Dermatomyositis
&
Cutaneous Lupus

how morphology can clue us in to systemic manifestations

DIS
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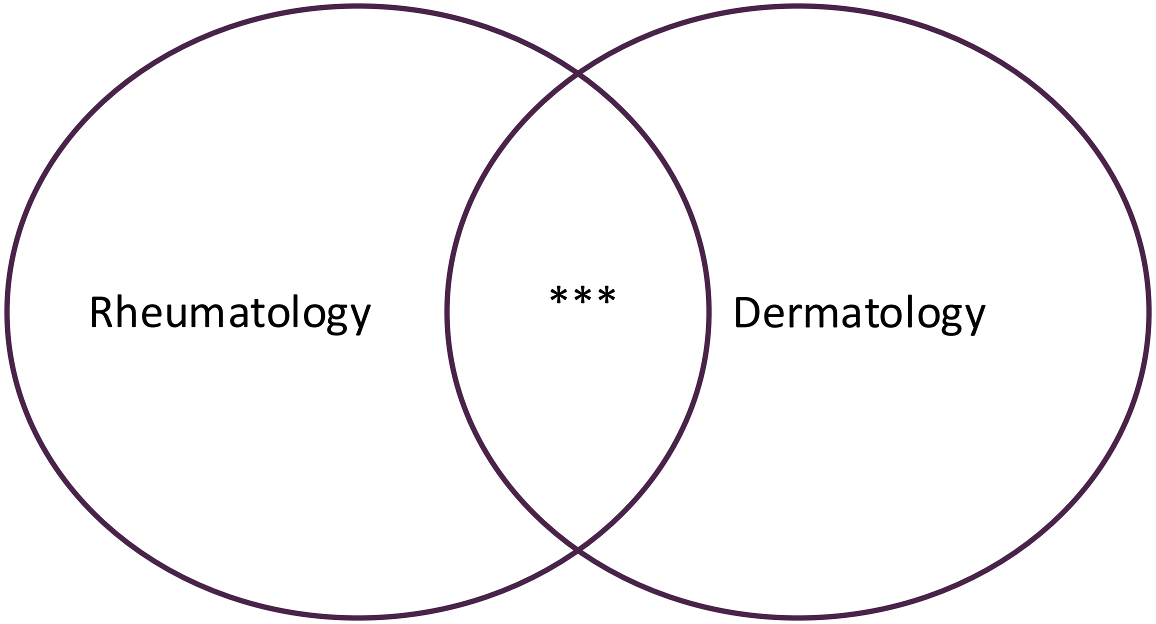
No financial disclosures

LAC-USC Clinic

USC University of Southern California

Dermatology is the best…


Rheumatology
***
Dermatology

Agenda- Focus on Morphology

- Dermatomyositis
  - Some new things to consider with a focus on morphology
- Cutaneous Lupus
  - Review, with a focus on systemic disease

Why Dermatomyositis?

Why Dermato?

-Frequent Diagnostic Delay

-Clinical Variability

-New information emerging diagnostically

-Derms are often on the cutting edge of this- and can serve as liaisons to medical community and advocates for our patients

Morphology

Morphology

- Classic cutaneous findings of DM
  - Pruritic, erythematous scalp
  - Heliotrope sign
  - Poikiloderma
    - Shawl Sign
    - Holster Sign
  - Gottron's sign
  - Gottron's papules
  - Nailfold changes

Photo credit American College of Rheumatology

Morphology

What's New?

Antibodies in DM

- Serologies can also be of some help and come in two categories
  - Non-specific- ANA is elevated in up to 80% of patients
    - Anti-synthetase antibodies are directed against cytoplasmic antigens- <u>so ANA may be negative</u>
  - Myositis-specific antibodies (MSA)
    - <u>Found in idiopathic inflammatory myopathies</u>

Callen JP. The Lancet 2002; 355: 53-57. Dermatomyositis.

A note on MSA's

- Which ones do we discuss?

