RhAPP

RHEUMATOLOGY ADVANCED PRACTICE PROVIDERS

# RHAPP NATIONAL CONFERENCE

## SEPTEMBER 8-10, 2022

# Inflammatory Myopathies- Fundamentals

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# Objectives

- Review the etiology of polymositis (PM) and dermatomyositis (DM)
- Describe the appropriate clinical work up for PM/DM
- Review management options for PM/DM

# Inflammatory Myopathies

Inflammatory Myopathies (IM) are a heterogenous group of disorders and are characterized by proximal muscle weakness and inflammation of skeletal muscles.  They are also frequently associated with extra-muscular manifestations that can affect the skin, lungs, and joints.

*Primer on the Rheumatic Disease*. 2001:12; 369-372

# Disease Subtypes

- Polymyositis (PM)
- Dermatomyositis (DM)
  - Amyopathic Dermatomyositis
- Inclusion Body Myositis (IBM)
- Overlap Myositis
  - Antisynthetase antibody syndrome (ASA)
  - Myositis Associated with other CTD
- Immune Mediated Necrotizing Myopathy
- Juvenile Myositis

*Secrets Rheumatology*,2020:4; 177-184

# Epidemiology

- 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 bimodal distribution with peak onset of <18 yo and again in midlife

Secrets Rheumatology

# Clinical Manifestations

| MSK | CUTANEOUS | EXTRAMUSCULAR |
|---|---|---|
| Symmetric Proximal Muscle Weakness | Photosensitive Rashes | Fever/Chills, Fatigue, and Weight Loss |
| Dyspnea due to diaphragmatic and intercostal muscle weakness | Heliotrope Rash; Shawl Neck Signs | Raynaud's Phenomenon |
| Dysphagia due to pharyngeal muscle weakness | Gottron's Papules; Mechanics Hands | Inflammatory Arthritis |
| | Cuticle Hypertrophy, Nailfold Capillary Abnormalities | Interstitial Lung Disease |

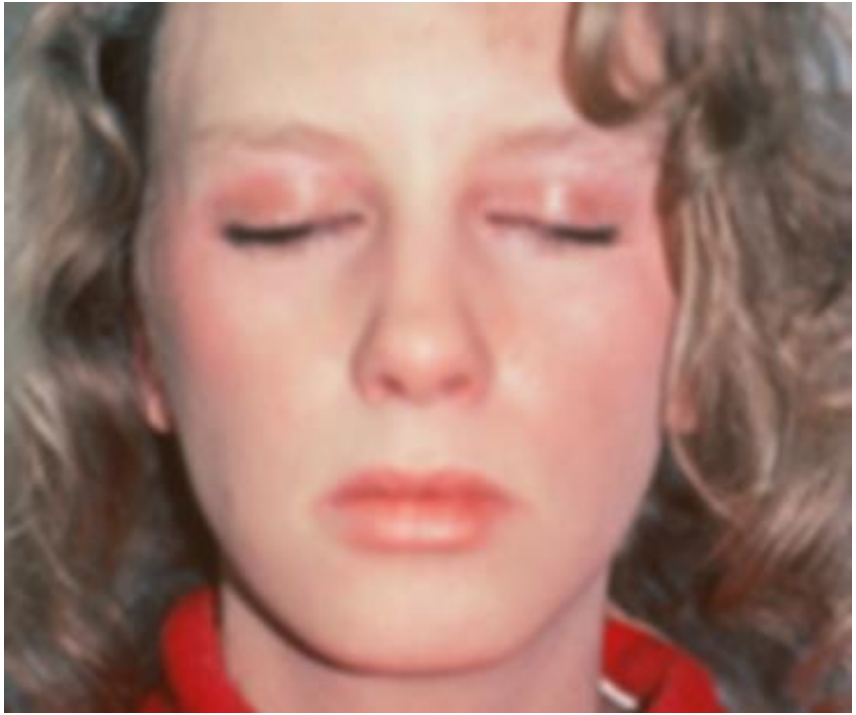
# Physical Examination

- Muscle strength testing
  - Extensor muscles are more affected more than flexor muscles
  - Proximal muscle weakness is hallmark and distal muscle strength is almost always maintained
  - Neck Flexor muscles are affected

