Demystifying weakness: how to approach refractory myositis

Jemima Albayda, MD
Assistant Professor
Johns Hopkins Myositis center

Disclosures

• Off-label uses for medications will be discussed

Objectives

• To develop the approach for evaluation of myositis and its mimics
• Describe the management challenges in refractory myositis
• To enumerate new treatments for myositis
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Framework for assessment

- Does the patient have myositis?
- If they have myositis, what organs are involved and active?
- What treatments have been tried/can be used?

2017 EULAR/ACR classification criteria for IIM

- Aim was to define minimum essential, easily available clinical and laboratory features to:
  1) Distinguish IIM from mimics
  2) Distinguish major subgroups of IIM
- Uses a weighted score; with and without muscle biopsy
- Total score corresponds to probability of having IIM
- Definite IIM: probability ≥ 90%, ≥ 7.5 (≥ 8.7 with muscle biopsy)
- Minimum score of 5.5; 6.7 with muscle bx to classify as IIM
Does the patient have myositis?

- Typical skin rashes
- Subacute proximal weakness
- Elevated muscle enzymes
- EMG myopathic changes
- MRI evidence of acute edema
- Myositis specific antibody
- Other signs of immune-mediated phenomena
- Response to medications
- Compatible muscle biopsy

Features suggestive of non-autoimmune myopathy

- Positive family history of muscle weakness
- Slow progressive evolution of weakness over months to years
- Presence of facial or extraocular muscle weakness
- Scapular winging
- Presence of distal weakness greater than or equal to proximal weakness
- Presence of asymmetric weakness
- Lack of myositis autoantibodies
- Lack of systemic manifestations of autoimmune disorders
**Major mimics to consider**

- Metabolic myopathies
  - McArdle’s, Pompe’s
- Muscular dystrophies
  - FSHD, dysferlinopathy
- Mitochondrial myopathies
- Endocrine myopathies
  - Thyroid, parathyroid, DM

**Considerations for treatment of IIM**

- Specific organ involvement
- Severity of presentation
- Known antibody
- Distinction of activity versus damage

**Therapeutic Strategies**

- Use medications that target involved organs
- Treatment with steroids is variable
- Consider the severity of presentation and how quickly medications take effect
- Consider comorbidities
- If cannot taper steroids readily, should optimize background therapy
### TREATMENT OPTIONS

- Methotrexate – 20-25mg/wk
- Azathioprine – 2mg/kg/day
- Mycophenolate mofetil – 2-3g daily
- IVIG – 2g/kg divided over 3-5 days every 4 weeks
- Rituximab – 1g on day 0 and 1g on day 14
  *Hydroxychloroquine

### TREATMENT OPTIONS

- Tacrolimus
- Cyclosporine
- Cyclophosphamide
- TNF inhibitors
- Plasmapheresis
- Acthar

### Recent Studies for Refractory disease

- Infliximab – 2/6 patients achieved DOI
- Abatacept – 8/19 patients achieved DOI
- ACTH gel – 7/10 patients achieved DOI
Treatments being investigated

- Tofacitinib
- Abatacept
- Tocilizumab
- Anabasum - a Cannabinoid receptor type 2 agonist

Some practical tips

- If with ILD, we generally start with azathioprine or mycophenolate
- When with cancer, Rituximab and IVIG are safest
- Aside from steroids, IVIG works fastest
- Must use therapeutic doses of medications and allow time to take effect
- Often need combined treatments: methotrexate + azathioprine; rituximab + methotrexate; IVIG and rituximab

Treatment challenge: Statin-induced myositis

- Stop the statin once confirmed
- Steroids usually started, together with another immunosuppressant
- Steroids can be avoided if with other comorbidities
  - If mild, can use oral immunosuppression
  - If very weak, we usually start IVIG
  - Rituximab is also an option
Case Example

- 62 year old man presented with chronic muscle weakness of over ten years duration, treated with steroids at one time with improvement.
- 4/5 strength in the arm abductors and 5/5 strength elsewhere
- There was mild scapular winging and abdominal laxity
- EMG showed a mild irritable myopathy with early polyneuropathy with predominantly axonal features.
- Biopsy of the deltoid showed degenerating and regenerating fibers
- CPK was 482
- FSHD as well as myotonic dystrophy were considered and ruled out by genetic testing.
- The myositis panel was negative for known antibodies.

He was then treated with steroids
- However on follow-up, he had symptoms of heart failure with a nadir ejection fraction of 20-25%, findings of cardiomyopathy, and atrial and ventricular arrhythmias.
- Endomyocardial biopsy showing a single foci of perivascular lymphocytes consistent with myocarditis.
- Azathioprine added, and eventually Rituximab
- THIS PATIENT HAD ANTIMITOCHONDRIAL AB ASSOCIATED MYOSITIS
Conclusions

• Treatment of myositis is challenging given lack of consensus guidelines and heterogeneity of disease
• Use of immunosuppressive/immunomodulatory agents is mostly guided by organ involvement and severity
• Many agents are in use and beneficial in myositis
• Exercise is integral part of treatment

Questions?

• Thank you for your attention

Johns Hopkins Myositis Center
Mamman AM. Which nonautoimmune myopathies are most frequently misdiagnosed as myasthenia? Curr Opin Rheumatol 2017, 29:616 – 622.