- A few varied clinical findings related to these MSA's and their underlying systemic associations

MSA's

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MyoMarker Panel 3

MAYO CLINIC LABORATORIES

Reference Values

PL-7, PL-12, EJ, OJ, SRP, MI-2, Fibrillarin (U3 RNP), U2 snRNP, Ku:

Reference Range: Negative

Anti-Jo-1 Ab, TIF1 GAMMA (P155/140), MDA-5 (P140) (CADM-140), NXP-2 (P140), Anti-PM/Scl-100 Ab, Anti-U1-RNP Ab, Anti-SS-A 52 kD Ab IgG:

Reference Range: <20

EIA Interpretation:

Negative:	<20 units
Weak Positive:	20 – 39 units
Moderate Positive:	40 – 80 units
Strong Positive:	>80 units

Myositis Specific 11 Antibodies Panel

Quest Diagnostics

Test Details

Includes

Jo-1 Ab, PL-7 Ab, PL-12 Ab, EJ Ab, OJ Ab, SRP Ab, Mi-2 Alpha Ab, Mi-2 Alpha Ab, Ab, TIF-1y Ab, NXP-2 Ab

Methodology

Line Blot

Assay Category

These tests were developed and their analytical performance characteristics ha by Quest Diagnostics. They have not been cleared or approved by the FDA. These validated pursuant to the CLIA regulations and are used for clinical purposes.

MSA's

- DM- specific MSA's most referenced in dermatology literature
  - Anti-
    - *TIF1 (transcription intermediary factor 1)
    - *Mi-2- anti helicase
    - *MDA5 (melanoma differentiation associated protein 5)
    - NXP2 (nuclear matrix protein 2)- adults cancer, juvenile DM calcinosis
    - SRP- cardiac involvement, poor prognosis
    - Anti-synthetase syndrome- Jo1, PL7, PL12, EJ/OJ- mechanics hands, raynauds, severe ILD
    - SAE (small ubiquitin-like modifier activating enzyme)

Dewane ME, Waldman R, Lu J. Dermatomyositis: Clinical features and pathogensesis. JAAD Feb 2020, 267-281

MSA's

- Caution
  - A "serologic gap" still exists (20-50% of DM patients positive)
  - Available tests vary in their sensitivity and specificity
  - Immunoprecipitation assay is the gold standard, not widely available and lacks standardization

**Now back to morphology and how it can tip us off to MSA's*

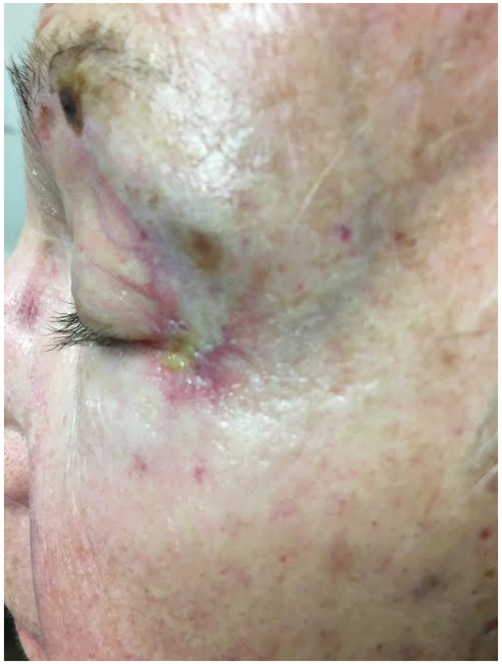
Ravishankar A et al. Accuracy of Commercial Panels to Evaluate Myositis Autoantibodies: A Single Institution Perspective, JAAD (2020).

