RhAPP

RHEUMATOLOGY ADVANCED PRACTICE PROVIDERS

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The ABC’s of Inflammatory Myopathies

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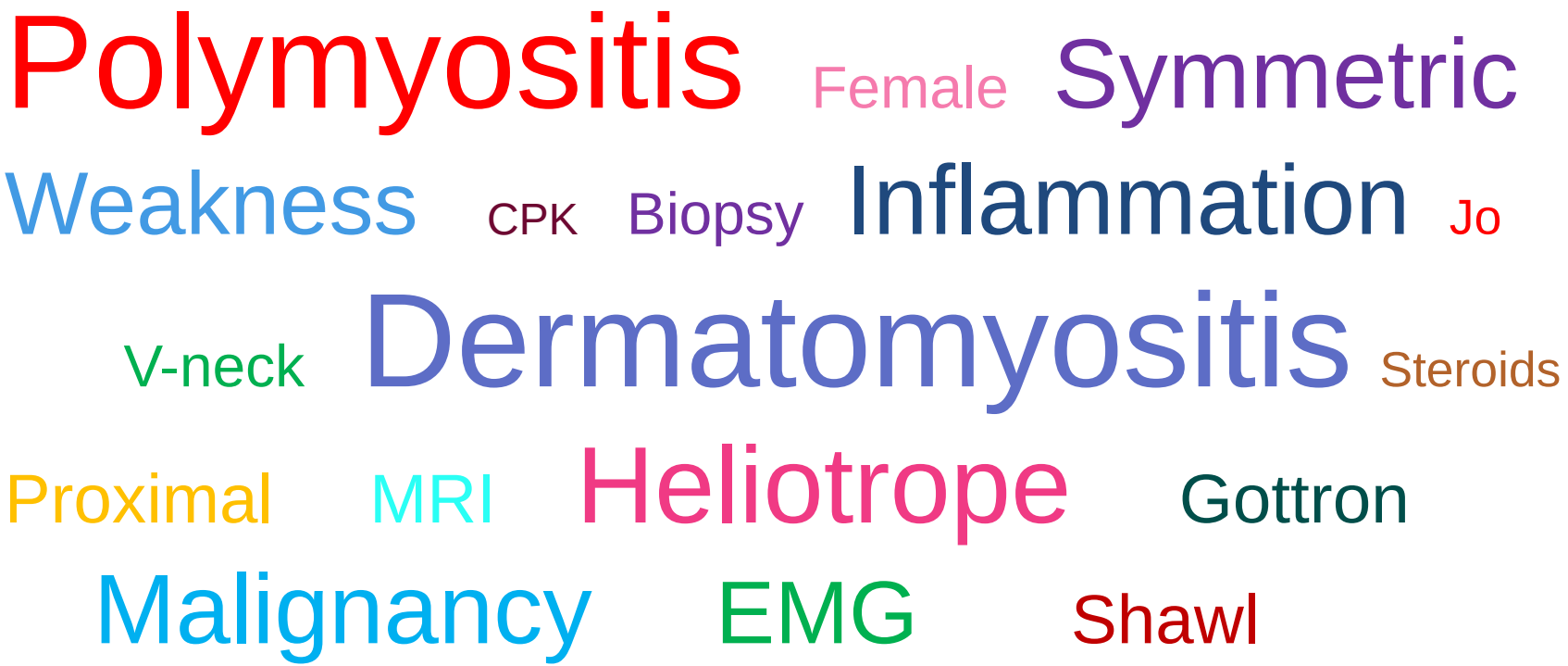
Polymyositis
Female
Symmetric
Weakness
CPK
Biopsy
Inflammation
Jo
V-neck
Dermatomyositis
Steroids
Proximal
MRI
Heliotrope
Gottron
Malignancy
EMG
Shawl

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Faculty Disclosures

- Consultant: Novartis

Objectives

- Overview of Polymyositis/Dermatomyositis
- Describe the epidemiology & pathophysiology of polymyositis (PM) and Dermatomyositis (DM)
- Formulate a diagnosis for PM/DM via
  - Physical exam
  - Diagnostic studies
- Develop a treatment plan for PM/DM

Inflammatory Myopathies- Overview

Inflammatory Myopathies (IM)

- Heterogeneous group of disorders
  - Characterized by proximal muscle WEAKNESS and inflammation of skeletal muscles.
  - Frequently associated with extra-muscular manifestations that can affect the skin, lungs, and joints.