- Muscle Pain as well as tenderness

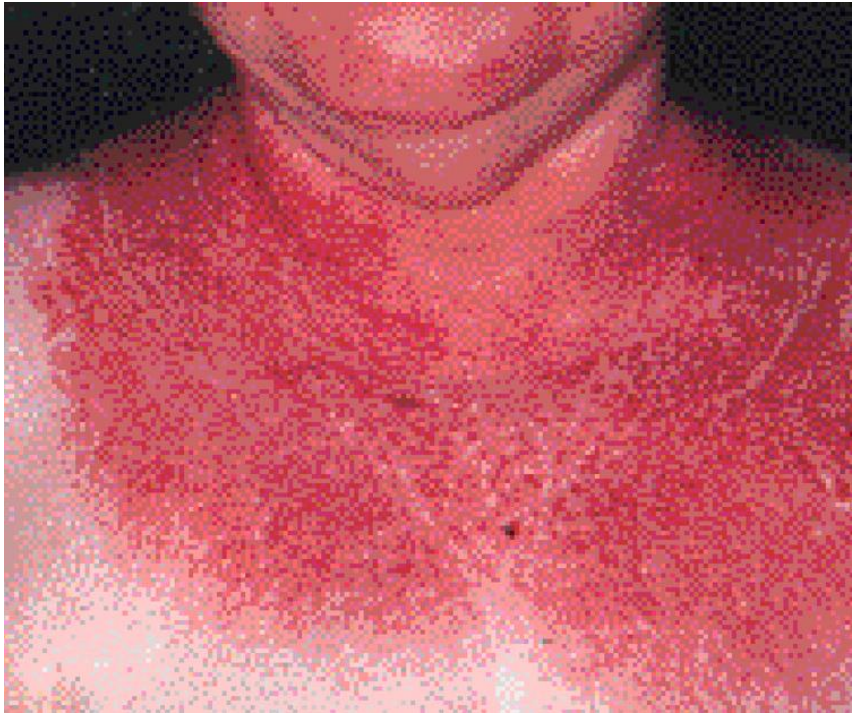
- Sensory exam will be normal and tendon reflexes will be preserved

# Typical DM Skin Manifestations



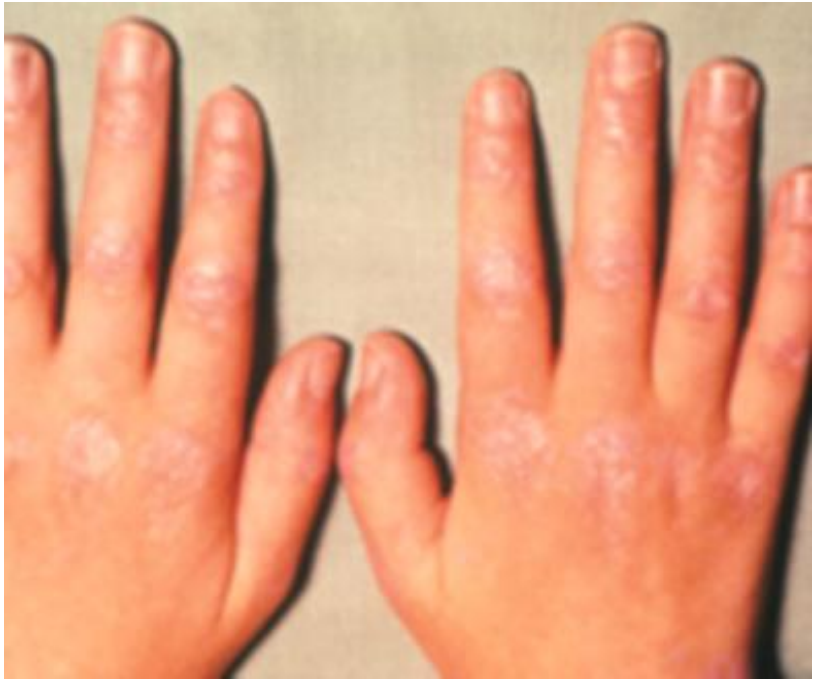
- Heliotrope rash- purple to erythematous rash affecting the eyelids, forehead, and nasolabial folds