Dewane ME, Waldman R, Lu J. Dermatomyositis: Clinical features and pathogensesis. JAAD Feb 2020, 267-281

TIF1- morphology

- Severe photosensitive cutaneous disease with heliotrope
- <u>Ovoid palatal patches</u>
- Atrophic hypopigmented patches with overlying telangiectasia
- Palmar hyperkeratosis/psoriasiform plaques

Image Bernet, Fiorintino JAMA Dermatol. Sept 2016



Dewane ME, Waldman R, Lu J. Dermatomyositis: Clinical features and pathogensesis. JAAD Feb 2020, 267-281

TIF1

- Approximately 20% all DM patients
- Hypomyopathic
- GI involvement
- *think cancer (tumor reports in the literature 20-65%)
- TIF1 tumor suppressor gene, antibodies may be generated during anti-tumor immune response

Fiorintino D, Casciola-Rosen L. TIF1 autoantibodies in dermatomyositis shed insight into the cancer-myositis connection. Arthritis Rheum. 2012 Feb; 64(2):348-49.

PNP DM- Beyond TIF

- Malignancy (paraneoplastic phenomenon)
  - Increased risk men, older patients (not pediatric), dysphagia, cutaneous ulcerations, anti-TIF gamma
  - Ovarian and GI over represented *
  - Increased risk for 3 years after symptoms develop then return to age adjusted risk/screening
  - Certain phenotypes/autoantibodies considered higher risk- but ALL adults should be screened

Oldroyd, Aggarwal. A systematic review and meta-analysis to inform cancer screening guidelines in inflammatory myopathies. Rheumatology 2021

Mi-2- Morphology

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- Classic DM findings

- Especially facial dermatosis, shawl sign, poikiloderma and flagellate erythema

Dewane ME, Waldman R, Lu J. Dermatomyositis: Clinical features and pathogensesis. JAAD Feb 2020, 267-281

Mi-2

- 4-35%
- Mild myopathic disease, lower associations with cancer or ILD
- Amendable to therapy but can relapse

Dewane ME, Waldman R, Lu J. Dermatomyositis: Clinical features and pathogensesis. JAAD Feb 2020, 267-281

MDA5 *Dermatomyositis*

MDA5 Morphology

Cutaneous patterns vary - can include *classic DM findings*, but also have more atypical patterns that have been noted

Dewane ME, Waldman R, Lu J. Dermatomyositis: Clinical features and pathogensesis. JAAD Feb 2020, 267-281

MDA5 Cutaneous Ulcerations

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- Typical Areas of Ulcerations
  - Lateral nail folds
  - Elbows
  - Gottron papules

MDA5 Painful Palmar Erythematous Papules

- Histology
  - Vasculopathy
  - fibrin deposition
  - Variable perivascular inflammation

Dewane ME, Waldman R, Lu J. Dermatomyositis: Clinical features and pathogensesis. JAAD Feb 2020, 267-281

MDA5 Clinical Patterns

- Also noted
  - Alopecia
  - Painful oral erosions/tender gums
  - Gottron's sign

J Am Acad Dermatol. 2011 July ; 65(1): 25–34. doi:10.1016/j.jaad.2010.09.016.

MDA5

- MDA5
  - 10-30%
  - *Amyopathic or myopathic
  - *Not* paraneoplastic
  - *Rapidly progressive interstitial lung disease
    - 43% incidence RPILD recent US cohort
    - Onset typically within 6 months of presentation
  - Acute pulmonary predominant presentation can mimic other causes of acute pneumonitis (infectious, drug induced)

Lin R, Warp P et al. Assessing Time of Onset for ILD in Anti-MDA5 Antibody-Positve DM. JAMA Dermatol. May 2024.

Dewane ME, Waldman R, Lu J. Dermatomyositis: Clinical features and pathogensesis. JAAD Feb 2020, 267-281

Anti–Melanoma Differentiation–Associated Gene 5 Is Associated With Rapidly Progressive Lung Disease and Poor Survival in US Patients With Amyopathic and Myopathic Dermatomyositis

SIAMAK MOGHADAM-KIA, MD[1], CHESTER V. ODDIS, MD[1], SHINJI SATO, MD[2], MASATAKA KUWANA, MD[3], and ROHIT AGGARWAL, MD, MSc[1]

- 61 cases of classic (Dermatomyositis) DM and Clinically Amyopathic (CADM) case controlled by age and gender
- Rates of ILD
  - DM 26.2%
  - CADM 31.1%
- Rates of RPILD
  - DM 5%
  - CADM 8.2%
- Rates of MDA5 positivity
  - DM 13.1%
  - CADM 13.1%

No **clinically relevant** difference in rates of ILD, RPILD or MDA5 positivity in DM vs. CADM

Arthritis Care Res (Hoboken). 2016 May ; 68(5): 689–694. doi:10.1002/acr.22728.