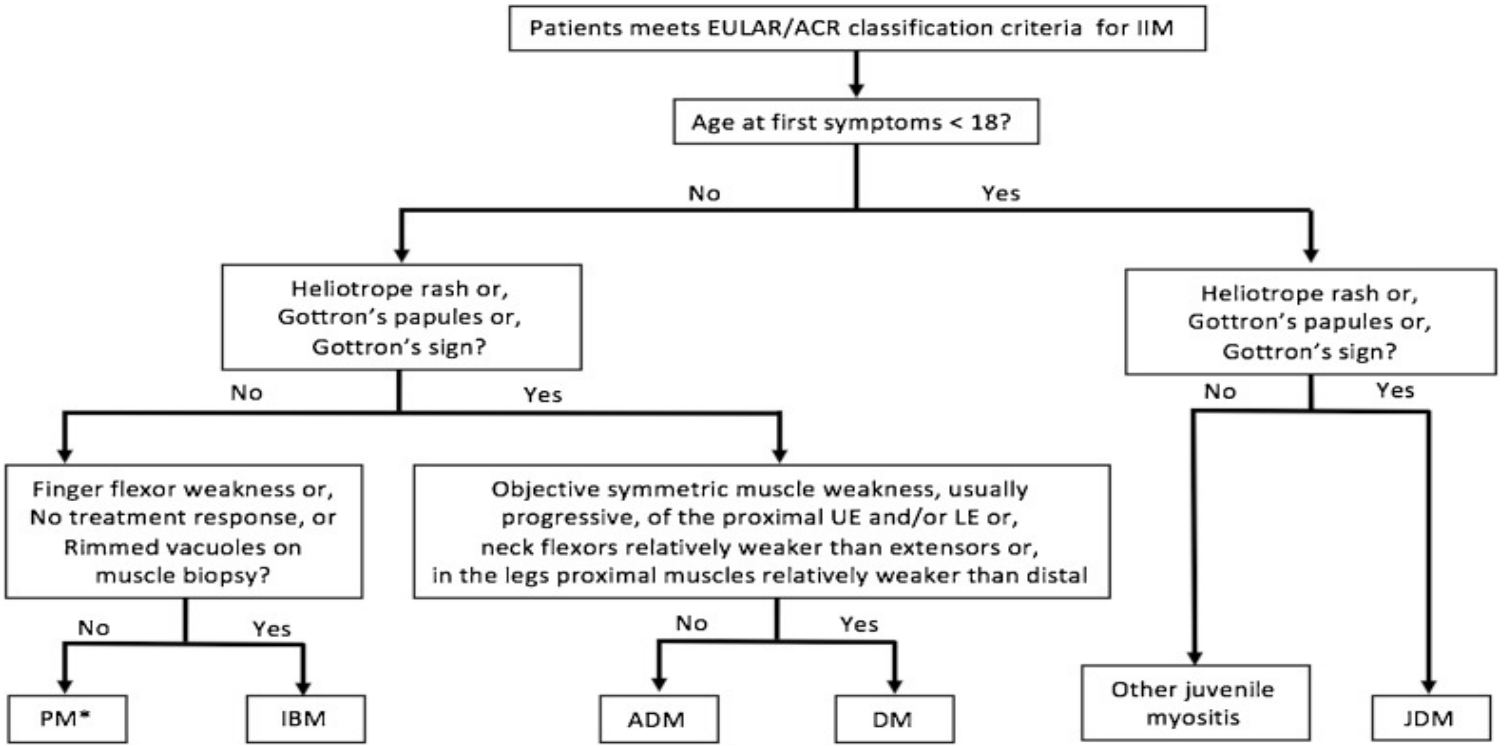
History-Overview

- Myositis was first documented in 1863 by Wagner in a patient with extensive skin findings in addition to muscle weakness.
  - Years later it was reported that muscle weakness could occur in the absence of cutaneous findings
- In 1891, the term Dermatomyositis was coined by Unverricht to describe patients with dermatological findings + myopathy

