PEARLS AND PITFALLS FROM DERMATOMYOSITIS CASES

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DISCLOSURE OF RELATIONSHIPS WITH INDUSTRY

Benjamin Chong, MD, MSCS
F123 – Complex Medical Dermatology Cases – Pearls and Pitfalls

DISCLOSURES

Biogen Inc.: Investigator – Grants
Daavlin Inc.: Investigator – Grants
Pfizer: Investigator
Celgene, Viela Bio: Consultant
PATIENT CASES
60 y.o. Caucasian female with history of rash on face, and chest

Past medications - hydroxychloroquine

Current meds – Prednisone 10 mg QD

Review of systems: + shortness of breath, negative for photosensitivity, joint pains in hands, cough, muscle weakness
CASE #1

- **Biopsy – SCLE vs. dermatomyositis**
- **Lab work**
  - ANA 1:160
  - Negative dsDNA antibodies
  - Negative extractable nuclear panel (Jo-1 antibody)
  - Normal CK (46), normal aldolase (6.6)
  - Myositis panel negative (Mayo Clinic)
    - Mi-2, Ku, PL-7, PL-12, SRP, U2RNP
ADDITIONAL TESTS

- Order additional myositis-specific antibodies
  - MDA5
  - TIF-1γ
  - NXP2

- Results (Oklahoma Medical Research Foundation)
  - MDA5 antibody negative
  - TIF-1γ antibody positive
Not necessary to order if diagnosis of dermatomyositis is straightforward

Consider ordering them:
- If dermatomyositis is in DDx
- Need supportive proof for your diagnosis of dermatomyositis
- Provide prognostic information
MYOSITIS-SPECIFIC AND MYOSITIS-ASSOCIATED ANTIBODIES ARE SEEN IN PATIENTS WITH DM

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<th>Myositis-specific and myositis-associated autoantibodies</th>
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<td>Dermatomyositis-Specific:</td>
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<td>• Anti-TIF-1 γ</td>
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Tartar DM et al, Clin Dermatol 2018; 36:508-524
Anti-Ro (SS-A) antibody most commonly reported with myositis
- Ro-52 > Ro-60 antibody
- Pm/ScI antibodies associated with mechanic’s hands
- U1-RNP Ab – myositis-SLE overlap

Tartar DM et al, Clin Dermatol 2018; 36:508-524
Most DM patients have one myositis-specific antibody present

- **Mi-2 Ab**
  - Favorable prognosis
  - Shawl sign, heliotrope rash, cuticular overgrowth

- **SAE-1 Ab**
  - Heliotrope rash
  - Dysphagia
TIF-1-γ is part of TRIM family of proteins
- Involved in transcription regulation
- Formerly known as p155/140 autoantibodies

Predilection for cancer-associated DM patients¹
- Malignancies occurring within 3 years of DM diagnosis²

Reported in 13-21% of adults with DM³

Associated with severe skin disease⁴

¹Targoff et al, Arthritis Rheum 2006; 54:3682-9
²Oldroyd A, et al, Rheumatology 2018 [epub]
³Fiorentino DF et al, Arth Rheum 2013; 65:2954-62
TIF-1-.gamma autoantibodies are associated with distinct skin findings

Psoriatic-like lesions\(^1\)

“Red on white”\(^1\)

Ovoid palatal patch\(^2\)

2. Bernet L et al, JAMA Dermatol 2016; 152; 1049-51
ANTI-MDA5 ANTIBODIES ARE ASSOCIATED WITH DM PATIENTS WITH RAPIDLY PROGRESSIVE ILD AND MILD MUSCLE DISEASE

- MDA5 encodes RNA helicase recognizing single-stranded viruses
- Present in 10-20% of all DM patients
- A/w rapidly progressive ILD and clinically amyopathic DM patients$^{1,2}$
- Antibody levels can mirror ILD activity$^{3}$

$^2$Hamaguchi Y et al, Arch Dermatol 2011; 147:391-8
ANTI-MDA5 ANTIBODIES ARE ASSOCIATED WITH SIGNS OF VASCULOPATHY

Palmar papules¹

Ulcers²

¹Fiorentino D et al, J Am Acad Dermatol 2011; 65:25-34
²Narang NS et al, Arth Car Res 2015; 67:667-672
ANTI-MDA5 ANTIBODIES ARE ASSOCIATED WITH SIGNS OF VASCULOPATHY

Painful violaceous macules in ear

1Okiyama N et al, Br J Dermatol 2018 [epub]
NXP2 AUTOANTIBODIES ARE ASSOCIATED WITH CALCINOSIS AND JUVENILE DERMATOMYOSITIS