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- Rates of ILD p 0.04
  - MDA5 + 50% (8 of 16)
  - MDA5 - 25.5% (27 of 106)

- Rates of RPILD significantly associated with MDA5+ 0.001%
  - MDA5+

Arthritis Care Res (Hoboken). 2016 May ; 68(5): 689–694. doi:10.1002/acr.22728.

Unique characteristics of anti-MDA-5 associated dermatomyositis in Southern California with a large Hispanic population

Eaman Alhassan [a,#,*], Belina Y. Yi [b,c,#], Jack Rodman [d], Michael H Weisman [e], Ashley Crew [f], Leanna Wise [a]

- 30 MDA-5 patients 4 Southern CA instsitutions
- 73% Hispanic
- ILD most common non myositis systemic manifestation, 5 deaths from RPILD
- Hispanic patients diagnosed at a younger age than non Hispanic patients
- All male patients inflammatory arthritis

Alhassan E, Wise L et al Sem in Arthritis and Rheumatism. March 2024.

MDA5

- Consider MDA5 Dermatomyositis
  - Painful erythematous palmar papules
  - Ulcerations
  - Rapidly Progressive Interstitial Lung Disease

- When you are concerned consider
  - **<u>Expedited referral to rheumatology</u>**
    - Rapid Pulmonary Screening
    - Close clinical monitoring, aggressive therapy

Summary

- Serologies for dermatomyositis can be non specific (ie ANA) and specific (MSA's)
- Certain <u>morphological findings</u> can raise your suspicion for a serologic subtype of dermatomyositis
- These clinical and serologic subtypes can be associated with higher risk of underlying complications and can aide in guiding subsequent workup

Cutaneous Lupus

Why Does It Matter

-As dermatologists, we need to be prepared to diagnose and treat cutaneous lupus

-We serve as the expert on this

-A part of this expertise is knowing when to be concerned about underlying systemic disease

CLE or CL+ SLE

- Cutaneous lupus 2-3 x as common as SLE
- Most cases will be just CLE- but we need to be prepared to flag when it is "more"

Brief Review- Lupus Specific

- Acute Cutaneous Lupus (ACL)
- Subacute Cutaneous Lupus (SCLE)
- Chronic Cutaneous Lupus (CCLE)
  - -DLE*
  - -Lupus panniculitis*
  - -Lupus erythematosus tumidus (LET)
  - -Chilblain lupus
- Other
  - -Bullous Lupus

You’re considering cutaneous lupus?

-Pause!

Does this patient have Systemic LE?