Disease Subtypes

- Polymyositis*
- Dermatomyositis*
  - Amyopathic dermatomyositis
- Juvenile PM/DM
- Inclusion Body Myositis

Classification Criteria



Leclair V. Curr Rheumatol Rep. 2018 Mar 17;20(4):18

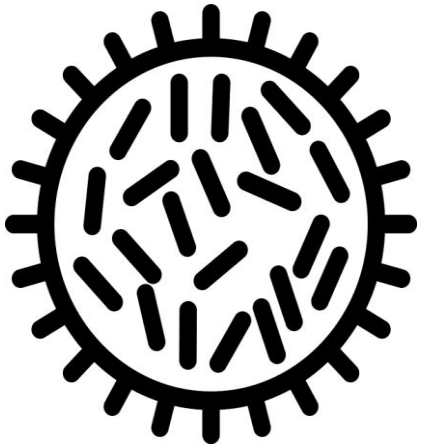
Classification Criteria

http://www.imm.ki.se/biostatistics/calculators/iim/

- 15 yes or no questions
- The probability of IIM (minimum to maximum) is displayed at the top of the page.
- You can save the webpage of the calculator on most mobile devices

Epidemiology

- The incidence of PM/DM is 2-19 per million annually
- Female to Male is 2-3:1 for PM/DM
- In the US, African American to Caucasian ratio is about 3-4:1
- Peak incidence of PM in adults occurs between 50-60 yo, but individuals of any age may be affected
- DM has a bimodal distribution with a peak onset of 5-15 yo and the other at 45-65



Secrets Rheumatology

Pathophysiology

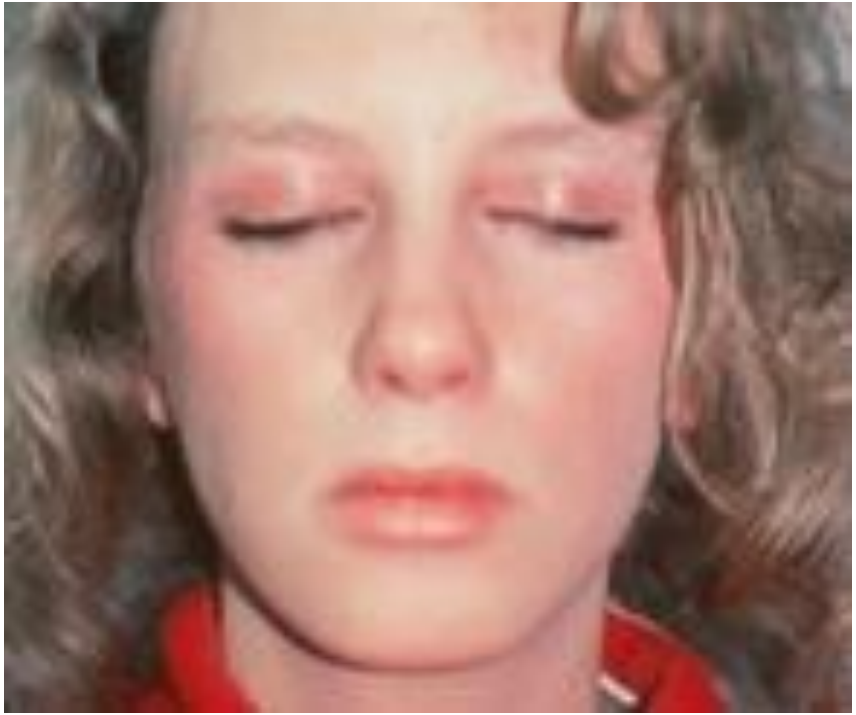
- Immune-mediated responses are believed to be triggered by environmental factors in susceptible individuals
  - Viruses have been strongly implicated
    - Coxsackie B virus
    - Hepatitis C
    - HIV
- Strongest known risk factors are
  - HLA- DRB1
  - HLA-DQA1
  - HLA- DQB1

