Reducing Placebo Response and Assessment Variability

March 2nd, 2024

Outline

- Why Are Placebo Responses and Assessment Variability so Important?
- Best Practices to Reduce Placebo Effects and Assessment Variability with the TIS
- Placebo Effect/Variability Case Studies
  - Potential Sources of Placebo Responses and Assessment Variability and What Can Be Done
  - Focus on High-quality Assessments

Why Are Placebo Responses and Assessment Errors So Important?

- **Placebo Effect:** (Latin: I will please) a beneficial effect produced by a placebo drug/treatment, which cannot be attributed to the properties of the placebo itself and must therefore be due to the patient's belief in that treatment

- **Placebo Response**: degree of clinical improvement reported in the placebo group; a major factor that can distort the measurement of net treatment effect in a randomized controlled trial; Colloca et al. 2019. It is a ***is a function of several factors***: the natural history of disease, regression to the mean, researcher bias, co-interventions, and the "placebo effect" itself (expectancy); Evans et al. 2021

  → In DM trials, these other factors beyond classic "placebo effect" may be even greater drivers of placebo response risk

- As the ***placebo response*** and/or ***assessment variability*** of the Total Improvement Score core set measures increase, it becomes more difficult for brepocitinib to demonstrate a net positive treatment effect in the Phase 3 DM registration study

- **Goal**: identify and decrease sources of *placebo responses and assessment errors/noise*

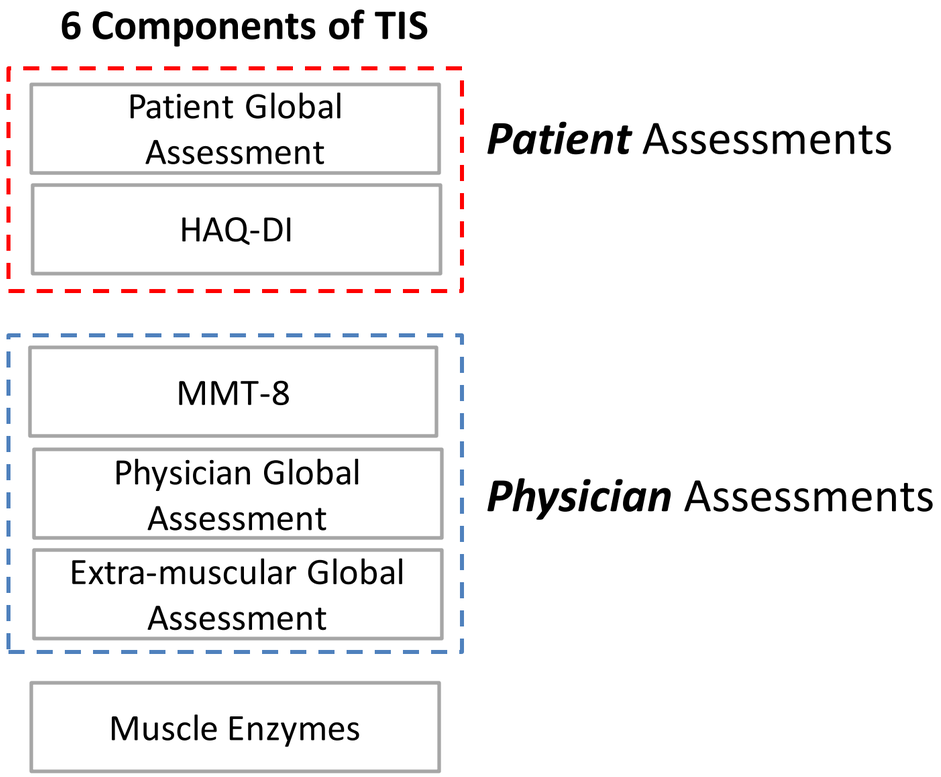
  → Important reminder: in therapeutic trials it is our job as clinical researchers to work to minimize placebo response (meaning some of our patients will not get better); this is different than ordinary clinical practice where placebo effect is a good thing if it leads patients to feel better

Placebo Response in DM Trials: IVIg Phase 3 DM Study

The Primary Endpoint (Total Improvement Score, TIS) is Susceptible to Placebo Effects and Measurement Errors

By Week 16 (Double-Blind Treatment Period)

