‘Weakness’ in MG

What’s MG and what’s not

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Myasthenia Gravis

- Autoimmune disease with antibodies against the acetylcholine receptor.
- Most patients present with ocular symptoms (ptosis, diplopia) - most go on to develop bulbar and extremity weakness.
  - Weakness is proximal and symmetric.
- Highly treatable
  - Symptomatic (mestinon)
  - Immunosuppressive (many Rx)

Adapted from Kuks 2002
Myasthenia Gravis - the symptoms

• Weakness
  – Fluctuates
  – Worse with use, at end of day
  – Periods of remission & worsening

• Involving
  – Eyes - double vision and droopy eyes
  – Face - facial weakness
  – Speech - slurred or hoarse
  – Swallowing problems
  – Breathing problems
  – Proximal arm weakness - carrying, lifting
  – Proximal leg weakness - stairs and chairs
Diagnosis of MG

• Suspect it clinically

• Diagnostic tests
  – Tensilon test / Ice pack test
  – Electrical tests
    • Repetitive nerve stimulation
    • Single fibre EMG
  – Detection of antibodies in blood
    • Anti-acetylcholine receptor (50% ocular MG are +, 85% generalized MG are +)
    • Anti-MuSK (5% of generalized MG are +)
  – Other
    • CT chest
    • Thyroid tests, Vitamin B12
<table>
<thead>
<tr>
<th>Clinical</th>
<th>Definite or Probable MG n = 680</th>
<th>Definitely or Probably NOT MG n = &gt; 300</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = &gt; 1100 Referred to clinic</td>
<td>Ocular MG 28%</td>
<td>Unknown cause</td>
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<tr>
<td></td>
<td>Generalized 72%</td>
<td>Other types of muscle diseases, thyroid eye problems, nerve problems etc</td>
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<tr>
<td>AChR ab Positive</td>
<td>Ocular 54%</td>
<td></td>
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<tr>
<td></td>
<td>Generalized 87%</td>
<td></td>
</tr>
<tr>
<td>MuSK Positive</td>
<td>n = 13 (≈ 3% of all generalized MG)</td>
<td></td>
</tr>
<tr>
<td>Congenital Myasthenic Syndromes (non-immune)</td>
<td>n = 11</td>
<td></td>
</tr>
<tr>
<td>Lambert Eaton Myasthenic syndrome</td>
<td>n = 12</td>
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</tbody>
</table>
Serology of generalized MG

- 85% AChR antibodies
- 10% Seronegative
- 5% MuSK positive
Weakness I

What’s not MG

The MG patient who improves with treatment, and then worsens……..(or who doesn’t improve at all)
The patient who doesn’t improve

• Treatment in MG is so effective (eventually) in most patients that a complete lack of response should raise concerns about diagnosis
The Seronegative MG patient who doesn’t improve

- Could be resistant / severe MG
- Or….not MG?
  - In a seronegative non-responsive patient always reconsider diagnosis
    - Other muscle diseases
    - Not MG
      - Internet search for ‘weakness’ or ‘fatigue’ always leads to MG
The Seropositive MG patient who doesn’t improve:
You know they have MG, but....

• MG plus:
  – Hypo- or hyperthyroidism
  – Dysthyroid ophthalmopathy
  – Inflammatory myopathy or neuropathy
• MG but non-compliance with Rx
• MG but medication doses not high enough
• MG but too early to see response
  – Be patient!!
• Really severe MG
• Too late in the game (bulbar especially)
• Other occupational, social, domestic issues
Treatment failure

"Please, Doc—nothing too aggressive. I'm kind of attached to my symptoms."
The MG patient who worsens again

• Severe MG – drug dependent
• Tapering of Rx too fast
• Intercurrent event
  – Infection
  – Pregnancy
  – Other Drug - macrolides, quinolones
• Symptoms not due to MG
  – Steroid myopathy
  – Sleep apnea
  – Depression
Not all weakness in an MG patient is secondary to MG
Weakness in a myasthenic

• Secondary to MG
  – Symmetric, proximal > distal - exceptions exist!
  – Fatigable - worsens at end of day, fluctuates from day-day

• Not secondary to MG
  – Adverse effects of drugs - steroid myopathy
  – Other diseases
    • thyroid, immune myopathy
    • Obstructive sleep apnea
  – Not MG (wrong Dx)
Weakness in an MG patient

• Many MG patients, after diagnosis and treatment complained that they weren’t getting better and were still ‘weak’

• The first step - Is it really weakness?