Pathophysiology

- Abnormal activation of cytotoxic T lymphocytes (CD8 cells) and macrophages against muscular antigens
  - Leads to direct damage to the muscle
- Complement activation
  - Leads to the release of proinflammatory cytokines and chemokines
    - Can also indirectly lead to muscle damage
- Affects endomysial layers of skeletal muscle

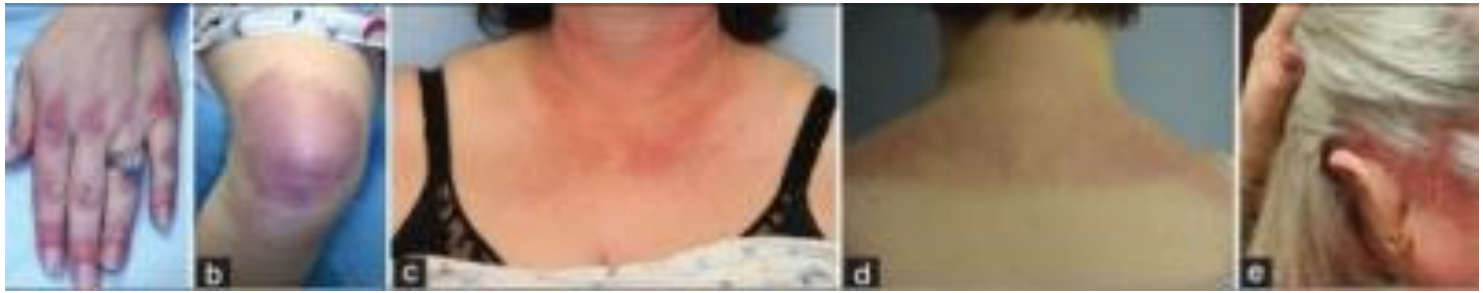
Sarwar et al. Treasure Island (FL): StatPearls Publishing; 2023

Physical Exam- Skin



- Heliotrope rash- purple to erythematous rash affecting the eyelids, forehead, and nasolabial folds

ACR Image Library. Available at: https://www.rheumatology.org/Learning-Center/Rheumatology-Image-Library.



A: Gottron's papules: Violaceous, scaling papules on the skin overlying the joints and proximal nailfolds

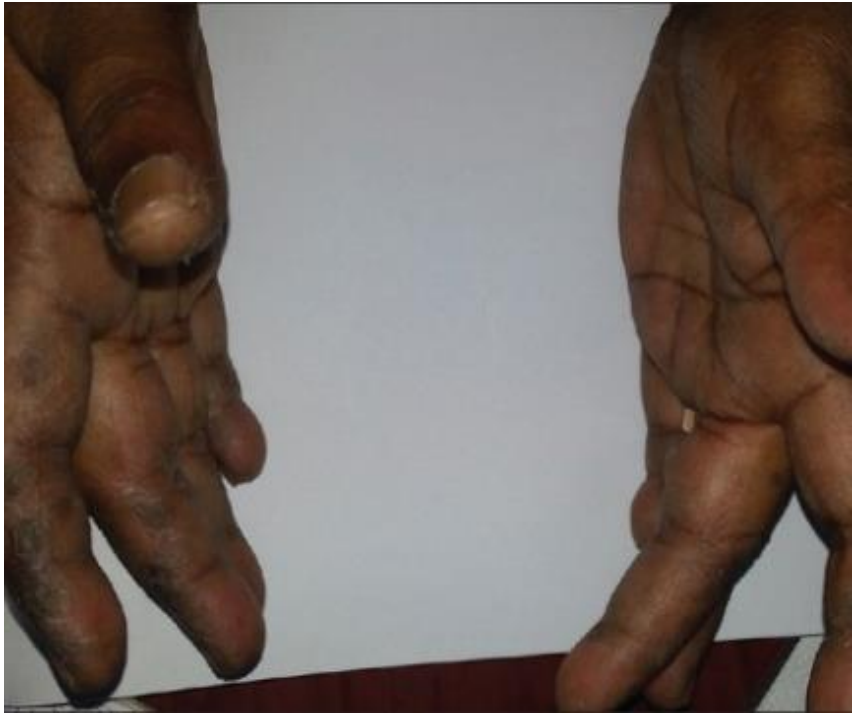
B: Gottron's sign: Violaceous patches overlying the knees