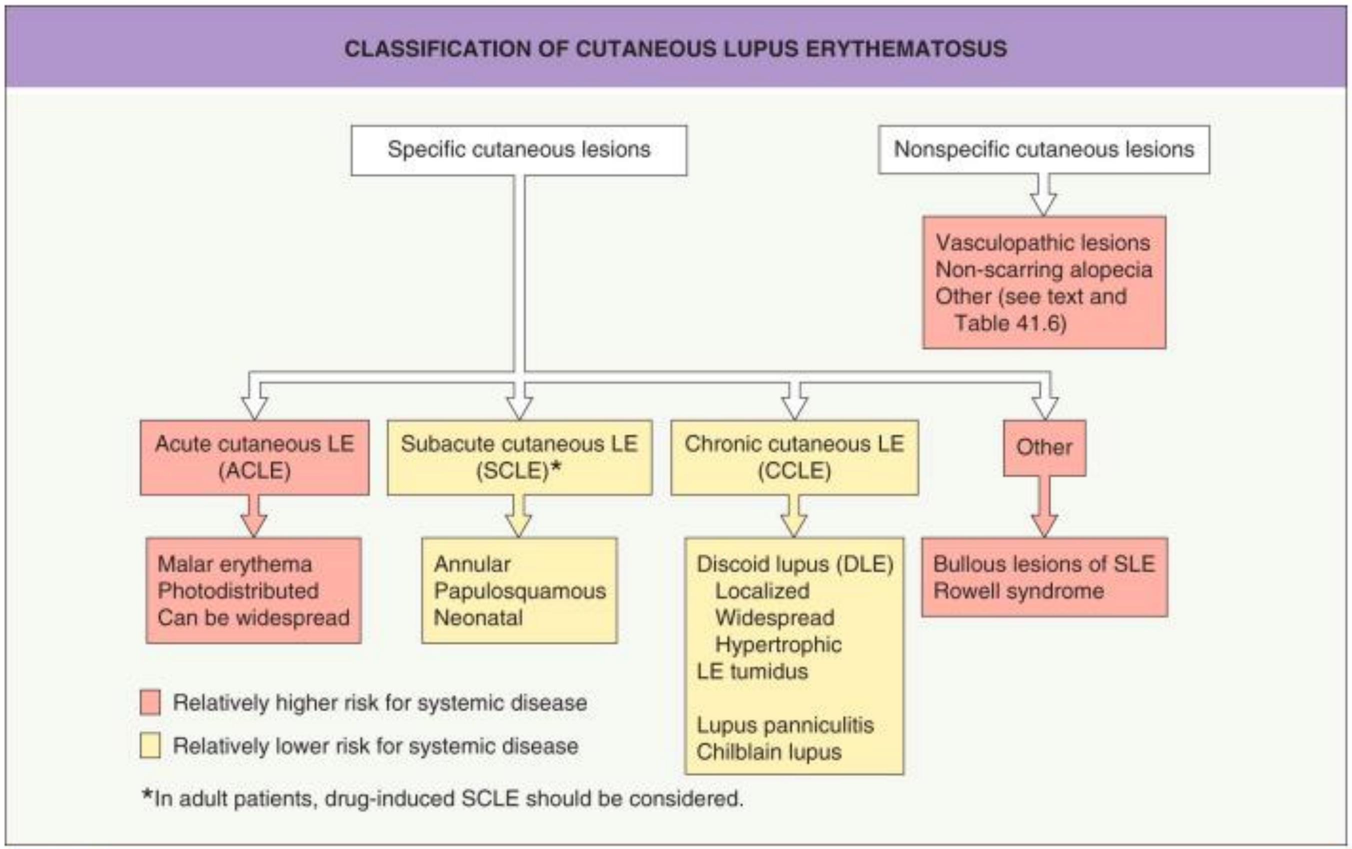


Fig. 41.2

Lee LA, Werth V. Dermatology. Dec 31, 2017. 662-680

SLE Diagnostic Criteria

4 needed for diagnosis, serially or simultaneously

1. Malar erythema
2. Discoid LE
3. Serositis (pleuritis or pericarditis)
4. Oral ulcers
5. Arthritis
6. Photosensitivity
7. Blood (hematologic) disorder (hemolytic anemia, leukopenia, lymphopenia, thrombocytopenia)
8. Renal (proteinuria or cellular casts)
9. ANA+
10. Immunologic disorder, anti ds-DNA/Smith, false positive STS (serologic test for syphilis), antiphospholipid
11. Neurologic disorder (unexplained seizures or psychosis)

SLICC Criteria

4 needed for diagnosis, at least one clinical and one immunologic OR Lupus Nephritis with ANA/dsDNA

Clinical criteria:

1. Acute cutaneous lupus
2. Chronic cutaneous lupus
3. Oral ulcers: palate
4. Nonscarring alopecia
5. Synovitis 2>joints
6. Serositis
7. Renal
8. Neurologic
9. Hemolytic anemia
10. Leukopenia
11. Thrombocytopenia

Immunologic criteria:

1. ANA
2. Anti-dsDNA
3. Anti-Smith
4. Antiphospholipid antibody
5. Low complement
6. Direct Coombs in the absence of hemolytic anemia

Morphology Review

Acute Cutaneous Lupus

Malar distribution

Can be widespread

Photo-exacerbated

Spares IP joints

ANA + , dsDNA, Sm

Flares correlate with systemic disease

Associated Alopecia (non scarring)

Associated leukocytoclastic vasculitis

Almost always associated with SLE

Bullous Lupus

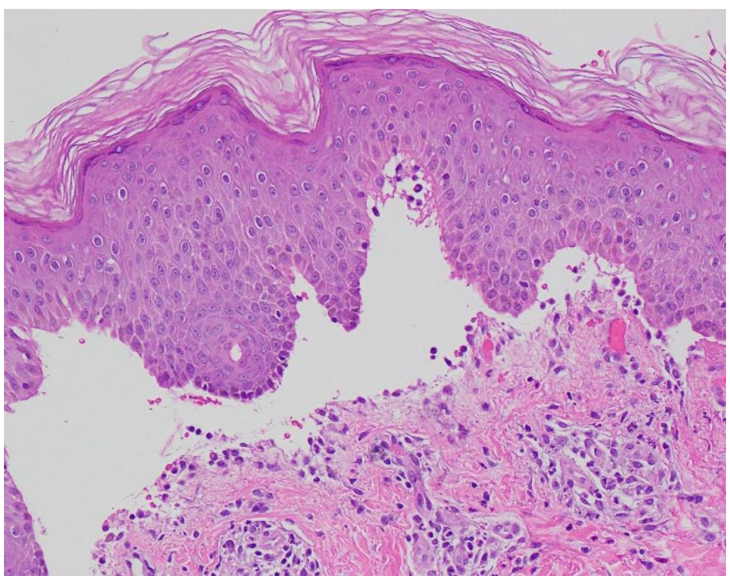
Tense vesiculobullous lesions

Autoantibodies to type VII collagen

Reported as presenting symptom in pediatric patients**

Flares do not always corelated with systemic disease

Very strong association with SLE



Subacute Cutaneous Lupus (SCLE)

Papulosquamous/Annular

Photosensitive but <u>spares central face</u>

Frequently triggered by a medication (>1/3)

Dyspigmentation

SSA + (70%), ANA (70-80%)

<u>Association with SLE = 30-50%</u>

Typically more mild- arthritis and myalgias

L.G. Okon, V.P. Werth / Best Practice & Research Clinical Rheumatology 27 (2013) 391–404

Discoid Lupus

Frequent skin manifestation of lupus

Head and Neck

Photosensitive +/-

Pigmentary alteration, scaling

Scarring Alopecia

<u>If initially SLE negative- may go on to develop SLE = 5-20%</u>

Risk of conversion may be higher if patients have associated high titer ANA and widespread disease

Lupus Panniculitis

Tender subcutaneous nodules

May be associated w overlying DLE (profundus)

Face, upper arms/legs, breasts

Heals with atrophy

Must be distinguished from Subcutaneous Panniculitis-like T Cell Lymphoma (SPTCL)

<u>Association with SLE = 5-20%</u>

CLE = SLE?

-Considering cutaneous lupus?

-Identify suspected subtype
- -Acute cutaneous lupus
- -SCLE
- -Chronic cutaneous LE

-Know pre-test probability

-Get to Work
- Full skin check
- Review of systems
- Biopsy
- Labs/referral
- Education
- Monitoring

Cutaneous Lupus AI Associations

University of Southern California

-If patients don't meet criteria for SLE- do we need to worry about other AI conditions?

-Yes!

