RhAPP

RHEUMATOLOGY ADVANCED PRACTICE PROVIDERS

Second Annual National Conference

September 30 – October 2, 2021

Phoenix, AZ

RhAPP
RHEUMATOLOGY ADVANCED PRACTICE PROVIDERS

Inflammatory Myopathies

Eileen Lydon ANP-BC
Emmy Katz PA-C

Disclaimer

Disclosure of Conflicts of Interest:

All individuals in control of the content of continuing education activities provided by the Annenberg Center for Health Sciences at Eisenhower are required to disclose to the audience any real or apparent commercial financial affiliations related to the content of the presentation or enduring material. Full disclosure of all commercial relationships must be made in writing to the audience prior to the activity. All staff at the Annenberg Center for Health Sciences at Eisenhower and the Rheumatology Advanced Practice Providers (RhAPP) have no relationships to disclose.

Faculty Disclosures

Eileen Lydon, ANP-BC

- Speaker: Abbvie, Sanofi Genzyme

Emmy Katz, PA-C

- There are no financial relationships to disclose.

Outline

- Overview
- Epidemiology
- Pathophysiology
- Clinical presentations
- Diagnostic overview
- Treatment strategies
- Case study

Inflammatory Myopathies

Inflammatory myopathies (IM), known as myositis, are heterogeneous disorders characterized by muscle inflammation, and frequently accompanied by extra-muscular manifestations that affect the skin, lungs, and joints.

The Lancet Neurology. 2018:17 (9); 816-828.

Disease Subtypes

- Dermatomyositis
  - Clinically Amyopathic Dermatomyositis
- Polymyositis
- Antisynthetase syndrome
- Overlap Syndromes
- Immune-mediated necrotizing myopathy
- Inclusion body myositis

PM/DM Epidemiology

- Annual incidence of 2-10 cases/million
- DM peak 5-15, and again 45-65, years of age
- PM rarely occurs <15; Mean 50-60 years of age
- F:M ratio is 2-3:1 overall
- U.S. AA >Caucasians 3-4:1

Sterling, W. 2015.

Dermatomyositis (DM) & Polymyositis (PM)

- Proximal, symmetrical muscle weakness & inflammation
- Elevated muscle enzymes
- DM, unlike PM, is associated with a variety of skin findings
  - Cutaneous often precedes weakness
  - Amyopathic DM
    - Skin findings without muscle weakness
- ILD, dysphagia, polyarthritis, constitutional, may be present

DM & PM Clinical Findings

- Deltoids and hip flexors muscles most often involved
- Pain often a symptom
- Muscle weakness occurs over days to weeks
- May cause difficulty getting up from a chair, walking, carrying heavy groceries, lifting object over head

DM/PM

Muscle Pathology

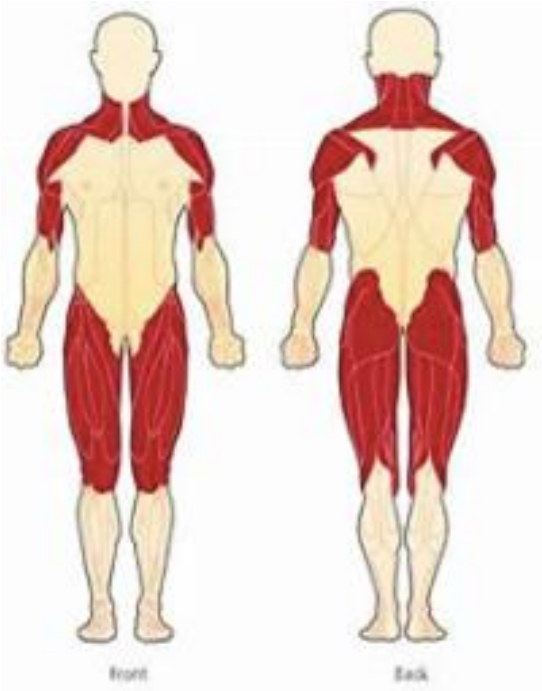
- DM tends to be vascular, located in the perifascicular region, while PM, the cellular infiltrate is within the fascicle, with inflammatory cells invading individual muscle fibers

