 54 male presented with dyspnea

  History of URI and generalized weakness 1week earlier
- On examination,Oriented

  C/N: Intact

  Neck:4/5

  Proximal upper limb:4/5 Distal upper limb:5/5

  Proximal lower limb:4-/5 Distal lower limb:5/5

  DTR:+ Plantar:down

Diffrential Diagnosis

- Myelitis Spinal MRI: Normal
- IIM CPK:1500
- MG
- GBS

- EMG_NCV: Normal
- RNS test: >10% decremental pattern in 2 muscles
- CPK:Normal

- Chest CT:Thymoma

- Pathology:TypeA(spindle shape)Thymoma

Epidemiology

- MC occurs in approximately 15% to 20% of patients and can be the first presentation.
- The annual incidence of MC is approximately 2.5% .

- The mean age of hospitalization with MC was 56.5.
- Patients in crisis requiring intubation spend a median of 17 days in the hospital
- mortality of MC is 4% .

CLINICAL MANIFESTATION AND EVALUATION OF MC

- MC typically present with increasing generalized or bulbar weakness ,and weakness of the inspiratory and expiratory muscles leading to reduced respiratory volume, and/or weakness of upper airway muscles causing respiratory obstruction.

- Due to the fatigable nature of MG, respiratory muscles may suddenly wear out, precipitating a respiratory collapse, and profound hypoxemia .

neurological examination

- Ophthalmoparesis and ptosis
- Facial weakness
- Jaw closure
- Hypernasal dysarthria,
- Dysphagia with nasal regurgitation
- weak cough
- Tongue weakness
- Neck flexion weakness
- Paradoxical breathing pattern
- Use of accessory muscles (sternocleidomastoid, scalenes, intercostals, and abdominal muscles)

TRIGGERS, PREDICTORS, AND PREVENTION OF MC

- Infections are associated with 30% to 50% of MC.
- medication change, which includes initiation of medications that could exacerbate MG or suboptimal MG treatment due to tapering of immunotherapy or medication nonadherence.
- Up to 42% of MG patients administered 40–80 mg of prednisone experienced a transient worsening, and those who are older, have bulbar symptoms, or have more severe MG are more likely to experience an exacerbation.
- In up to 30% to 40% of MC cases, no obvious trigger can be identified.

TABLE 1 Common triggers of myasthenic crisis

Infection including bronchitis, pneumonia, and sepsis
Aspiration pneumonitis
Reduction of immunotherapy, under-treatment, or medication nonadherence
Surgery or trauma
Pregnancy/postpartum
Medications (most frequent triggering medications):
Corticosteroid
Antibiotics (e.g., aminoglycosides, macrolides, and quinolones)
Intravenous magnesium
D-penicillamine
Botulinum toxin
Immune checkpoint inhibitors (e.g., pembrolizumab, nivolumab, ipilimumab)
Vaccination
Emotional distress
No obvious precipitant

Case2

• A 50 y/o man with diplopia and dysarthria from 6months ago.

History of psychiatric problems .

• On examination, mild bilateral ptosis with fixed eye

facial weakness

Neck4/5

M/F 5/5

DTR++

Brain MRI:NL

AchR-

RNS:NL

- Lactat:Normal
- AchR-
- MUSK++
- Single fiber:abnormal

MUSK Myasthenia

Start treatment

- Surgery
- Pregnancy
- Perimenstrual state
- Physical or emotional stress
- Medications

  Quinidine,procainamide,BB, CCB

  Penicillamine

  Botulinium toxin

  magnesium

  antibiotics (telithromycine,ampicillin, gentamicin,ciprofloxacin)

  phenytoin, gabapentin,

  a-interferon

  immune checkpoint inhibitors

Risk factors for MC

I. Previous MC
II. Oropharyngeal weakness
III. Severe MG symptoms
IV. MuSK antibody positivity
V. Thymoma

Cholinergic crisis

- Patient taking an excess of acetylcholinesterase inhibitor dosage

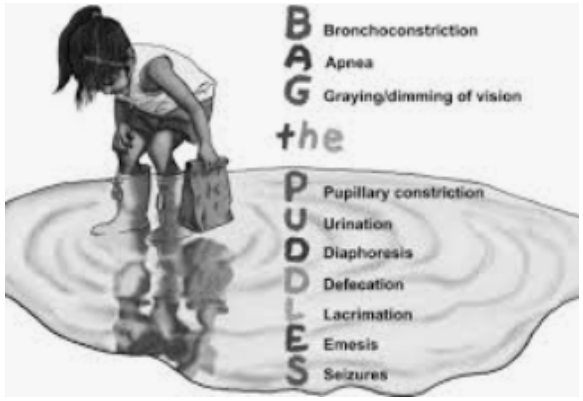

Table 2. Symptoms of Cholinergic Crisis

Nicotinic toxicity
Muscle weakness
Fasciculations
Muscarinic toxicity
Diaphoresis
Excessive tearing
Increased oral and pulmonary secretions
Nausea and vomiting
Diarrhea
Bradycardia

Assesment of respiratory

- **Myasthenic crisis can involve the upper airway muscles, respiratory muscles, or a combination of both muscle groups,manifesting as dyspnea.**
- **Inspiration is performed primarily by the diaphragm and external intercostal muscles and secondarily by the sternocleidomastoid and scalene muscles.**
- **Expiration is primarily passive, the abdominal and internal intercostal muscles can be recruited to assist.**