# Typical DM Skin Manifestations



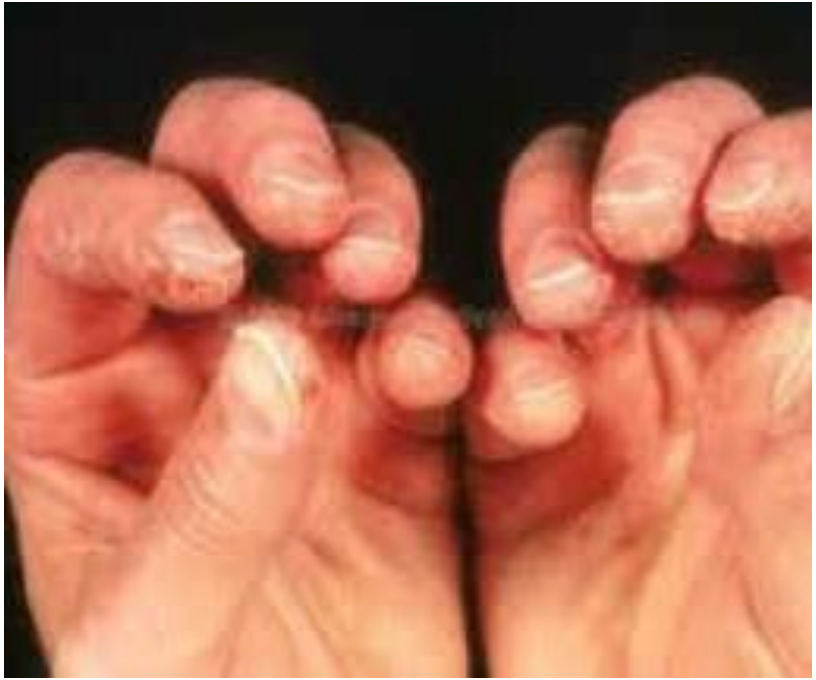
- V-sign rash confluent erythematous rash over the anterior chest and neck.
- Shawl-sign erythematous rash over the shoulders and proximal arms
- Holster-sign rash erythematous rash over the lateral aspect of the proximal thighs

# Typical DM Skin Manifestations



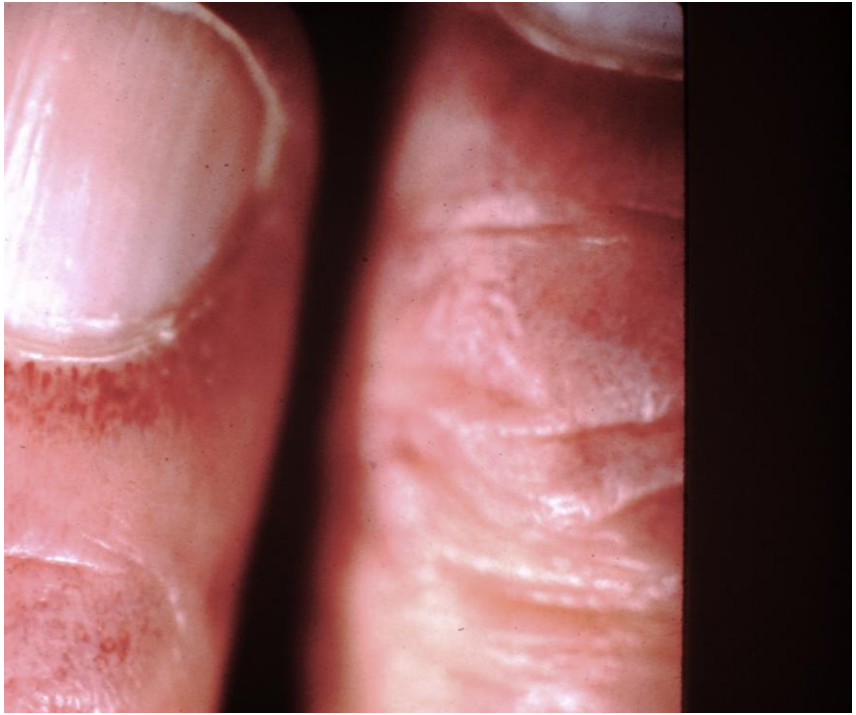
- Gottron's Papules: Purple to erythematous flat or raised lesions over the dorsal surface of MCPs, PIPs, or DIPs