Auto-antibodies

- DM:
  - Mi-2, MDA5 (ILD), TIF-1y(malignancy), NXP2(malignancy), SAE
- PM
  - Unspecific

DM/PM Muscle Exam

- Muscle strength testing
- Extensor muscles more affected than flexor
- Distal strength almost always maintained
- Neck flexor weakness may be seen
- Muscle pain and tenderness
- Sensation is normal and tendon reflexes are preserved



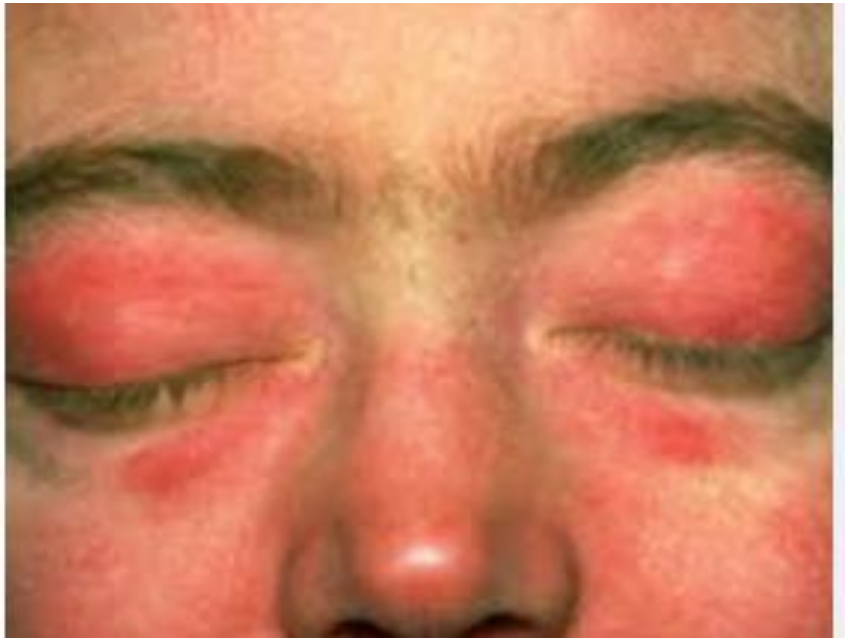
Myositis.tumbir.com

DM Skin Findings

- Hallmark features of DM
  - Gottron’s papules and heliotrope eruption
- Other characteristic findings
  - Gottron’s sign, photodistributed erythema, poikiloderma, nailfold changes, scalp involvement and calcinosis

Heliotrope Eruption

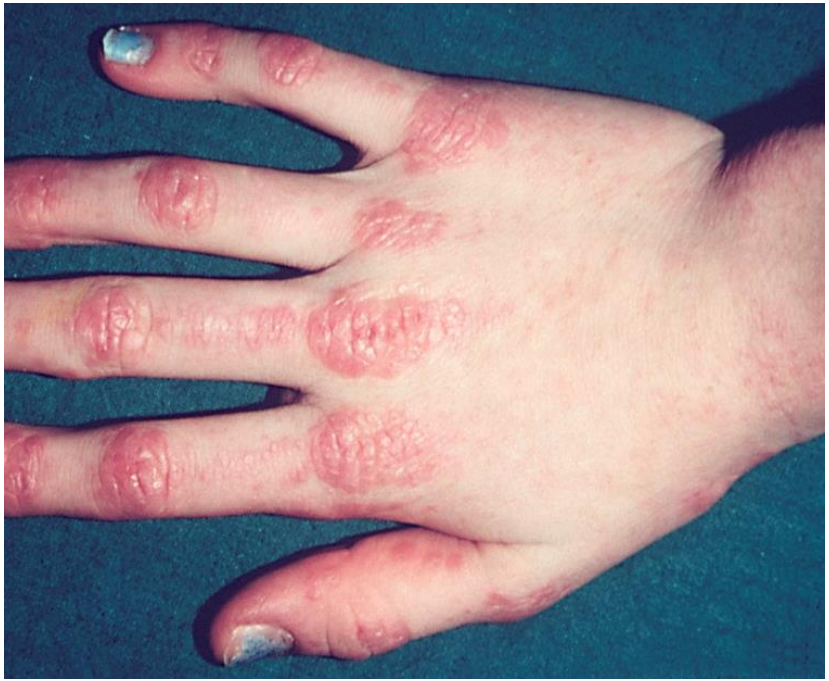
- Violaceous to erythematous rash, on the upper eyelids, sometimes accompanied by eyelid edema



