A Dermatologist’s Approach to Dermatomyositis

Northwest Rheumatism Society
4/27/2018
Nicole Fett MD MSCE
Associate Professor of Dermatology
Oregon Health and Science University

Conflicts of Interest and Disclosures

• All medications discussed are off label
• Investigator for Pfizer and F. Hoffman-LaRoche
• I have no pertinent disclosures
  — UpToDate Author
  — Assistant Section Editor JAMA Derm
  — Education committee MDS
  — Education committee ROS
  — Materials review panel medical expert in dermatology for the Lupus Foundation of America
  — Executive committee member, Pacific Dermatology Association
  — Immediate-past President, Oregon Dermatology Society

Additional Disclosure

• Myositis
• Interstitial Lung Disease
• Malignancy Screening
Objectives

• Recognize the cutaneous manifestations of dermatomyositis

• Understand the “antibody: cutaneous phenotype” relationships in dermatomyositis

• List the cutaneous differential of dermatomyositis

• Compare and contrast dermatomyositis mimickers with dermatomyositis

What does “Dermatomyositis” mean?

In the 1970s Peter and Bohan came up with the following criteria to define dermatomyositis

- Bohan and Peter Criteria
  - Compatible cutaneous disease
    • AND...
  - Proximal symmetrical weakness
  - Elevated muscles enzymes
  - Abnormal electromyogram
  - Abnormal muscle biopsy

We now know that some patients with dermatomyositis do not develop myositis
What does “Dermatomyositis” mean?

- Classic DM
  - Cutaneous features
  - Clinically significant muscle weakness
  - Objective evidence of myositis

- Amyopathic DM
  - Cutaneous features > 6 months
  - No evidence of myositis (and not treated)

- Hypomyopathic DM
  - Cutaneous features > 6 months
  - No clinically significant muscle weakness
  - Objective evidence of myositis

- Early treated ADM
  - ADM treated with > 2 mos immunosuppressants w/in first 6 mos

- Early treated HDM
  - HDM treated with > 2 mos immunosuppressants w/in first 6 mos

- Premyopathic DM
  - Cutaneous features for < 6 mos and no evidence of myositis

- Clinically ADM
  - ADM + HDM

- Skin-predominant DM
  - All patients with cutaneous findings of DM without history of myositis

---


Characteristic Exam Findings in Dermatomyositis

Cutaneous Features of Dermatomyositis
- Facial erythema that includes the nasolabial folds
- Heliotrope sign
- Gottron's sign
- Gottron's papules
- Mechanics hands
- Ragged cuticles
- Nailfold capillary dilation and hemorrhage
- V-neck erythema
- Shawl sign
- Poikiloderma
- Holster sign
- Band of involvement on the low back
- Calcinosis
- Ulcerations

Dermatomyositis

Involvement of the nasolabial folds
Dermatomyositis - Periorbital Edema


- Heliotrope rash


Heliotrope

Gottron’s sign

• Shawl sign
• V-neck sign

Characteristic cutaneous findings in Dermatomyositis

Gottron’s Sign

Nailfold Capillary Dilation

Characteristic cutaneous findings in Dermatomyositis

- Mechanic's hands

Dermatomyositis: Holster sign
Dermatomyositis: Diffuse Scalp Involvement

Dermatomyositis: Ulceration

Objectives

- Recognize the cutaneous manifestations of dermatomyositis
- Understand the “antibody : cutaneous phenotype” relationships in dermatomyositis
- List the cutaneous differential of dermatomyositis
- Compare and contrast dermatomyositis mimickers with dermatomyositis
Dermatomyositis Antibodies: MDA5

- Cytosolic RNA sensor
- Antibodies to MDA5 in dermatomyositis are linked to:
  - Amyopathic disease
  - Interstitial lung disease
  - Arthritis
  - Cutaneous ulcerations
  - Palmar papules
  - Mechanics hands
  - Alopecia

Cutaneous findings associated with MDAS (CADM 140) abs
Dermatomyositis Antibodies: Mi-2

- Complexes with nucleosome-remodeling deacetylase (NuRD) and binds chromatin, repressing gene transcription
- Found in regenerating muscles
- Increased in basal keratinocytes and up-regulated with UV


Dermatomyositis Antibodies: Mi-2

- Mi2 antibodies are present in 11 to 59% of patients with dermatomyositis
- Mi2 antibodies are associated with
  - Classic cutaneous findings
  - Myositis
  - Treatable disease
  - Low mortality

Dermatomyositis Antibodies: Mi-2

Cutaneous Features

- Classic cutaneous findings
- Myositis
- Treatable disease
- Low mortality
**Dermatomyositis Antibodies:**
Small ubiquitin-like modifier activating enzyme (SAE)

- SAE is involved in post-translational modification of proteins, altering function, localization and stability
- SAE antibodies are found in 6 to 8% of adults with Dermatomyositis
  - SAE antibodies are not associated with ILD or cancer
  - SAE antibodies may be associated with dysphagia