- NXP2 – nuclear matrix protein, involved in transcription regulation
- Reported in 1.6%-30% of adult DM patients
- Associated with calcinosis in dermatomyositis\(^1,2\) and juvenile dermatomyositis\(^2\)
- Higher disease severity (dysphagia, myalgia (distal weakness))\(^3\)
- Also seen in DM patients with cancer\(^4\)

\(^1\)Valenzuela A et al, JAMA Dermatol 2014; 150:724-9
\(^2\)Gunawardena H et al, Arth Rheum 2009; 1807-14
\(^4\)Fiorentino DF et al, Arth Rheum 2013; 65:2954-62
\(^5\)Bowman KA, Chong BF. Dermatomyositis. Dermatology Atlas for Skin of Color. 2014
Cellcept was started, and later d/c’d (urosepsis)
Methotrexate initiated
Now on 25 mg SQ weekly with prednisone weaned off
Later diagnosed with ILD
TREATMENT LADDER FOR DERMATOMYOSITIS

**Mild (skin-limited)**
- Sun protective methods
- Topical Steroids/Immunomodulators
- Hydroxychloroquine (200 mg QD-BID)
- Add quinacrine (100 mg QD)
- Switch hydroxychloroquine to chloroquine (125-250 mg QD)

**Moderate/Severe (with systemic symptoms)**
- Prednisone (0.5-1 mg/kg/day)
- Mycophenolate mofetil (1000-1500 mg BID)
- Methotrexate (15-25 mg QWK)
- IV Immunoglobulin
- Rituximab
- Tofacitinib
CASE #2

- 61 y.o. female with complaints of rash of face, neck, upper chest, forearms, hands
- Triggers – sun exposure
- ROS – positive for shortness of breath, cough, negative for muscle weakness
- Current medications - none
CASE #2

Labs:
- CK high (299), aldolase (11.5)
- ANA positive
- Negative dsDNA Ab, ENA Ab
- Myositis panel – positive PL-7 antibody
ANTI-SYNTHE TASE SYNDROME

- Autoantibodies against tRNA synthetase
  - Jo-1, PL-7, PL-12, EJ, OJ, KS, Ha, Zo
- Triad – ILD, myositis, arthritis
- Additional findings – fever, mechanics hands, Raynauds
FURTHER WORKUP FOR INTERSTITIAL LUNG DISEASE?

- A. Refer to pulmonary
- B. Order pulmonary function tests.
- C. Order high-resolution lung CT
- D. All of the above
CASE #2 – PULMONARY WORKUP AND F/U

- PFTs – Moderate restriction with severely reduced diffusion capacity (DLCO)
- High-resolution CT chest – consistent with non-specific interstitial pneumonia
- Prednisone 40 mg QD (taper), Cellcept 500 mg BID started
Non-specific Interstitial Pneumonia (NSIP)

- The most frequent ILD in both scleroderma and DM
- Presentation – subacute to chronic dyspnea/cough
- Constitutional symptoms in up to 1/3

Rx – steroids, mycophenolate mofetil, cyclosporine, azathioprine, cyclophosphamide

Courtesy of Dr. Craig Glazer
MOST DM PATIENTS WITH INTERSTITIAL LUNG DISEASE ARE STABLE OR SHOW IMPROVEMENT

- 107 DM/PM patients with ILD
  - 32.7% had their ILD resolve
  - 51.4% showed disease improvement or stability
  - 15.9% worsened
  - Factors associated with worsening – older age, having dyspnea or cough, having symptomatic acute onset, lower FVC, DLCO

Marie I et al Arth Rheum 2011; 3439-3447
RISK FACTORS ASSOCIATED WITH ILD IN PATIENTS WITH DM

- Mechanic’s hands
- Autoantibodies – Anti-MDA5, anti-synthetase antibodies

Ang CC et al, Br J Dermatol 2017; 176:231-233
MY INTERSTITIAL LUNG DISEASE SCREENING IN DERMATOMYOSITIS PATIENTS

- Initial testing
  - High-resolution chest CT
  - PFTs (with DLCO)
- Follow-up testing – PFTs (with DLCO) annually
- When to Refer to Pulmonary
  - Unexplained respiratory symptoms
  - Abnormal HRCT
  - Abnormal PFT
    - Abnormal FVC or DLCO (<80% predicted)
Myositis-specific and associated antibodies can help support diagnosis of dermatomyositis.

- Newer myositis-specific antibodies have been characterized in a larger percentage of DM patients.
  - Anti-MDA5 Abs – a/w rapidly progressive ILD, clinically amyopathic patients
  - Anti-TIF-1γ Abs – a/w malignancies in DM patients
  - Anti-NXP2 Abs – a/w calcinosis in DM patients, juvenile DM, malignancy

- Screening for ILD includes HRCT and PFTs.