1. **Bedside spirometry can be performed to measure VC, NIF, and maximal expiratory pressure (MEP).**
2. **VC and NIF reflect the strength of inspiratory muscles, while MEP measurements correlate to the strength of expiratory muscles.**
3. **a decline in MEP by 30% indicates a high risk of needing non-invasive or invasive respiratory support.**
4. **patients with VC >20 mL/kg, MEP >40 cm H2O, or a NIF is better than 40 cm H2O are at low risk.**
5. **useful measure of diaphragmatic weakness is a fall in VC in the supine position when compared to a seated VC.**
6. **Due to difficulty sealing and fluctuating nature of weakness, the decision to intubate should always be clinically .**

- **All myasthenic patients with questionable respiratory status should be admitted to ICU.**
- **Patients with severe and rapidly increasing generalized weakness secondary to an exacerbation of MG should be admitted to an ICU.**
- **Sign and symptom of respiratory failure:**

a) **Dyspnea**

b) **Severe dysphagia**

c) **Hypophonia,pausing ,use of accessory muscle and paradoxical abdominal breathing**

d) **VC <30ml/kg**

I. Early intubation and mechanical ventilation are perhaps the most important steps in the management of MC, and emergency intubation should be avoided.

II. If doubt exists, it is recommended to intubate and ventilate immediately.

III. When there is a suspicion for MC, the patient's vital signs, VC, NIF, and MEP as well as patient's appearance, clinical status, and their trajectory should be frequently assessed. Worsening trends in these measurements should prompt early intubation.

IV. Oxygen saturation and arterial blood gas measurements are generally not considered.

V. The 20/30/40 rule (VC < 20 mL/kg; NIF worse than 30 cm H2O; and MEP < 40 cm H2O) is a helpful tool to guide decisions regarding intubation

- Neuromuscular blocking agents (paralytics) should be used with caution when intubating MG patients.
- Depolarizing agents (for example, succinylcholine) are less potent in MG.
- Nondepolarizing agents (for example, vecuronium) have increased potency, and reduced doses are required for paralysis.

a. Weaning from the ventilator should be initiated after the patient demonstrates clinical improvement, typically at a vital capacity of more than 15 mL/kg.

b. The patient should be alert, hemodynamically stable, and free of triggers for MC.

c. After extubation, a period of close observation for 48 h in the ICU.

d. Predictors of extubation failure include age > 50 y, history of prior MC, pulmonary complications (atelectasis, pneumonia), long intubation duration, and low VC at time of extubation

Risk factors for prolonged intubation>14 days

1) **Age>50**
2) **Peak VC <25 ml/kg on post-intubation days1to6**
3) **Serum bicarbonate>30mmol/l**
4) **Thymoma**

To prevent atelectasis, early intubation, aggressive chest physiotherapy, and frequent suctioning should be implemented and high positive end-expiratory pressure given while the patient is mechanically ventilated.

- Use of non-invasive ventilation Non-invasive ventilation (NIV) can be helpful in patients prior to intubation and post extubation.
- Hypercapnia ($PaCO_2 > 50$ mmHg), pneumonia, and older age predict NIV failure.
- intubation and mechanical ventilation should be initiated if the patient has continued or worsening shortness of breath, increased work of breathing, tachypnea, or hypercapnia (and less frequently hypoxemia)
- Overall, the initial use of NIV is associated with a shorter duration of ventilatory support and ICU stay.

Treatment of Myasthenic Crisis

1) *I*ntravenous immunoglobulin (IVIg) 400 mg/kg daily for 5 days

More serious adverse events can include aseptic meningitis, hypertension, cardiac arrhythmia, thrombocytopenia, and thrombotic events, including stroke, myocardial infarction, and pulmonary embolism.

2) Plasma Exchange, 5 exchanges (40–60 mL/kg) per session.

fever, symptoms from hypocalcemia (primarily paresthesias), a transient decrease in blood pressure, and tachycardia.

- Corticosteroids
- Corticosteroid-sparing agents
- eculizumab has been used in 13 patients with MC who did not respond to IVIG, plasmapheresis or both, most being AChR antibody positive. In all 13 patients, rapid and sustained improvements were observed, usually occurring within 10 days of the first eculizumab dose. In most patients, invasive and non-invasive ventilation were discontinued, while no significant side effects were observed.

- Fc Rn plays a central role in immunoglobulin G (IgG) homeostasis by rescuing IgGs from lysosomal degradation. By binding to the FcRn, efgartigimod interrupts this IgG recycling process and lowers the levels of IgG including AChR antibodies in the blood.
- Efgartigimod may serve as a rescue therapy for patients in MC as an alternative to plasmapheresis, thus "medical plasmapheresis". Its onset of action may not be as fast as traditional plasmapheresis, but improvement can still be seen within the first 1 to 2 wk. Theoretically, it can be considered in patients with contraindications to plasmapheresis like hemodynamic instability, or patients not responding to traditional rescue therapies.

- anti-CD 20 antibodies such as rituximab have been used in the treatment of long-lasting MC after failing initial treatment of IVIG or plasmapheresis.

- Pyridostigmine should be discontinued in patients intubated for MC.

summary

- 15 to 20 %of people living with MG experience at least one crisis in their lives.
- It is a true emergency.
- Elective ventilation
- PLEX and IVIG are used as short-term treatment.
- MG should be on the list of differential diagnoses for unexplained respiratory failure in patients without an established MG diagnosis.

Thank you