---

**Dermatomyositis Antibodies:**
Transcription initiation factor (Tif-1γ)

- Regulates gene transcription
- Associated w/malignancy
  - Sensitivity of 78% (45-94%)
  - Specificity of 89% (82-93%)


---

**Dermatomyositis Antibodies:**
Transcription initiation factor (Tif-1γ)

- Less likely to have:
  - Raynaud’s phenomenon
  - Arthritis and arthralgia
  - Calcinosi
  - Interstitial lung disease
  - High creatinine kinase
  - High aldolase


Dermatomyositis Antibodies: Transcription initiation factor (Tif-1γ)

Dermatomyositis Antibodies: tRNA synthetase


• Patients with anti-synthetase antibodies are more likely to have:
  – Raynaud's phenomenon
  – Interstitial lung disease
  – Mechanic's hands
  – Arthritis
  – Fever
Dermatomyositis Antibodies: tRNA synthetase cutaneous features

- Nuclear Matrix Protein 2 (NXP2)
  - Make up internal structural framework of nucleus
  - Associated with DNA replication and RNA synthesis
  - Regulate p53-induced cellular senescence in response to oncogenic signals

- 2 to 30% of adults with dermatomyositis and are associated with calcinosis, Gottron’s sign, peripheral edema and dysphagia, myalgia, and possible malignancy
- NXP-2 antibodies are associated with calcinosis, severe muscle weakness, joint contractures, intestinal vasculitis and polyarthritis in children with dermatomyositis


Dermatomyositis Antibodies: NXP2 Cutaneous Features

• Calcinosis

Objectives

• Recognize the cutaneous manifestations of dermatomyositis

• Understand the “antibody : cutaneous phenotype” relationships in dermatomyositis

• List the cutaneous differential of dermatomyositis

• Compare and contrast dermatomyositis mimickers with dermatomyositis
Cutaneous Differential of Dermatomyositis

- Hydroxyurea-induced Dermatomyositis
- Acute Cutaneous Lupus
- Psoriasis
- Multicentric Reticulohistiocytosis

Hydroxyurea-induced Dermatomyositis

- 36 cases
  - 69% CML, 14% essential thrombocytosis, 14% PVC, 3% psoriasis
  - Mean time to onset 60 months
  - Low rate of ANA positivity (16%)
  - No myositis
- Stop the hydroxyurea = cutaneous signs resolve

Acute Cutaneous Lupus Erythematosus
Face: CLE vs Dermato

Hands: CLE vs Dermato

CLE vs Dermato

ITCH
Does NOT distinguish b/w CLE and dermatomyositis

**Differentiating Features:**

**Acute Cutaneous Lupus**
- Malar rash **without** nasolabial fold involvement
- Skin manifestations **do not** localize to joints
- Not a lot of pruritus
- Concomitant DLE
- Mucosal ulcerations
- Systemic involvement
  - Arthritis, Serositis, Nephritis, Seizures/Psychosis, Cytopenias
- Autoantibodies
  - ANA, anti-dsDNA, anti-salmon, SSA, SSB

**Dermatomyositis**
- Facial rash **WITH** nasolabial fold involvement
- Skin manifestations **localize to joints**
- **LOTS** of PRURITUS
- Heliotrope
- Poikiloderma
- Holster sign
- Confluent scalp involvement
- Systemic involvement
  - Myositis, ILD, Malignancy

**Psoriasis**
Psoriasis: Helpful exam hints

- Nail pits
- Nail “oil spots”
- No nailfold capillary dilation
- Involvement of gluteal cleft
- Involvement of occipital scalp and EAC
- Koebernerizes
- Does not usually localize to dorsal hand joints
- Better demarcated than DM
- Rare facial involvement

Psoriasis

- Regular acanthosis
- Thinning of epidermis
- Neutrophils in the epidermis
- Dilated vessels within the superficial dermis
Psoriasis vs Dermatomyositis

- Mild dermatomyositis and mild psoriasis can be difficult to distinguish

- Nail changes (pits and oil spots), absence of eyelid and dorsal hand joint involvement, absence of nailfold capillary dilation, and well demarcated plaques favor psoriasis

- When in doubt, biopsy

Multicentric reticulohistocytosis

MRH
• Rare, systemic non-Langerhans (class II) histiocytosis (CD 68+, S100-, CD1a-)
• Symmetric erosive polyarthritis and mucocutaneous nodules
  – Can also infiltrate other tissues
• Female predominance
• Approximately 30% associated with internal malignancy
  – Breast and gastric most common

• Classic cutaneous findings
  – Coral beads
  – Facial papules and nodules
MRH

- Classic radiographic findings
  - Punched out erosions
    - Can mimic RA or PsA
  - Reabsorption of juxta-articular space


MRH

- Etiology unknown
- TNF-α and osteoclasts
  - Increased TNF-α in skin and synovial fluid in MRH
  - TNF-α known to induce osteoclast formation
    - Up-regulates RANKL
  - Osteoclasts contribute to mutilating arthritis


