Myasthenia Crisis in the Hospital Setting

Definition and Epidemiology

- Myasthenia crisis is a life-threatening exacerbation of myasthenia gravis (MG), characterized by severe muscle weakness leading to respiratory failure or bulbar dysfunction requiring mechanical ventilation or intensive care. MG is an autoimmune neuromuscular disorder caused by antibodies against the neuromuscular junction.
- Prevalence MG affects ~20 per 100,000; myasthenia crisis occurs in 10-20% of MG patients within the first 2 years of diagnosis.
- Risk Factors Infection (40% of crises), medication changes, surgery, pregnancy, non-compliance with therapy.
- Rare Demographics Anti-MuSK MG (more bulbar symptoms), juvenile MG, paraneoplastic MG (small cell lung cancer).

Pathophysiology

- Mechanisms Autoantibodies (anti-AChR, anti-MuSK, or anti-LRP4) impair neuromuscular transmission by blocking or destroying acetylcholine receptors (AChR) or associated proteins, reducing the endplate potential and causing muscle weakness.
- Effects Severe weakness affects respiratory muscles (diaphragm, intercostals) and bulbar muscles (pharyngeal, laryngeal), leading to hypoventilation, aspiration, or airway obstruction. Fatigue worsens with repetitive activity.
- Molecular Pathways Anti-AChR antibodies (85% of cases) trigger complement-mediated destruction of the postsynaptic membrane. Anti-MuSK antibodies disrupt agrin signaling, impairing AChR clustering. Cytokines (IL-6, IL-17) amplify autoimmune response.
- Key Pathway Autoantibody attack → Reduced AChR function → Neuromuscular transmission failure → Respiratory and bulbar weakness.

Causes

Category	Common Causes	Rare Causes	Notes
Infectious	Pneumonia, UTI, viral illness	Sepsis, CMV reactivation	Infection is the leading trigger (40%)

Category	Common Causes	Rare Causes	Notes
Medication-Related	Aminoglycosides, beta-blockers	Quinine, immune checkpoint inhibitors	Check contraindicated drugs (e.g., telithromycin)
Surgical	Post-thymectomy, anesthesia	Abdominal surgery	Neuromuscular blockers exacerbate weakness
Systemic	Stress, pregnancy	Thyroid storm, adrenal crisis	Pregnancy: 30% risk of exacerbation
Neurological	Non-compliance with pyridostigmine	Paraneoplastic (anti-titin antibodies)	Paraneoplastic MG linked to lung cancer
Idiopathic	Unknown triggers	Anti-LRP4 MG, juvenile MG	LRP4 antibodies rare, ocular-predominant

Clinical Presentation

Symptoms

- Progressive weakness (ptosis, diplopia, dysphagia)
- Respiratory distress (dyspnea, orthopnea)
- Bulbar symptoms (dysarthria, nasal speech, choking)
- Rare Generalized weakness mimicking GBS, cognitive changes (hypoxia)

Exam

- Fatigable weakness (worsens with repetitive testing, e.g., sustained upgaze)
- Reduced forced vital capacity (FVC <1.5 L or <20 mL/kg)
- Nasal speech, weak gag reflex, neck flexor weakness
- Rare Fasciculations (MuSK-MG), autonomic instability (paraneoplastic)

Red Flags

FVC <1 L, inability to clear secretions, SpO2 <92% despite O2

Labs and Studies

Labs

- Anti-AChR Antibodies Positive in 85% of generalized MG; binding antibodies most specific
- Anti-MuSK Antibodies Positive in 5-10%, associated with bulbar crises
- CMP Hypokalemia (pyridostigmine overuse), elevated glucose (steroids)
- CBC Leukocytosis (infection trigger), anemia (chronic disease)
- Advanced Anti-LRP4, anti-titin (paraneoplastic), cytokine panel (IL-17, research)

Imaging

- CT Chest Rule out thymoma (10-15% of MG), thymic hyperplasia
- CXR Pneumonia, aspiration, or atelectasis
- Advanced MRI brain/spine (rule out stroke, GBS mimic), PET-CT (paraneoplastic workup)
- Other
- Electromyography (EMG) Decremental response on repetitive nerve stimulation (>10% amplitude drop)
- Single-Fiber EMG Jitter, most sensitive for MG (95%)
- Spirometry FVC <1.5 L or negative inspiratory force (NIF) <-20 cmH2O indicates crisis
- EKG Rule out arrhythmia from QT-prolonging drugs (e.g., azithromycin)
- Advanced Neuromuscular ultrasound (diaphragm thinning), autoantibodies against agrin

Diagnosis

Criteria

Severe weakness (respiratory or bulbar) in known MG or new MG diagnosis + FVC <1.5 L or need for ventilatory support.

Differential

Guillain-Barré syndrome (GBS), botulism, Lambert-Eaton myasthenic syndrome (LEMS), organophosphate poisoning.

Flowsheet

- Step 1 Stabilize ABCs Hypoxia (SpO2 <92%) → BiPAP; airway compromise → Intubation
- Step 2 History/Exam Known MG, recent infection, or medication change; assess FVC, bulbar function
- Step 3 Labs Anti-AChR/MuSK, CMP, infection workup (blood cultures, UA)
- Step 4 Studies EMG (if new MG), CT chest (thymoma), spirometry (FVC, NIF)
- Step 5 Differential Rule out GBS (areflexia, CSF protein), LEMS (proximal weakness, autonomic)

Treatment

General Principles

Reverse triggers, enhance neuromuscular transmission, suppress autoimmunity, and support respiration.