Flicker.com

Gottron’s Papules

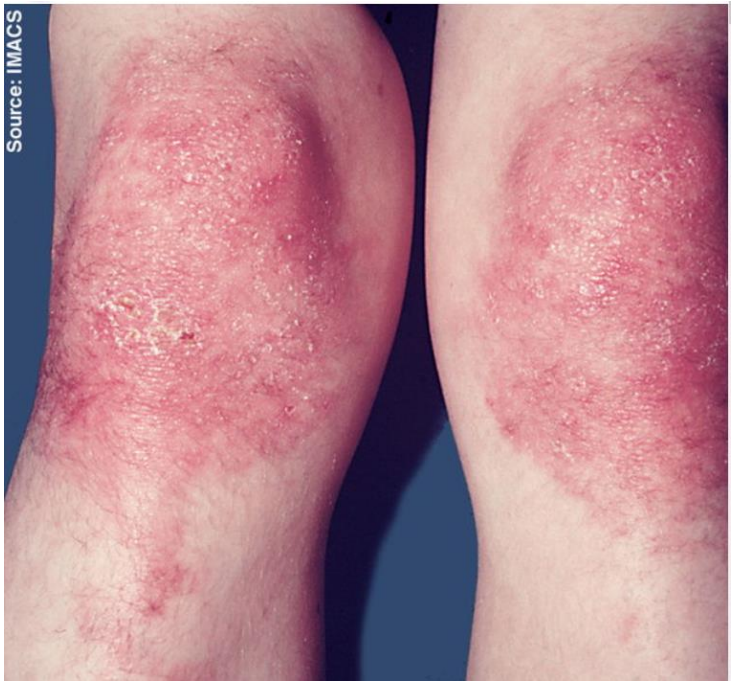
- Flat topped, erythematous to violaceous papules
- Found over MCP, PIP or DIP joints
- May have a scale overlying papules



Source: IMACS

Gottron’s Sign

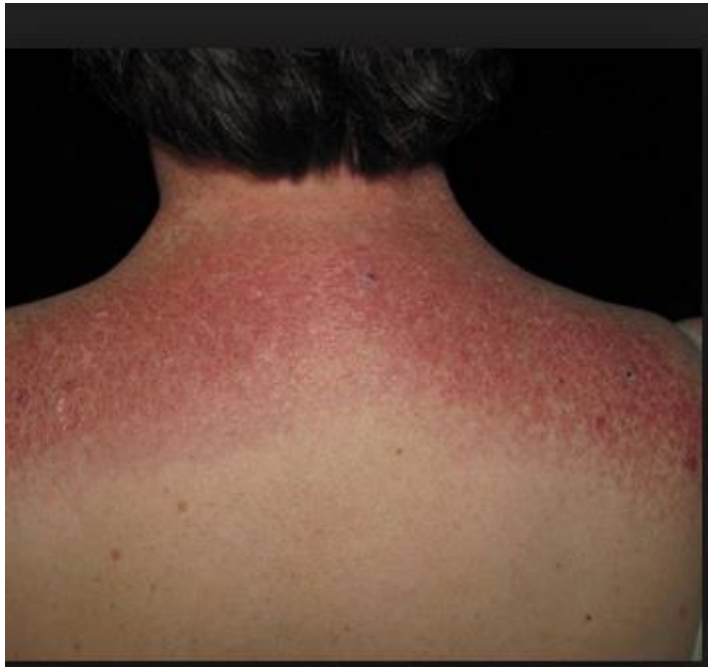
- Erythematous to violaceous macules, papules or patches, on the extensor surfaces of joints other than the hands
- Particularly the elbows, knees or ankles