# Typical DM Skin Manifestations



- Hyperkeratotic fissured skin on the palmar and lateral aspects of the fingers
- Linked to an increased risk of pulmonary disease

# DM Skin Manifestations



- Capillary nail beds with dilated capillary loops, cuticular overgrowth, and periungal erythema

# Diagnosis

- Lab values including marked elevated of creatinine phosphokinase (CPK), and sometimes other enzymes such as LDH, AST or ALT

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

  - Myositis specific autoantibodies may be detected.

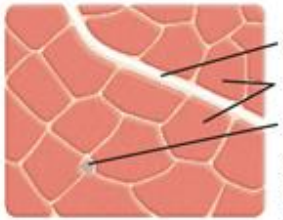
  - Important to also check CTD autoantibodies such as ANA, RNP, SSA/SSB to monitor for an overlap syndrome

# Diagnosis

- EMG of affected muscles displays a myopathic pattern.
- MRI can be helpful to identify areas of active muscle inflammation. This can help determine the appropriate muscle site to biopsy.
- Muscle biopsy – This is the most important and most invasive step to make the correct diagnosis and is sometimes the only way to distinguish between the different subtypes of myositis (which is important when considering treatment options).

# Pathology

**Normal Muscle**



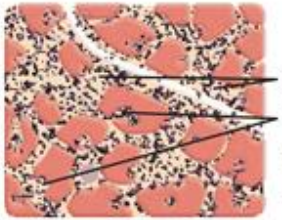
*border of muscle bundle (fascicle)*

*normal muscle fibers*

*blood vessel*

*When normal muscle fibers are viewed under a microscope, they look like puzzle pieces that fit together neatly.*

**Polymyositis**



*inflammatory cells*

*invasion of fibers by inflammatory cells*

*In polymyositis, inflammatory cells of the immune system invade previously healthy muscle cells, which become rounded and varible in size.*

# Amyopathic Dermatomyositis

- Classic skin changes of dermatomyositis in the absence of muscle weakness
- About 50% of patients presenting with ADM will develop muscle disease overtime
- Can be associated with malignancy
- Monitor for extra-muscular manifestations such as rapidly progressive Interstitial Lung Disease

# Antisynthetase Antibody Syndrome (ASA)

- Antibodies are directed against tRNA synthetase- Identifying myositis specific antibodies (MSA) and/or muscle biopsy can help identify specific clinical subsets
- Proximal Muscle weakness is typically presenting symptoms and CK is 5-10X upper normal limit
- Mechanic's hand is common
- ILD, inflammatory arthritis, Raynaud's, and fever can occur
- 5 -year survival rate is 80%

# Myositis Associated with other CTD

- Most common overlap occurs with systemic sclerosis
- Frequently have myositis associated antibodies (anti-PM-Scl, anti-U1-RNP, anti-KU, anti-U3RNP
- Other CTD associated with myositis include MCTD, SLE, and Sjogren’s syndrome

# Inclusion Body Myositis

- Most common idiopathic inflammatory myopathy in patient's >50.
- Bilateral weakness may develop gradually.  May involve distal muscles (foot extensor and finger flexors) and may be asymmetric. May cause atrophy of forearms and quads.  Dysphagia is common.
- CPK is elevated but typically less than 1000U/L
- Muscle biopsy is typically necessary for diagnosis because there is no MSA.
- Slowly progressive and poorly responsive to immunosuppressive therapy