Supportive Care

- Airway Management BiPAP for FVC <1.5 L; intubate if FVC <1 L or unable to protect airway
- Nutrition NG tube for dysphagia, TPN if prolonged NPO
- Infection Control Broad-spectrum antibiotics (e.g., ceftriaxone 2 g IV q24h) if infection suspected

Specific Therapies

- Plasmapheresis (PLEX) 5 sessions over 7-10 days, first-line for rapid response (removes antibodies)
- IV Immunoglobulin (IVIG) 2 g/kg over 2-5 days, alternative if PLEX unavailable
- Corticosteroids Prednisone 1 mg/kg/day (max 60 mg), start low (10-20 mg) to avoid transient worsening
- Pyridostigmine Hold during crisis (risk of secretions); resume at 60 mg q4-6h once stable
- Immunosuppression Azathioprine 2-3 mg/kg/day, rituximab 1 g IV (MuSK-MG), eculizumab (refractory AChR+)

Advanced

Thymectomy (if thymoma), complement inhibitors (ravulizumab), FcRn inhibitors (rozanolixizumab)

Rare Causes

Treat paraneoplastic (chemotherapy for lung cancer), thyroid storm (PTU, beta-blockers)

Monitoring

FVC/NIF q2-4h during crisis

Daily neuro exam (ptosis, diplopia, gag reflex)

ECG monitoring (pyridostigmine, QT drugs)

Complications

Acute

- Respiratory Failure Hypoventilation, CO2 retention (mortality 5-10% if untreated)
- Aspiration Pneumonia From dysphagia, bulbar weakness
- **Cholinergic Crisis Pyridostigmine overdose (muscarinic symptoms:** diarrhea, salivation)

Long-Term

- Steroid Myopathy Proximal weakness, cushingoid features
- Immunosuppression Risks Opportunistic infections (PCP, TB)

Rare

Thymic malignancy (thymoma progression), permanent ventilator dependence

Clinical Scenarios

Case 1 Typical Myasthenia Crisis

Presentation 60 y/o F with known AChR+ MG presents with dyspnea, dysphagia, and worsening ptosis after URI. Vitals BP 140/80, HR 90, SpO2 90%, RR 24. Exam FVC 1.2 L, weak gag, nasal speech.

Labs/Studies Anti-AChR positive, WBC 14K, CXR normal. EMG Decremental response.

Interpretation Myasthenia crisis triggered by infection, respiratory compromise.

Management BiPAP, PLEX (5 sessions), prednisone 20 mg/day (taper up), ceftriaxone 2 g IV q24h. Hold pyridostigmine. ICU monitoring. FVC improves to 2 L by day 5.

Case 2 MuSK-MG Crisis (Rare)

Presentation 45 y/o M with MuSK+ MG presents with severe bulbar weakness, choking, and neck flexor weakness. Vitals BP 130/70, HR 100, SpO2 92%, RR 20. Exam FVC 1.4 L, fasciculations.

Labs/Studies Anti-MuSK positive, CT chest thymic hyperplasia. EMG Jitter on SFEMG.

Interpretation MuSK-MG crisis, high bulbar risk.

Management IVIG 2 g/kg over 3 days, rituximab 1 g IV, methylprednisolone 1 g IV x 3 days. NG tube for nutrition. Neurology consult. Discharge with rituximab maintenance.

Case 3 Paraneoplastic MG Crisis

Presentation 70 y/o M with new-onset weakness, diplopia, and cough. Vitals BP 150/90, HR 88, SpO2 94%, RR 18. Exam Generalized weakness, FVC 1.3 L, cachexia.

Labs/Studies Anti-AChR and anti-titin positive, CT chest 3 cm lung mass. EMG Decremental response.

Interpretation Paraneoplastic MG crisis, likely small cell lung cancer.

Management PLEX, prednisone 40 mg/day, BiPAP, oncology consult for lung biopsy. Chemotherapy planned. Monitor for LEMS overlap (autonomic symptoms).

Expert Tips

- Measure FVC q2h in crisis; intubate early if FVC <1 L or NIF <-20 cmH2O to prevent crash
- Use PLEX over IVIG in severe bulbar crisis (faster antibody removal, less volume)
- Avoid magnesium-containing drugs (e.g., IV MgSO4); they worsen neuromuscular block
- Suspect MuSK-MG in bulbar-predominant crises; fasciculations and atrophy are clues
- Check for thymoma in all new MG; anti-titin antibodies suggest paraneoplastic etiology
- Pitfall Missing cholinergic crisis (miosis, sweating); hold pyridostigmine if secretions excessive
- Advanced Trial rozanolixizumab (FcRn inhibitor) in refractory AChR+ MG; monitor for hypogammaglobulinemia

Key Pearls

- Myasthenia crisis requires urgent airway assessment; FVC <1.5 L signals impending failure
- Infection is the most common trigger; treat aggressively while starting PLEX/IVIG
- Anti-MuSK MG has bulbar predominance, responds better to rituximab
- Hold pyridostigmine in crisis to avoid worsening secretions
- Rare paraneoplastic MG (anti-titin) requires cancer workup (CT chest, PET)

References

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