-17.8% of CLE only patients had at least 1 co-existing autoimmune condition

-4 fold higher than general population

- AI thyroid disease most commonly reported

Kunzer E, Chong B et al. Autoimmune Diseases in Patients With Cutaneous Lupus Erythematosus. JAMA Dermatol. 2018; 154(6):712-716

Last, But Not Least

All that Glitters Isn't Gold

-Once a patient has been diagnosed with CTD, impulse is to attribute all skin findings to this disease

-Remember- **common things** still happen in this patient population

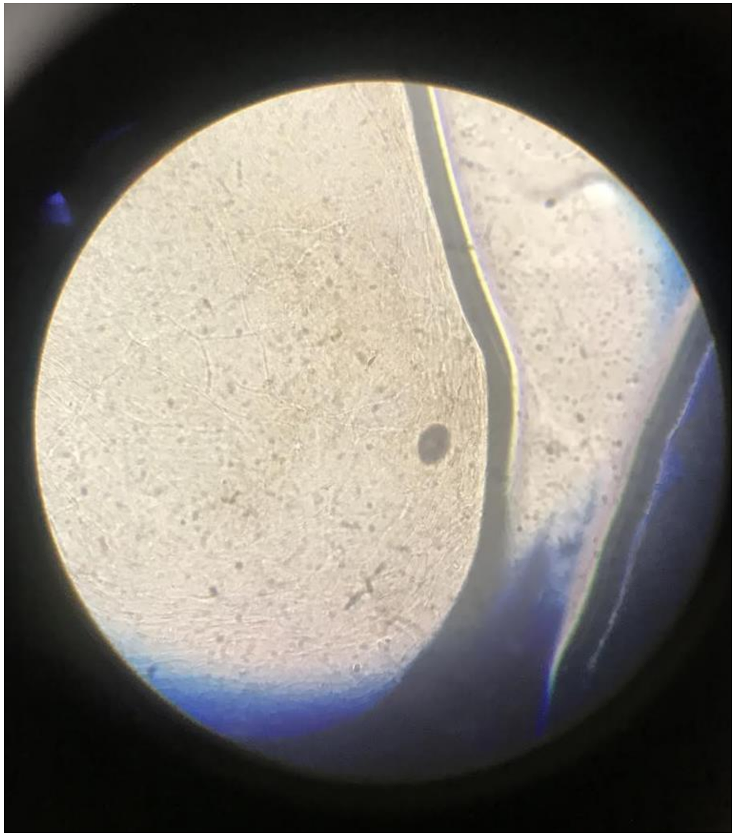
-As derms, we can help distinguish what is what, and **avoid unnecessary or escalating systemics**

All that Glitters Isn't Gold

- 56 year old female with dermatomyositis- myositis well controlled but skin continues to flare despite steroids, mycophenolate mofetil, IVIG, tacrolimus

All that Glitters Isn't Gold

- 49 year old male, with psoriasis and psoriatic arthritis, referred for persistent psoriasis, concern that he has failed several classes of biologics



Thank you!

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Wieczorek I, Propert K, Okawa J, Werth V. Systemic Symptoms in the Progression of Cutaneous to Systemic Lupus Erythematosus. JAMA Dermatol. 2013, Published online January 29, 2014

Xu Y1, Yang CS2, Li YJ1, Liu XD1, Wang JN1, Zhao Q1, Xiao WG1, Yang PT3. Predictive factors of rapidly progressive-interstitial lung disease in patients with clinically amyopathic dermatomyositis. Clin Rheumatol. 2016 Jan;35(1):113-6. doi: 10.1007/s10067-015-3139-z. Epub 2015 Dec 10.

- Treatment notes CLE
- Some compact fluorescent bulbs emit more UVB than incandescent bulbs, and thus shielding of bulbs is important [53]. It is important to consider the risk of vitamin D deficiency in sun-avoiding patients, as sunlight is required for vitamin D synthesis. 25-Hydroxyvitamin D levels should be monitored and supplementation with at least 400 IU of vitamin D3, or cholecalciferol, is advised [54].