Sex differences among patients with different forms of autoimmune muscle disease

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Disclosures

• I have patented an anti-HMGCR autoantibody test, but do not receive compensation for this

• I will discuss off-label treatments for myositis
Overview

• Describe the four major types of autoimmune muscle disease
• Review sex differences among the different types
• Do a deeper dive in one type
Four major types of autoimmune muscle disease

- Dermatomyositis
- Antisynthetase syndrome
- Immune-mediated necrotizing myopathy
- Inclusion body myositis
Dermatomyositis

- Symmetric proximal muscle weakness progressing over weeks or months
- Typical skin rash progressing over weeks or months
- Elevated muscle enzyme levels
- Autoantibodies
- Myopathic electromyography
- Abnormal muscle biopsy
Dermatomyositis skin rashes

Heliotrope rash

Gottron’s papules
Dermatomyositis skin rashes

Ulcerating lesion

Ulcerating Gottron’s papules
Dermatomyositis skin rashes

Nailbed changes
Normal muscle biopsy

Low power

Higher power
Dermatomyositis muscle biopsy

Perifascicular Atrophy

Perivasculuar Inflammation
The antisynthetase syndrome

- Autoantibodies recognizing one of the aminoacyl-tRNA synthetases
  - Histidyl-tRNA synthetase (Jo1)
  - Alanyl-tRNA synthetase (PL12)
  - Threonyl-tRNA synthetase (PL7)
  - Glycyl-tRNA synthetase (EJ)
  - Isoleucyl-tRNA synthetase (OJ)
The antisynthetetase syndrome

Arthritis
Myositis
Mechanic’s Hands
Interstitial Lung Disease
Rash
Raynaud’s Phenomenon
Immune-mediated necrotizing myopathy

- Muscle biopsy: myofiber necrosis
- Autoantibodies targeting...
  - Signal recognition particle
  - HMG-CoA reductase
- Rapidly progressive
- Severe weakness
- Minimal extra-muscular involvement
- Often difficult to treat
Inclusion Body Myositis

- The most common myopathy in patients over 50 years old
- Insidious onset
- Asymmetric weakness
  - Quadriceps
  - Distal finger flexors
  - Wrist flexors
  - Ankle dorsiflexors
  - Obicularis occuli
- Dysphagia common
Inclusion body myositis muscle biopsy

Rimmed vacuoles and invasion of myofibers by CD8+ T cells

Figure courtesy of Dr. Anthony Amato
Most forms of myositis preferentially effect women

<table>
<thead>
<tr>
<th>Disorder</th>
<th>% Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermatomyositis</td>
<td>70%</td>
</tr>
<tr>
<td>Antsynthetase syndrome</td>
<td>69%</td>
</tr>
<tr>
<td>IMNM</td>
<td>64%</td>
</tr>
<tr>
<td>IBM</td>
<td>39%</td>
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</tbody>
</table>
Inclusion Body Myositis

- Slowly progressive
- Poor response to therapy
- Clinical heterogeneity may influence treatment responsiveness
- Data regarding heterogeneity (e.g., sex differences) are limited
Methods

- Clinical, histologic, radiologic, and electrophysiologic data analyzed for all patients with IBM and other forms of myositis enrolled at The Johns Hopkins Myositis Center from 2003 to 2018

- Univariate, multivariate, and graphical analyses were used to identify prognostic factors in IBM

- The evolution of creatine kinase and muscle strength was studied using multilevel linear regression models. Nonmodifiable risk factors (sex, race, disease duration, and age at the onset of first symptoms) were used as adjusting covariates for the regression analyses
Results I

• 335 patients with IBM included
• 64% were male
• Average age of disease = 58.7 years
• Average delay to diagnosis = 5.2 years
• Initial misdiagnosis (52%) was common
• Black patients had significantly weaker arm abductors, hip flexors, and knee flexors compared with non-Black patients
Results II

- Compared to males, females had*
  - stronger knee extensors
  - stronger finger flexors
  - increased prevalence of dysphagia (OR 1.8)
  - slower rate of strength decline
  - less spontaneous activity on EMG
  - increased rate of misdiagnosis and mistreatment
  - a longer time to correct diagnosis (6.2 vs. 4.7 years)

*Using multilevel regression models including time from onset
Implications for women with IBM

- Female IBM patients have a distinct clinical phenotype and trajectory compared to men.
- These unrecognized differences may have contributed to delay of correct diagnosis in women.
- Women may have different responses to therapies, which may influence the design of future clinical trials in IBM.
Thank you!