# Immune Mediated Necrotizing Myopathy

- Muscle histology is consistent with scattered necrotic fibers and macrophages.
- Muscle disease is acute in onset with progressive muscle weakness and myalgias.  Weakness is typically severe.
- CPK>10-50 times UNL.
- MSAs are present in 80% and very helpful to identify clinical subsets- SRP autoantibodies and anti-HMGCR autoantibodies
- Not typically associated with ILD, rash.
- May be refractory to therapy

# Differential Diagnosis

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

# Poor Prognostic Features

- Clinical manifestations including severe weakness, dysphagia, respiratory muscle weakness, ILD
- Antibodies associated with poor prognosis
  - anti-SRP, anti-MDA-5, anti-155/140
- Necrotizing myopathy on pathology
- Malignancy

# Treatment- Corticosteroids

- Dose usually starts at 1-1.5mg/kg/day (up to 80mg/day) in divided doses. 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 3-6 months, then taper further

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

# Treatment-Corticosteroids

- Potential long-term side effects
  - Osteoporosis
  - Cataracts
  - Skin Atrophy
  - Diabetes Mellitus
  - Hypertension
  - Mood Swings; Psychosis
  - Weight Gain
  - Increased risk of infection
  - *Steroid myopathy*

# Treatment- 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 require routine lab monitoring including a CBC and Hepatic Function.*

# Treatment

- 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

- Important to continue to monitor for malignancy
- If underlying ILD is suspected, an interdisciplinary approach to treatment with pulmonology is important
- At onset of diagnosis, referral for physiotherapy is essential to help maintain muscle strength until clinical symptoms are fully resolved

# Case Study #1

38 year old AA male with a past medical history of asthma presented with 6+ month history of arm and shoulder pain and described difficulty using his arms. He had seen ortho and had cortisone injections and was referred to PT. Symptoms progressed and therapist mentioned the possibility of RA and that he should see a rheumatologist. 1 week prior to his initial OV, he began having swelling in his left foot. At his initial OV (which was a virtual visit), he also described weakness with walking up steps and trouble getting up from a seated position. He admitted to frequent falls due to pain.

- Positive history for Raynaud's phenomenon

He denied any weight changes, fever/chills, recent steroid use.

PE- Very limited due to virtual visit and obviously could not assess muscle weakness.

No obvious rash, mild vitiligo. PIPs appeared puffy- when he was finally able to be seen in the office he had left elbow contracture and bilateral fused wrists.

# Case Study #1

Labs- +ANA, +SSA, ESR 33, CBC-Platelet counts 470,000, CRP 5.80, CK 17365, CMP- ALT/AST 248/520; Anti-Jo1 antibody >100

X-rays showed erosive changes in hands consistent with RA.

Based on work up so far, it was determined that muscle biopsy would not be necessary and diagnosed with RA/PM overlap.

# Case Study #1

- He was initially started on 60mg Prednisone but had significant side effects (tachycardia, anxiety, insomnia). Dose was decreased by 10mg each week (X 2 weeks) and he was started on MTX 15mg/week and Folic Acid 1mg QD.
- At 20mg/day Prednisone and 20mg/week of MTX- Patient felt better but still unable to get up from a seated position and still significant muscle weakness on exam
- Prednisone decreased to 15mg; MTX increased to 25mg/week and discussed adding Rituxan
- It took about 10 weeks to get patient assistance for Rituxan but did begin 1000mg on Day 0 and 15. Prednisone was slowly tapered