C: "V neck" sign: Erythematous and hyperpigmented macules on the chest

D: Shawl sign: Violaceous macules and patches on the upper back and shoulders

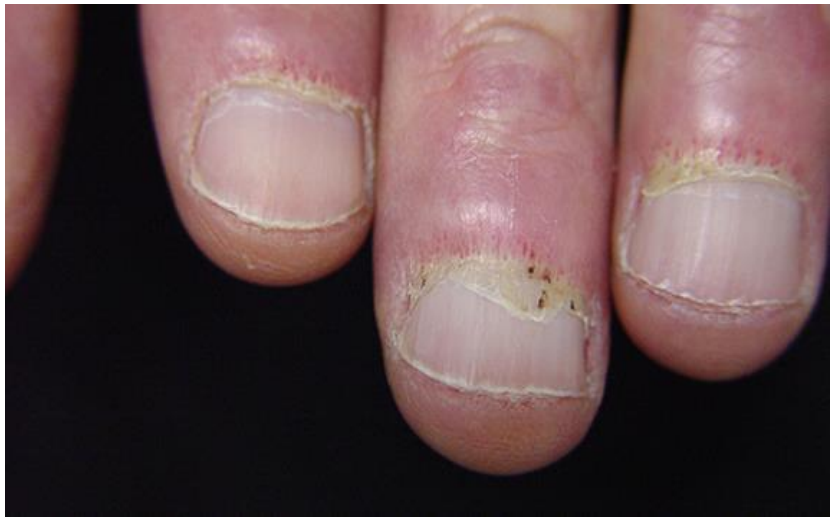
E: Scalp disease in dermatomyositis: Deeply erythematous scaling plaques are seen diffusely on the posterior scalp

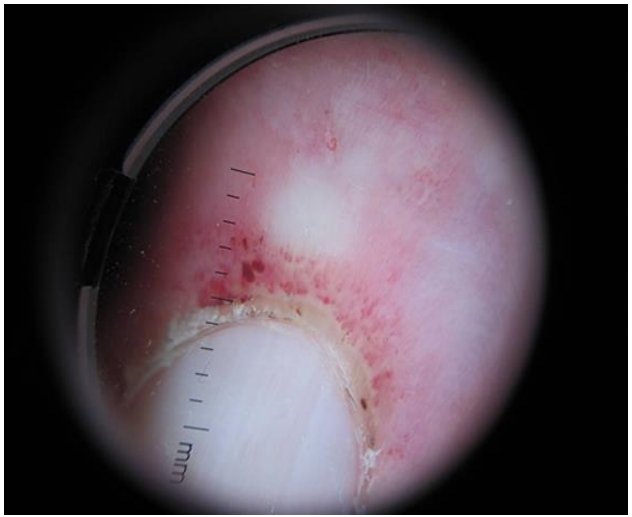
https://openi.nlm.nih.gov/detailedresult?img=PMC3482801_IJD-57-375-g001&query=dermatomyositis&it=xg&req=4&npos=49



- Mechanic's hands (dermatomyositis)
  - hyperkeratosis
  - fissuring
  - associated increased risk of pulmonary disease

https://openi.nlm.nih.gov/detailedresult?img=PMC5372453_IDOJ-8-79-g013&query=dermatomyositis-%20mechanics&it=xg&req=4&npos=2





Periungual erythema and capillary telangiectasia along the distal nail folds on both hands

https://www.uptodate.com/contents/clinical-manifestations-of-dermatomyositis-and-polymyositis-in-adults?search=dermatomyositis%20treatment&topicRef=5133&source=related_link