Source: IMACS

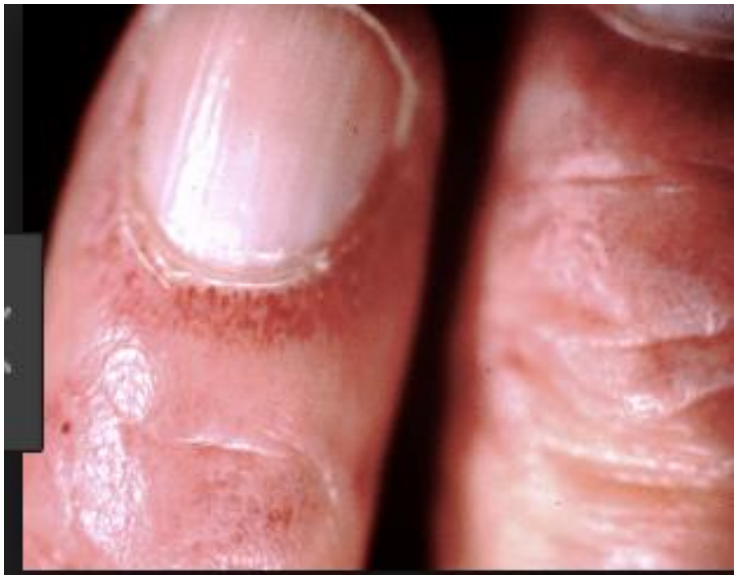
Photodistributed Poikiloderma

- Hyper & hypopigmentation, telangiectasia, epidermal atrophy
- May occur on any photo-exposed skin
  - Upper back (shawl sign) and upper chest (V sign)



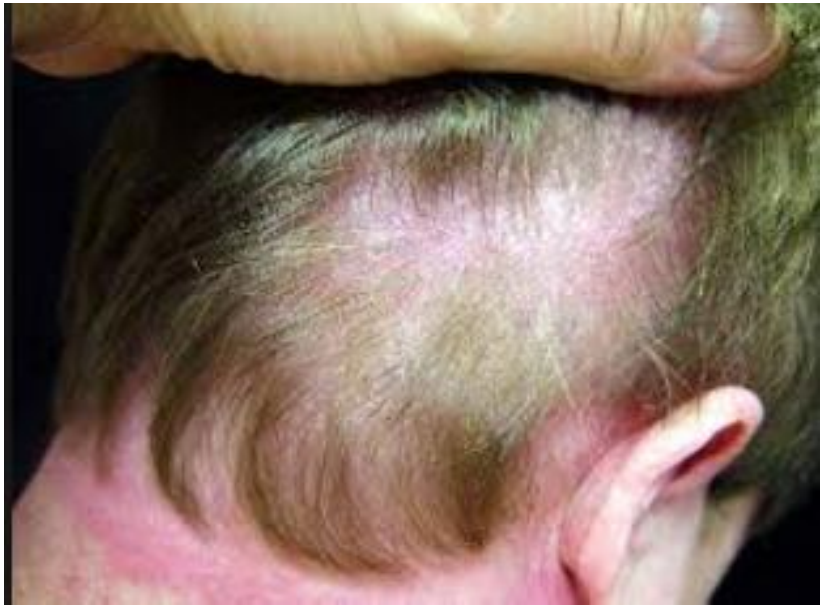
Periungual Abnormalities

- Capillary nail beds with dilated capillary loops, with dropout and periungal erythema
- Cuticular overgrowth, “ragged cuticles”



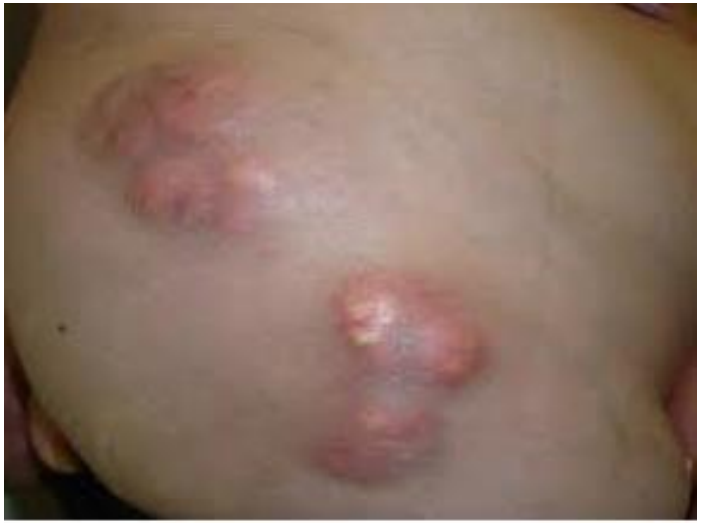
Psoriasiform Changes in the Scalp

- May resemble seborrheic dermatitis or psoriasis
- Diffuse, often with poikilodermatous changes and scaling
- May result in burning, pruritus and sleep disturbance