# Case Study #1

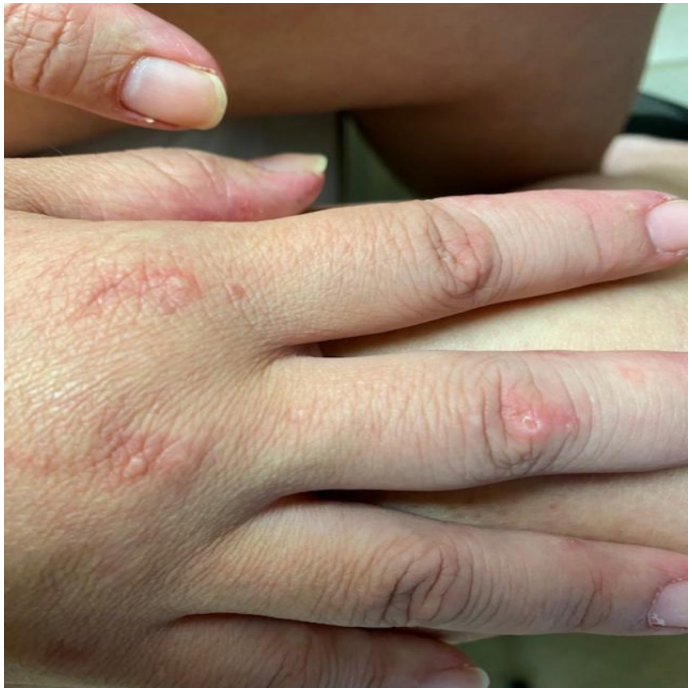
- Lost to follow up for about 6 months.  Stopped MTX and Prednisone because her was feeling better.  Returned with severe flare and muscle weakness.  CK 43,610, ALT/AST 475/1194
- Restarted Prednisone 40mg, MTX 17.5mg/week and received Rituxan that week.
- Seen last month, walking 3X/week for exercise, denied joint pain/stiffness, muscle pain, muscle weakness.  Muscle strength 5/5 both upper and lower extremities- Last CK was 647

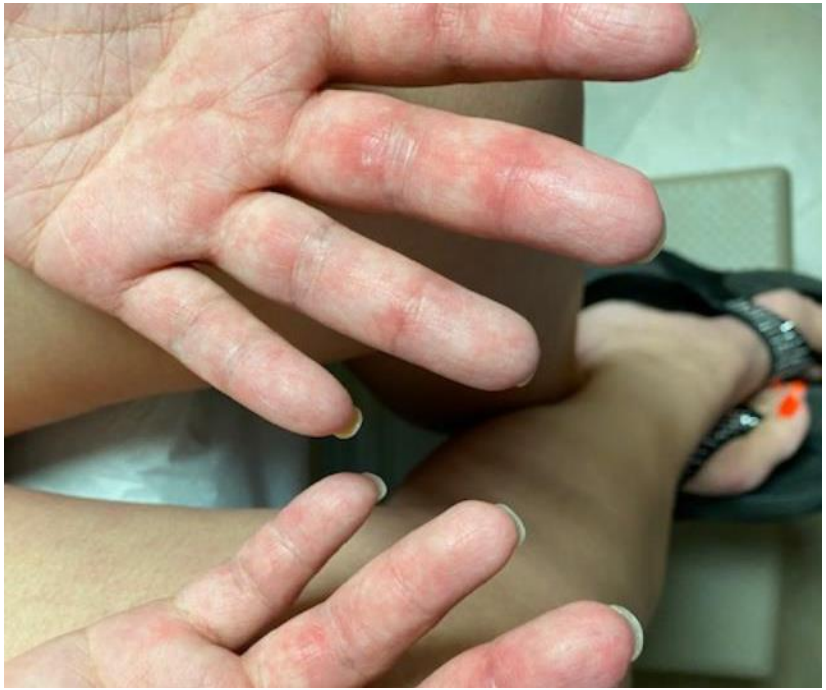
# Case study #2

- 41 yo Asian female referred by her dermatologist due to recent skin biopsy of the left thigh consistent with interface dermatitis.
  - 4 months prior she developed erythematous papular exanthem on her forehead. Also noticed rash along the hairline and inner ears. 2 weeks later, sudden onset of an intensely painful rash over the palmar aspect of her hands involving the digital pads and lateral fingers. This rash was erythematous, raised and had a callous appearance. Then developed lesion over left olecranon which formed an eschar. Rash developed over temporal and nasal aspects of her eyes (but not her eyelid) with flaking. Violaceous rash over the lateral and posterior thighs.
  - Early on she developed painful apthous ulcers involving tongue and buccal mucosa lasting one week.
  - One week after rash she developed arthralgias of MCP and PIP joints, wrists, and elbows.

