An Unusual Presentation of Myasthenia Gravis: Rapidly Progressive Distal Muscle Paralysis

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Background

- Myasthenia Gravis (MG) is an autoimmune disorder with antibodies against neuromuscular junction proteins:
  - Acetylcholine receptor (AChR, 80%)
  - Muscle-specific kinase (MusK, 4%,)
  - Lipoprotein-related protein 4 (LPR4,2%)
- **Prevalence:** 1 in 7500, affected all ages, peak incidence 20-30s (women), 60-70s (men)
- MG has an association w/ thymoma (15% of AchR MG)
- **Clinical Manifestation:**
  - Fluctuating weakness - worse w/ repetitive use & relieved by rest "fatigability"
  - 60% initially present w/ ocular symptoms (ptosis, diplopia)
  - 20% only have ocular symptoms
  - 15% will have bulbar symptoms (difficulty with chewing, dysarthria, dysphagia)
  - Proximal limb weakness > distal, DTRs are preserved
- **Progression:** Early in the disorder symptoms may be episodic - being asymptomatic intervals lasting hours, days, or even weeks. Over time, manifestation typically worsens and becomes more persistent.
  - Usually it takes years to progress to maximal severity (requiring respiratory support)
- **Prognosis**: Varies by symptom severity and response to treatment.
  - Factors associated w/ worse prognosis: frequent exacerbations, severe bulbar symptoms, Myasthenic crisis, presence of thymoma, onset at age > 50 YO

Significance

Herein, we report a case in which the patient presented with distal muscle weakness and his symptoms progressed within days. The case will depict an unusual, unique presentation of rapidly progressive muscle paralysis which is likely due to MG.

MG is known to have proximal muscle weakness. There are a few case studies published where the patient's symptoms affect the distal extremities. Many of these case study reports upper extremity weakness. This case study would be unique in the sense that it reports both upper and lower distal extremity weakness.

The cause of MG in most patients is the presence of acetylcholine receptor antibodies. However, in 10-20% of MG patients, these antibodies are not found in the serum. In that patient group, some have an antibody to muscle-specific kinase. However, neither antibody was located in this patient on immunology testing. One study by Romi et al has shown that disease severity is not increased compared to seropositive patients, but the study was small and not randomized.

Case Details

- **38 year old male patient with no reported past medical history presented with right eyelid droop that began several hours prior upon waking and paresthesias in distal extremities.**
  - Numbness, tingling, initially mild but progressive over the last day/night
  - Weakness in bilateral hands and feet since the early morning
  - Denied blurry vision, loss of vision, speech changes, shortness of breath, skin changes, recent outdoor activity, or camping.
  - Was recently sick with a "cold" the week before, with a cough that resolved by presentation.
- **Initial workup:**
  - Physical exam:
    - Nearly complete ptosis of right eyelid; mild fatigability of left eyelid with sustained upward gaze
    - No facial asymmetry or paresis; normal sensation in bilateral trigeminal nerve distribution; no other sensory loss
    - Diffuse weakness, proximal (4-, 4-) > distal (4, 4+) in bilateral upper and lower extremities, symmetric
  - Labs:
    - CBC: normal
    - CMP: normal except for glucose of 113 (74-106)
    - TSH: normal
    - Vitamin B12: 229 (239-931)
    - Folate: normal
    - UDS: negative
    - Immunology: AChR Ab test, MusK Ab test negative, otherwise negative
    - Serology: negative
    - Lumbar puncture: negative
  - Imaging
    - CT brain, CT angiography, MRI brain, MRI spine, CT chest all normal. No thymoma noted.
- **Hospital course**
  - Ice pack test performed in ER: no improvement noted.
  - Neurology consulted, recommend pyridostigmine 60mg TID, with plan for steroids or IVIG if no response
  - Admitted to ICU for respiratory status monitoring.
  - Following admission, became progressively weaker despite pyridostigmine. Eventually developed significant proximal and distal weakness. He developed difficulties with speech articulation.
  - Dose of pyridostigmine was increased, and IVIG was added with resultant improvement.
  - Following some improvement on regimen of supplemental cyanocobalamin, pyridostigmine 120mg q4h, 33 mg IVIG daily, requested transfer to hometown (Boston) to see family.
  - Was transferred directly (hospital to hospital) by MediFlight.

Discussion

- Typically Myasthenia Gravis manifests as presents as ocular, bulbar, and proximal muscle weakness. It tends to progress over weeks to months. In this case study, the patient presented with distal muscle weakness and his symptoms progressed within days.
- As the patient saw symptomatic improvement w/ IVIG and pyridostigmine, our working diagnosis of seronegative MG was supported.
- Many times steroids are used for immunosuppression in patients with MG. Steroids were not given in the case because there was concern for myasthenic crisis. In which, steroids may worsen a patient's symptoms. Myasthenic crisis is a medical emergency that occurs when respiratory muscles weaken to the point the patient needs mechanical ventilation to support their breathing. Myasthenia crisis may be the initial presentation of up to 20% of the patients.
- When treating patients with pyridostigmine, patients are at risk for a cholinergic crisis which is weakness secondary to overtreatment with anticholinesterase medications. Signs and symptoms of cholinergic crisis are: excessive salivation, abdominal cramping, and diarrhea. Plasmapheresis and IVIG are immunomodulating "rapid" therapies in that they start to work quickly over days but benefits only last for weeks. This is why they are usually only used in exacerbations of MG. In a limited small study, IVIG and plasmapheresis had similar efficacy (Barth et al, 2011).

Conclusion

- In this case study, a patient presented with atypical symptoms of MG - including rapid progression and distal weakness. This case is a reminder that as physicians we should continue to include a broad differential diagnosis when evaluating patients and be persistent with diagnostic evaluations in order to help our patients.

References

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