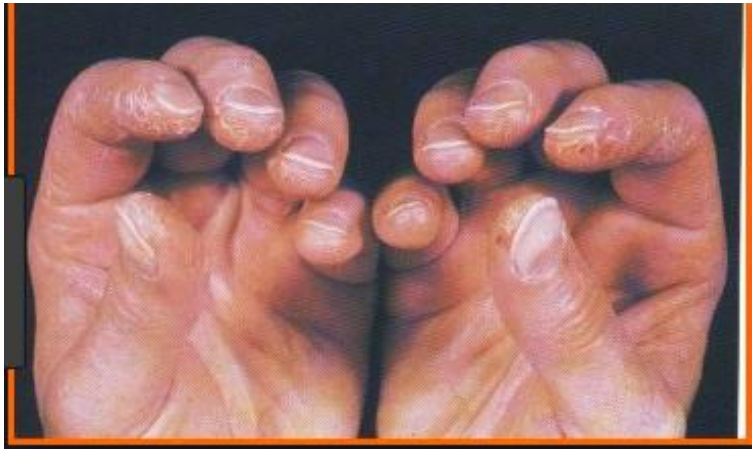
Calcinosis Cutis

- Deposition of calcium within the skin, occurs commonly in juvenile DM.
- May also be seen in SSc, SLE (rarely) and overlap connective tissue disorders.



“Mechanics Hands”

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



Antisynthetase Syndrome

- Inflammatory myopathy and/or extra-muscular findings with antibody directed against tRNA synthetase
  - ILD
  - Mechanics hands
  - Inflammatory arthritis
  - Raynaud’s
- Onset more acute than primary DM

Overlap Syndrome

- IM with another systemic rheumatic disease (SLE, SSc; scleroderma, and MCTD)
- Muscle involvement often subclinical or mild
- Mild elevation of muscle enzymes
- Largest group with up to half the myositis cases

Immune-Mediated Necrotizing Myopathy

- Muscle necrosis with scare inflammatory infiltrate on bx
- Leads to a rapid and severe proximal weakness
- Muscle enzymes usually very high
  - SRP autoantibodies
  - Anti-HMGCR autoantibodies and hx of statin use
    - Malignancy higher in Anti-HMGCR than SRP

Inclusion Body Myositis

- Affects older individuals, more commonly men
- More insidious onset and slower progression over years
- Weakness more distal in upper extremities and asymmetric
- May have progressive dysphagia
- Elevation of CK much milder

Malignancy and Extra-Muscular Manifestations

- All forms of myositis except IBM associated with malignancy
- Lung disease
  - Severe ILD associated with increased rate of mortality
    - Antisynthetase antibodies, anti-U-snRNP, PM/Scl, anti-Ku, anti-MDA5, and anti-SRP
- Joints
- GI

Diagnostic Overview

Typically three distinct presentations:

1. Patients with evidence of muscle weakness only
2. Patients with evidence of extramuscular disease only
3. Those with both muscle weakness and extramuscular manifestations

Laboratory Investigation

- Can have one or more elevated muscle enzymes: Creatinine Kinase, LDH, AST, ALT
- CK is the most sensitive and commonly followed
- CK can be normal in 20% of patients with Dermatomyositis even with patients with evidence of muscle inflammation on diagnostic tests
- Follow CK for relapse or response to treatment, but remember CK levels do not correspond with disease severity

Lab Work Up:

- Check for overlap syndromes
- SSA, SSB, Anti smith, RNP
- Inflammatory markers: ESR, CRP may or may not be elevated
- +ANA can be found in up to 60 % of patients with Dermatomyositis or PM, but it is not diagnostic

Diagnostic Work Up:

- **EMG:** can help to differentiate from other disease conditions such as Myasthenia Gravis, motor neuron diseases.
- EMG can also help to point out area best for muscle biopsy.
- **MRI:** Identify areas of muscle inflammation, fibrosis, edema and calcification.
- **Muscle/Skin Biopsy:** Useful for patients who present with muscle weakness but without other typical findings such as rash or specific antibody testing.