Physical Exam-

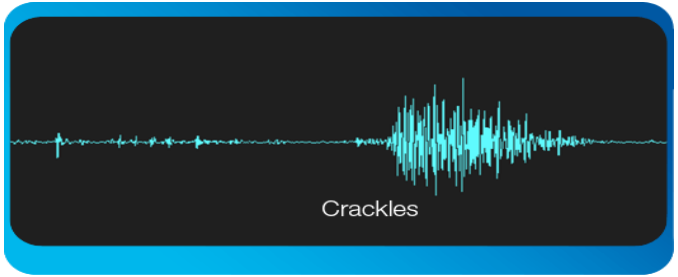
Hallmark feature is Proximal and Symmetric Muscle Weakness

- Muscle strength testing
  - Extensor muscles are more affected than flexor muscle
  - Proximal muscle weakness with distal muscle strength almost always maintained
  - Neck Flexor muscles are often affected
  - Pharyngeal muscles are often affected
  - Respiratory muscles are affected in advanced cases

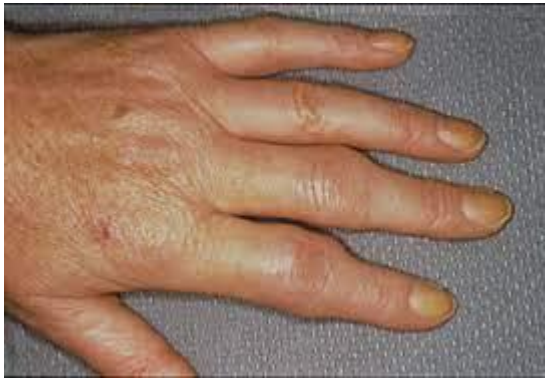
Sensory Examination is normal!

Physical Exam

- Crackles may be heard on pulmonary exam in the presence of interstitial lung dz.



- Joint Tenderness and Synovitis May be seen in the presence of overlap syndrome (PM/RA).



Laboratory Abnormalities

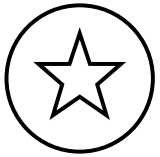
↑ Creatinine Phosphokinase (CPK)is elevated in almost all patients with PM/DM.

- CPK levels can be followed in order to monitor treatment. However, CPK levels do not necessarily correlate to the severity of the disease

L-aldolase, AST/ALT and LDH may also be elevated

Laboratory Abnormalities

- Myositis Specific Antibodies (MSA)



Anti-Jo1 antibody is the most common MSA in polymyositis

- Anti-HMGCR- hx of statin exposure
- Anti-Mi-2, Anti-T1F-1Y, Anti-NXP2- Associated with DM
- Anti-cN1a- Associated with inclusion body myositis (IBM)

Laboratory Abnormalities

- Myositis-associated autoantibodies (MAA) are found in patients with myositis, but also present in patients with other autoimmune diseases such as RA scleroderma, or Sjogren's syndrome
- *Workup for PM/DM should always include ANA, SSA/SSB, scl-70, anti- RNP, anti-Smith, RF, and anti-CCP to evaluate for overlap polymyositis*