  – Normal strength initially then fatigues - MG
  – Exhaustion, no energy - not MG
  – Sleepy - not MG
Sleep apnea in MG

- **Obstructive Sleep apnea (OSA)**
  - 10-15% of general population
  - ?? more prevalent in MG
    - Bulbar/respiratory weakness
    - Weight gain on steroids
  - If patient’s complaint is daytime sleepiness consider sleep apnea as Dx
    - Somnolence
    - Snoring
    - Morning headaches or confusion
    - Painful non-specific weakness (fibro-type)
Prospective study of sleep apnea in MG
Sara Rask, Wilma Koopman RN, Charles George MD, Sam Wiebe MD and Mike Nicolle MD

• 100 definite MG patients
  – Chosen randomly from data base of ≈ 400 MG patients
• Assessed prospectively
  – Clinical assessment
    • Weight and BMI, MG severity, treatment present and past
    • Sleep questionnaire
  – ‘MAP index’ calculated
    • Includes components based on age, gender, symptoms of OSA and weight/BMI
    • Score of 0-1, score > 0.5 indicates higher risk of OSA
  – Those scoring above cut-off for MAP - overnight polysomnographic studies
Risk Stratification for Sleep Apnea

• Multivariable Apnea Prediction (MAP)
• Developed and validated at University of Pennsylvania and Johns Hopkins University
• Includes
  – frequency of symptoms of apnea,
  – measurement of body mass index (the major risk for sleep apnea),
  – age
  – gender.
Prospective study of sleep apnea in MG
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• Results
  – Of 100 patients
  – 50 had MAP of > 0.5 (“high risk” of OSA)
    • 13 refused/could not have sleep studies done
    • 37 had sleep studies, 34 of whom had OSA
      – 10 mild, 9 moderate, 15 severe
      – 11 had OSA syndrome (OSA + daytime somnolence)
  – 50 had a MAP < 0.5 (“low risk” of OSA)
    • None studied with PSG for study
    • 2 diagnosed with OSA outside of study
Prospective study of sleep apnea in MG
Sara Rask, Wilma Koopman RN, Charles George MD, Sam Wiebe MD and Mike Nicolle MD

• Results
  – OSA prevalence in MG 36% vs 10-15% in general population (95% CI 27-45%, p < 0.001)
  – OSA syndrome 11% vs 3% in general population (95%CI 5-17%, p < 0.001)
Prospective study of sleep apnea in MG
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• Risks - MG patients with OSA more likely to be:
  – Male
  – Older
  – Overweight (increased BMI)
  – On steroids last 12 months

• But - patients selected for PSG using MAP index which is weighted for older overweight males.
  – This obscures other risk factors

• and...25% of OSA+ patients had never been treated for their MG and 50% had never used CST when OSA dx
Sleep apnea in MG

• Not all weakness in MG is a problem with neuromuscular transmission
• Consider sleep apnea as a cause
  – Treatment quite different – If MG, increase doses of Rx. If OSA – no need to increase (and should perhaps reduce doses of prednisone!)
• Ask the right questions
• Arrange sleep studies
Weakness II

What might be caused by MG
Clinical - The classical presentation

• Ocular
  – Diplopia
    • Can mimic any EOM abN - VI\textsuperscript{th}, pupil sparing III\textsuperscript{rd}, INO
    • Often difficult to ‘map’ as multiple muscles involved
    • Almost always with ptosis
  – Ptosis
    • Unilateral or asymmetric
  – Photophobia
    • worsening of ptosis/diplopia in bright sunlight
Clinical - The classical presentation

• Bulbar
  – Dysphagia
    • Painless, suprasternal
  – Dysarthria
    • nasal, hoarse
  – Jaw - problems chewing,
    • weakness of closure > opening
  – Facial weakness
  – Head drop
    • neck extensor weakness – although flexor weakness is more common
Clinical - The classical presentation

• Respiratory
  – Orthopnea, dyspnea bending over

• Extremity
  – Proximal and symmetric arm
    • Deltoid and triceps > biceps
  – Proximal legs less common
Patterns of Weakness in MG

• Most weakness in MG is proximal and symmetric
  – Ocular & Bulbar
  – Proximal Arm
    • Deltoid and triceps
  – Axial
    • Neck flexion or extension
  – Proximal Leg
    • Uncommon
Patterns of Weakness in MG

Wrist and Finger Drop in Myasthenia Gravis

Michael W. Nicolle