Differential Diagnosis:

- Infectious/drug induced myopathy
- Sarcoid myopathy
- Motor neuron diseases
- Myasthenia Gravis
- Amyloid myopathy
- Hypothyroid myopathy
- PMR (pain rather than weakness)
- Fibromyalgia (pain rather than weakness)
- Cutaneous lupus
- Psoriasis, Atopic dermatitis

Treatment Strategies:

Focused on the subtype of the disease

- *Aside from IBM (Inclusion body myositis) the mainstay of treatment is initial glucocorticoids followed by steroid sparing agent*

Also important to individualize based on disease severity, organ involvement, if there is malignancy associated

Take into consideration comorbidities of each patient

Treatment:

Prognosis and outcome: those with the following tend to have poorer response/outcome:

Underlying malignancy

Older age

Pulmonary involvement

Dysphagia

Delay in diagnosis/treatment

Treatment: DM and PM

- Initially glucocorticoids
  - (Inform patients they will likely be on glucocorticoids for approximately 1 year tapering)
  - There is no gold standard regimen
- Initially 1mg/kg/day for dosing up to 80 mg/day for approximately 4-6 weeks
- Continue to assess clinical response (CK levels may improve within several weeks but muscle strength lags behind typically)
- Be mindful of steroid myopathy

Treatment: DM and PM

- Test proximal muscles at each visit
- ILD: PFTs for monitoring *consider close co-management with Pulm

Prior to tapering steroids want to ensure near resolution of muscle weakness and muscle enzymes

- Typically taper down by 10 mg per week until patient reaches 40 mg/day
- Then begin tapering down by 5 mg per week until reaching 20 mg/day
- Taper by 2.5 mg/week until reaching 10 mg/day
- After patient is on 10 mg for a week begin taper by 1 mg every two weeks until tapered to 5 mg then continue slow taper

Treatment: Steroid Sparing Agents

- Helps to reduce the cumulative need for glucocorticoids and long term ramifications
- Azathioprine or MTX typically first line (avoid MTX in patients with ILD due to concern for pulmonary toxicity as well as those with liver disease)
- Initial Azathioprine dosing: 50 mg/day. Serial labs to watch for blood cell counts
- Then increase by 50 mg each week until 1.5 mg/kg/day
- Those with inadequate response may need up to 2.5 mg/kg/day
- Watch CBC, LFTs monthly

Treatment: Steroid Sparing Agents

- Methotrexate: use same dosing as for RA patients beginning with 15 mg/week increasing to maximum of 25 mg/week depending on clinical response
- Side effects may include GI upset, stomatitis, hair loss, leukopenia
- Monitor for hepatotoxicity
- Folic acid daily or Leucovorin weekly

Treatment: DM and PM, Other Therapies

- IVIG: reserved for patients with dysphagia who are at aspiration risk, those with life threatening disease
- Hydroxychloroquine (200-400 mg/day) helpful for skin in up to 75% of patients but not helpful for muscle involvement
- **Refractory disease:** Rituximab, Mycophenolate Mofetil, Tacrolimus, Cyclosporine

Treatment: DM and PM

Duration of therapy:

- Preference to discontinue corticosteroids prior before stopping steroid sparing agents
- Goal is to achieve remission and taper steroids prior to slow discontinuation of steroid sparing agents
- Tapering over month intervals with close attention to relapse

Treatment Considerations:

- **Patients with dysphagia:** aspiration precautions. Thickened diets, elevated head of bed, speech therapy consult
- **Skin manifestations:** importance of adequate sun protection
- **Osteoporosis prevention:** bisphosphonate therapy
- **Infection risk:** PJP infection prophylaxis with Bactrim
- **Immunizations:** ideally prior to initiation of immunosuppressive therapies

Case Study

56 year old Caucasian male with pmhx of hypertension presents with progressive muscle weakness in his upper and lower extremities bilaterally over the course of 4 months. His weakness had gotten to the point where it was difficult for him to climb up his stairs or raise his arms to wash his hair in the shower. He had also noticed an erythematous and somewhat pruritic rash on his face, chest, back and arms bilaterally. Patient denied recent fevers, chills, illness. Patient denied new medication use, use of new detergents or soaps.