Diagnosis

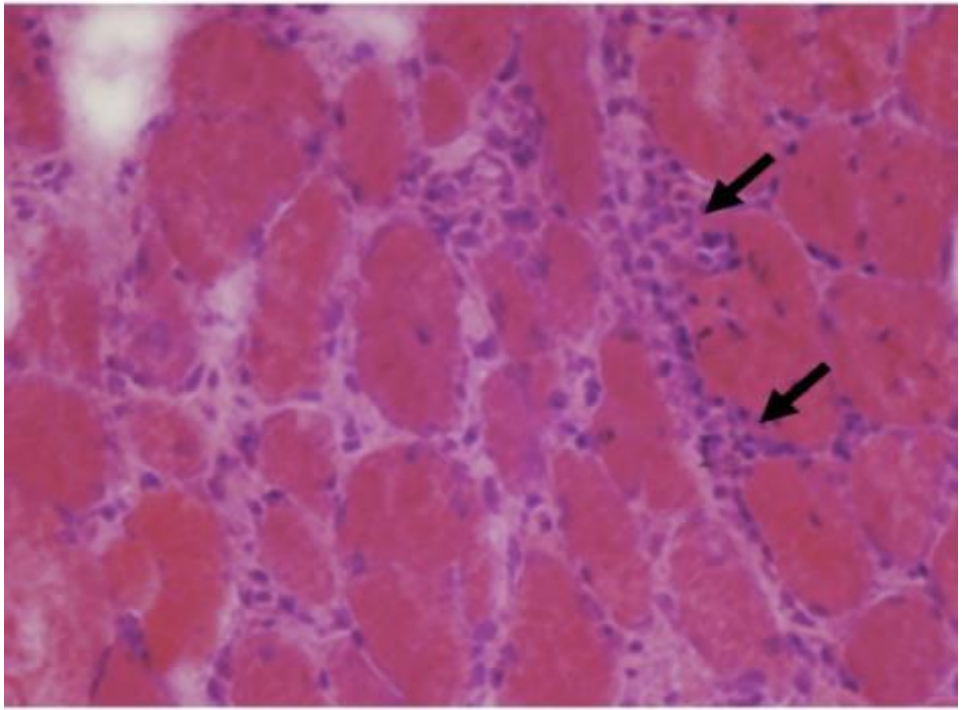
- **MUSCLE BIOPSY- Gold standard for diagnosis**

  – This is the most important and most invasive step to make the correct diagnosis and this is sometimes the only way to distinguish between the different subtypes of myositis (which is important when considering treatment options).

- EMG of affected muscles displays a myopathic pattern.
  - 10-15% of patients have a completely normal EMG
  - Can be helpful to distinguish between other motor neuron disorders such as myasthenia gravis

- MRI can be helpful to identify areas of active muscle inflammation.
  - This can help determine the appropriate muscle site to biopsy.

Histopathology



- Muscle biopsy shows muscle fibers in varying stages of inflammation, necrosis, and regeneration.
- Infiltrates consist mostly of CD8 T lymphocytes and macrophages

https://openi.nlm.nih.gov/detailedresult?img=PMC4873503_fneur-07-00064-g008&query=Polymyositis&it=xg&lic=by&req=4&npos=19

Rule Out Malignancy

- Perform age-appropriate evaluation for malignancy
  - Chest Radiography
  - Computed CT scan- chest, abdomen, and pelvis
  - Mammography
  - Pelvic U/S
  - Upper and lower GI endoscopy
  - MRI

Differential Diagnosis

- Neuromuscular disorders
- Endocrine Disorders
- Infectious Myositis
- Metabolic Myopathies
- Sarcoid Myopathy
- PMR; Fibromyalgia; inflammatory arthritis
- Acute Rhabdomyolysis

Treatment- Corticosteroids

- Dose usually starts at 1-1.5mg/kg/day (up to 80mg/day) in divided doses. The dose is maintained until remission is achieved. This typically takes 4-6 weeks.
- Taper by 20% each month until 20mg/day
- Then, taper by 5mg a month to 10mg/day
- Maintain this dose for 3-6 months, then taper further

- IV Pulse steroids may be used for life-threatening disease

Treatment- Corticosteroids

Potential Long-Term Side Effects

- Osteoporosis - Skin Atrophy
- Cataracts - Diabetes Mellitus
- Hypertension - Mood Swings, Psychosis
- Weigh Gain - Increased Risk of Infection
- *Steroid Myopathy*

Steroid-Sparing Agents

- Methotrexate up to 25mg/week (po or SC)
- AZA up to 2-3mg/kg/day
- MMF 1-1.5g BID
- Leflunomide 20mg/day

  - *each of these medications requires routine lab monitoring including a CBC, creatinine and Hepatic Function.*

Other- Immunosuppressive Agents

- IVIG- 2g/kg over 5 days; this is followed by monthly 2g/kg over 2-3 days.
  - *Effective in anti-HMGCR disease and/or patient's with dysphagia*
- Rituximab- 1g on Days 1 and 15; followed by 1g every 6 months
  - *Effective in DM/PM patient with anti-Jo1, anti-Mi-2,anti- HMGCR, and others*
- Tacrolimus, Cyclosporine, and Acthar Gel
- HCQ can be effective in treating skin manifestations of DM but not muscle weakness

Treatment Considerations

1.) Important to continue to monitor for malignancy

2.) If a patient fails to respond to appropriate doses of steroids, you should reevaluate for Inclusion Body Myositis

3.) If underlying ILD is suspected, an interdisciplinary approach to treatment with pulmonology is important

4.) At the onset of diagnosis, referral for physiotherapy is essential to help maintain muscle strength until clinical symptoms are fully resolved

Case Study

A 48-year-old woman was referred to our office for evaluation of muscle weakness, myalgias, and rash X 4 weeks.