ROS + hair loss; otherwise unremarkable

# Case Study #2





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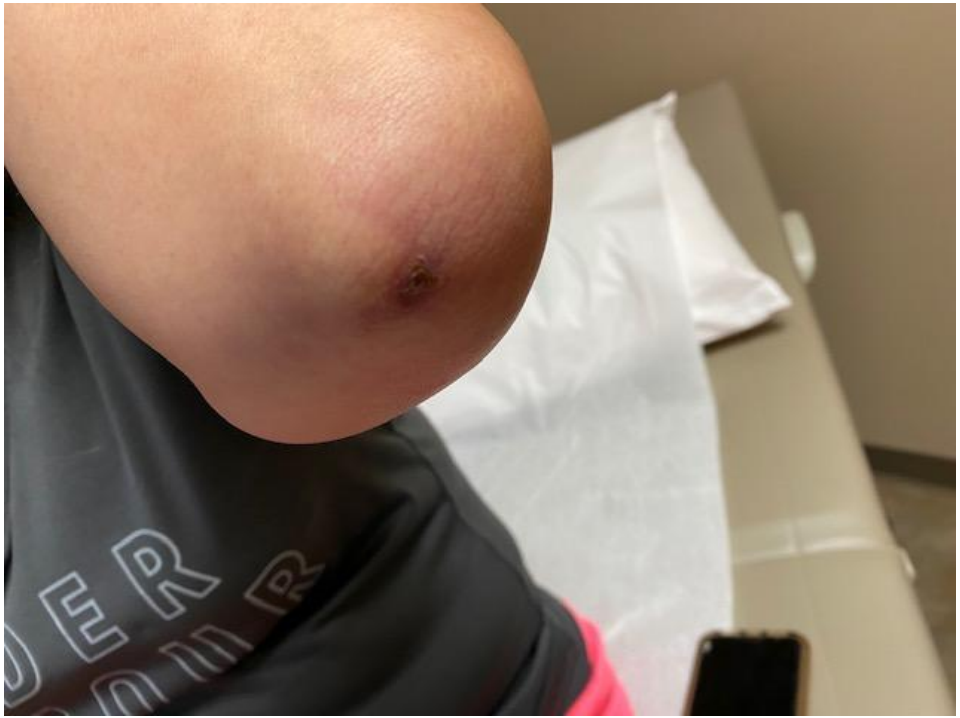

# Case Study #2

- Labs- Hepatitis Core total antibody +, Hepatitis B core IgM antibody negative; Hepatitis B surface antigen +; viral load low; ALT/AST 128/84; CPK 129
- - RF, CCP, ANCA, ANA and ANA 7 Profile were negative
- Mayo Clinic Myositis Panel- +MDA 5 ab, +IgG SSA 52kD antibody
- Chest X-ray normal; PFTs with DLCA normal; hrCT nonspecific, minimal fibrotic changes

# Cast Study #2

- Rash over the MCPs and PIPs was suggestive of DM
- However, the rash over hands, thighs, and face with early ulcerations and a vasculitis appearance were atypical.
- **DM with MDA 5 phenotype**
  - Normal CPK and elevated aldolase
  - Apthous ulcers, alopecia, and vasculitis lesions are frequently described in this phenotype

# Case Study #2

- Treatment
  - Rituximab 1000mg at 0, 15 days. Consider 1g IV Solu Medrol prior to Rituxan
  - Discuss antivial therapy with GI prior to initial Rituxan
  - Continue AZA and Prednisone

# Case Study #2

- Once she was started on Rituxan, she responded quickly.  She has maintained on Rituxan 1000mg every 6 months, Imuran 100 QD, and Prednisone 5mg QD.
  - We did discuss lowering Prednisone by 1mg each month to attempt to taper completely off.

# Thank you

Questions?