Case Study

Physical examination revealed stable vital signs and the patient did not appear in acute distress. Violaceous papules were noted over dorsal aspect of hands. Periorbital edema and erythema observed bilaterally along with maculopapular rash extending on anterior chest, back and forearms. Cranial nerves were intact. Motor exam revealed ⅕ in upper proximal arms bilaterally, ⅖ in distal arms. ⅖ noted in proximal legs bilaterally and ⅗ noted in distal legs bilaterally.

Case Study

Lab work revealed mild ESR elevation of 30, elevated CK of 10,264 IU/L (range 26-192 IU/L), CBC within tolerable limits, mildly elevated ALT, AST, LDH. ANA 1:160 speckled pattern. Specific myositis panel was nonrevealing.

Patient underwent EMG, Muscle biopsy consistent with inflammatory myopathy.

Patient was also referred to PCP for malignancy screening. Patient found to have RBCs on UA and subsequently referred to urology and diagnosed with bladder cancer.

Case Study: Dermatomyositis

In conjunction with discussion with Urologist treatment initiated with oral prednisone with dosing of 1 mg/kg/day. Patient's CK levels, and symptoms were followed closely and began to trend down. Rash continued, HCQ was added at 400 mg/day. Patient underwent BCG treatment for his bladder cancer with his urologist.

Steroid sparing agent added after BCG treatment and MTX 20 mg/week was added to patient's regimen. He was able to slowly taper off prednisone and has begun to taper off MTX and HCQ without disease recurrence.

Case

- 81 year old female presents with 2 months of progressive walking difficulties. Also worsening weakness in the upper extremities, particularly in the shoulders. Also, unable to rise from a chair without push-off and unable to lift arms above the head. The night prior she rolled down off her bed and fell on the floor and could not get up until her daughter came to help a few hours later. For the past 1-2 months she has also been experiencing intermittent swallowing difficulties. Reports being on Lipitor for many years since her 60’s

Case

Medical History

- PMH
  - Anxiety
  - Depression
  - Ulcerative Colitis
  - HL
  - Hyperthyroid
- PSH
  - Cholecystectomy

Medications

- Lipitor 40 mg daily
- Synthroid 125 mcg daily
- Toprol XL 50 mg daily
- Vitamin d 2,000 u daily
- Calcium 500 mg daily

Laboratory Evaluation

- CPK 1,389
- AST 66 (5-34)
- ALT 78 (0-37)
- Aldolase 19.4 (1.5-8.1)
- HMGCR 182 (0-19)
- SAE1, NXP2, MDA5, TIF-1 gamma – negative
- Anti-cN-1A – <20, PL-12, PL-7, OJ, EJ, SRP, Jo-1 – negative
- Smith/RNP negative, PM/ScL IGG, SSA,
  SSB – negative

Continued Workup

- EMG: compatible with primary myopathic process with irritative features
- CT Chest solid LUL mass highly suspicious for invasive primary lung adenocarcinoma
- CT abdomen/pelvis: No acute abdominopelvic pathology

Case

- Pt found to be HMG-CoA antibody +. Lipitor discontinued. Initiated high dose corticosteroids (prednisone 50mg daily), with improvement in her symptoms and CPK (down to 830). Prednisone taper initiated and steroid sparing agent Methotrexate 15 mg weekly started along with FA daily. Pt underwent CT CAP. Due to suspicion of LUL nodule, underwent lung biopsy which was negative for malignancy.
- Pt admitted for hip fracture after falling from standing height, likely steroid induced osteoporosis.
- CK continued to trend down (now 138), on 20 mg prednisone.

Case

- Plan
  - Continue steroid taper
  - Monitor CPK
  - Continue steroid sparing agent MTX/FA
  - F/u pulmonary
  - Continue age appropriate malignancy evaluation
  - Continue PT
  - Refer for osteoporosis eval
  - Cont. vitamin d, calcium