MRH

- Treatment
  - Immunosuppressives
    - Prednisone in combination with methotrexate
    - Cyclophosphamide
  - TNF-α inhibitors
    - Known increase in TNF-α in synovial fluid
    - May work by decreasing formation of osteoclast
  - Aminobisphosphonates
    - Prevent MNGC differentiation into osteoclasts
    - Cause apoptosis of formed osteoclasts

---

MRH presenting as Dermatomyositis

<table>
<thead>
<tr>
<th>Case</th>
<th>Author</th>
<th>Sex/Age</th>
<th>Cutaneous features</th>
<th>Joint involvement</th>
<th>Other manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hsiung, JAAD 2003</td>
<td>F/37</td>
<td>Photodistributed erythematous rash</td>
<td>Severe polyarthritis</td>
<td>Raynaud’s, Periungual telangiectasia</td>
</tr>
<tr>
<td>2</td>
<td>Hsiung, JAAD 2003</td>
<td>F/56</td>
<td>Photodistributed erythematous rash</td>
<td>No</td>
<td>Photosensitivity, PBC</td>
</tr>
<tr>
<td>3</td>
<td>Hsiung, JAAD 2003</td>
<td>M/57</td>
<td>Photodistributed erythematous rash</td>
<td>Arthritis and ankylosis</td>
<td>Myalgia</td>
</tr>
<tr>
<td>4</td>
<td>McRae, JRM 1996</td>
<td>M/49</td>
<td>Rash over knuckles, elbows, neck</td>
<td>Erosive polyarthritis</td>
<td>Proximal muscle weakness</td>
</tr>
<tr>
<td>5</td>
<td>Nitta, Derm 2007</td>
<td>F/50</td>
<td>Rash over elbows, hands, wrists</td>
<td>Erythematous plaques</td>
<td>Periungual telangiectasia</td>
</tr>
<tr>
<td>6</td>
<td>Munoz-Santos, Dermatology 2007</td>
<td>M/68</td>
<td>Photodistributed erythematous rash</td>
<td>Photosensitivity, Raynaud’s</td>
<td>Myalgia</td>
</tr>
<tr>
<td>7</td>
<td>Fett, Liu, 2011</td>
<td>F/50</td>
<td>Photodistributed erythematous rash</td>
<td>Photosensitivity, Polynervitis</td>
<td>Periungual telangiectasia, Photosensitivity</td>
</tr>
</tbody>
</table>

---

Are these the only cases?

- Pubmed search “multicentric reticulohistiocytosis”
- 234 manuscripts referencing MRH
  - Assessed for physical exam findings reminiscent of dermatomyositis
    - “dermatomyositis-like” = photo-distributed erythema, photodistributed patches, photo-distributed plaques, V-neck, erythematous patches or plaques over extensor surfaces, heliotrope, poikilodermatous patch, telangiectatic patch
    - One patient in cardiology literature included based on photographs of gottron’s sign on elbows
MRH can present with DM-like features

- Additional 27 cases MRH w/DM-like features
  - Total of 32 cases in the literature
- 26% w/malignancy
- 74% female
- 31/32 w/papules pathognomonic for MRH

---

MRH can present with DM-like features

- DM-like skin findings = MRH pathologically
  - Not DM-MRH overlap syndrome
  - MRH with DM-like clinical findings

---

MRH can present with DM-like features

- Important for screening and therapeutic purposes
  - Both = malignancy screening
  - MRH = severely deforming erosive arthritis, infiltration of internal organs, muscles, and salivary glands
  - Dermatomyositis = myositis, ILD, UV minimization

---
MRH can present with DM-like features

- TNF-α inhibitors may help patients with MRH
- TNF-α inhibitors may exacerbate/cause dermatomyositis

MRH a DM mimic

- MRH may present with DM-like cutaneous features
- MRH is easily differentiated from dermatomyositis histologically, and therefore cutaneous biopsy is an effective diagnostic tool
- Differentiating MRH from dermatomyositis is important for management decisions and comorbidity screening

Objectives

- Recognize the cutaneous manifestations of dermatomyositis
- Understand the “antibody: cutaneous phenotype” relationships in dermatomyositis
- List the cutaneous differential of dermatomyositis
- Compare and contrast dermatomyositis mimickers with dermatomyositis
Treatment of Dermatomyositis

• Three separate potential targets
  – Skin disease
  – Muscle disease
  – Lung disease

The therapeutic ladder for cutaneous manifestations of dermatomyositis

Dermatomyositis Skin Disease Treatment

- Topicals
- Corticosteroids
- Calcineurin inhibitors
- Antimalarials
  - HCQ vs. CQ
  - HCQ + quinacrine
  - CQ + quinacrine
- Strict photoprotection
- Antipruritics
Dermatomyositis skin disease treatment that also treats ILD

- Topicals
- Corticosteroids
- Calcineurin inhibitors

- Antimalarials
  - HCQ vs. CQ
  - HCQ + quinacrine
  - CQ + quinacrine

- Strict photoprotection
- Antipruritics

- Azathioprine
- Rituximab
- Calcineurin inhibitors
- JAK inhibitors
- Dapsone
- Thalidomide/Selenomide
- Cyclophosphamide
- Basiliximab