- Aching pain worse with activity
- Thigh and proximal arm muscle fatigue and weakness
- Mild peripheral joint pain and stiffness
- Photosensitivity
- V-shaped rash on neckline, rash on eyelids
- Reported difficulty getting out of a chair, brushing her teeth, and combing her hair

Case study

- PMhx
  - Hashimoto’s thyroiditis; mild anxiety
- Surgical Hx
  - 2 prior C-sections;
- Social History
  - Nonsmoker
  - Drinks about 2-3 glasses of wine/week
  - Married and has a 16 yo son and 13 yo daughter
  - Works full-time at the postal service

Case study

- Physical Examination

  - slight periorbital heliotrope rash around the eyelid margin and erythematous plaques with a thin scale overlying the forehead, scalp line, nose, cheeks, and anterior chest

  - symmetrical weakness: 2/5 in the neck flexors, hip flexors, quadriceps and deltoids and 3/5 in the biceps, and triceps

  - tenderness to palpate over forearms, deltoids, and thighs

  - mild tenderness over MCPs, no synovitis

Case study

- Lab values
  - CPK 2348 U/L
  - CRP 1.3mg/dL; ESR 45 mm/hr
  - ALT/AST 74/69 U/L; LDH 220 U/L; Aldolase 11.8 U/L
  - ANA + 1:40 titer; ANA 7 Profile negative
  - Negative RF and anti-CCP antibody
  - Myositis Panel- + anti-Mi2 antibody

Case Study

- EMG studies were ordered and results were consistent with myositis
- We determined that based on classic skin findings consistent with DM; proximal and symmetric muscle weakness on PE; elevated CPK,+ anti-Mi2 antibody and EMG results, an invasive biopsy was not needed.

Case Study

- Think Malignancy until proven otherwise

Associated cancers are present in 10-20% of adults with PM

-Over 50% of patients who develop PM/DM after 65yo

Case Study

- Initiated Prednisone 30mg BID- after two weeks patient reported significant side effects including tachycardia, insomnia, worsening anxiety
- MTX initiated 15mg/week and Prednisone was decreased by 10mg each week X 4 weeks
- 6 weeks after treatment initiated CPK 628; liver enzymes normalized; ESR and CRP normal
- MTX increased to 25mg/week SC and Prednisone decreased to 15mg X 2 weeks; then 10mg X 2 week, 7.5mg X one month, then 5mg

Case Study

- At a 3 month follow-up (42 weeks after treatment was initiated)
  - Skin exam normal
  - Muscle strength 5/5 both U.E. and L.E
  - CPK 295 U/L
- Patient has done very well on MTX 25mg/week CK and Prednisone 5mg QD

Conclusion

- PM/DM are rare diseases
  - Incidence of 2-19 million annually
  - Incidence is higher in women and African-Americans
- Polymyositis is characterized by symmetric and proximal muscle weakness
  - Occurs insidiously over 3-6 months
  - Most severely affecting shoulder/pelvic girdles
- Dermatomyositis is characterized by distinct skin manifestations (and can occur without muscle involvement)

Conclusion

- While EMG and MRI can be helpful in making diagnosis, muscle biopsy is the gold standard for the diagnosis of PM
- Glucocorticoids are the mainstay of treatment
  - Due to high doses typically required to obtain and sustain remission, other immunosuppressants are typically added early (MTX, AZA, MMF)
- Malignancy is commonly associated with PM/DM
  - Especially if age at diagnosis is >65
  - Must be ruled out

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