- The placebo group achieved a *mean TIS = 21.6*
- *44%* of placebo patients achieved **mild improvement in TIS (≥ 20)**, the primary endpoint
- *23%* of placebo patients achieved a **moderate improvement in TIS (≥ 40)**
- Note: VALOR is a 52-week placebo-controlled trial, there is risk of placebo increasing further over time



Minimizing **placebo effects and doing high quality assessments** <u>**across these 5 components of the TIS is critical**</u> to demonstrate the treatment benefit vs placebo

Patient Assessments

Best Practices to *Decrease* Placebo Response and Assessment Variability

Issue	Best Practice
Patient incorporates factors other than myositis disease activity into their assessments	**Remind patient at each visit what these tools are intended to measure (myositis disease burden, not co-morbidities or side effects)**
Patient thinks they "should" be getting better because they are in a clinical trial	**Remind patients they may or may not be receiving an active drug. Openly talk about "the placebo effect" and how it can influence perception – empowers patients to evaluate their own symptoms and experiences more rigorously.**
Patient does not devote sufficient attention and introspection to assessments (e.g., "survey fatigue")	**Investigator or coordinator should take time to review VAS and HAQ before and after completion with the patient and ensure the patient understands how to complete them accurately to ensure high quality and no missing data.** **Communicate the importance of introspection (patient focuses/increases awareness of their own thoughts/feelings/ experiences) and understanding their symptom severity to generate high quality data for the trial.**

Physician Assessments

Best Practices to *Decrease* Placebo Response and Assessment Variability

Issue	Best Practice
Risk of bias around assessments at screening/baseline for borderline patients	**For patients with mild disease (skin and/or muscle), assess holistically whether patient has meaningful (even if mild), stable disease activity that corroborates the MMT-8 and CDASI scores** **For patients with severe muscle, assess holistically (beyond just MMT-8 score) whether patient suffers from excessive non-reversible muscle damage (e.g., via serum creatinine, MRI or other prior assessments in medical history)** **Scores at baseline should be assigned without regard for time invested in screening and preparation to randomize. Patient should screen fail on day of randomization if no longer meet eligibility criteria for disease activity**
Rushing due to busy schedules	**As physicians, we are all very busy, which can lead to mistakes due to lack of time. Make sure to allocate sufficient physician/rater time for each study visit. The rater performing global disease activity assessments must spend sufficient time holistically evaluating patient.**
Rater consistency	**As ratings have an element of subjectivity, raters for each patient should be kept consistent to the greatest extent possible; at a minimum, same individual should perform the baseline rating, primary endpoint rating, and majority of ratings in between**
When to look back at previous ratings	**Every assessment should be scored based on the day of visit. For MDAAT and PhysGA review previous visit for anchoring. PhGIC is compared to start of study.**

Natural Disease Course (Impacts All Assessments)

Best Practices to *Decrease* Placebo Response and Assessment Variability

Issue	Best Practice
Patient selection	**Avoid enrolling patients during self-limiting flares (may resolve post-baseline absent therapeutic intervention), particularly for more mild patients where degree of improvement is capped** **Avoid enrolling patients that have not achieved the full effect of concomitant drugs initiated or with dose changes near enrollment. Some immunosuppressive drugs (e.g., mycophenolate) do not reach full efficacy for up to 6 months. Muscle improvement in strength is slow and is typically weeks to months after controlling disease process.**
Steroid taper	**Steroid taper is critically important for keeping placebo response in check in a 52-week study; it is also valuable for demonstrating steroid-sparing benefit of brepocitinib – if patient is hesitant to taper, we must remind them of why it is important for the study and in their own interest given long-term side effects of chronic steroid use**
Prohibited medications	**Use of prohibited medications across the trial will decrease the ability to demonstrate a drug treatment effect** **Ask patients about medications being taken at home at every visit. Remind patients that they should not use additional dermatomyositis medication they have at home (including topical OTC). If these are needed, patients should reach out to the site In addition to common DM meds, initiation of chronic NSAIDs, topicals and opioids are prohibited per protocol.** **If an acute event requires short-term treatment, please consult with medical monitor in advance and ensure the medication is stopped as soon as possible.**
Exercise regimen stability	**Ask about and document any exercise regimen at the start of the study. Remind patient at each visit to maintain same exercise regimen that was in place prior to randomization, and to avoid strenuous activities outside their normal routine during the week prior to each visit. Document any changes to exercise regimen that occur.**

CASE 1

A Complex Case of Progressive Muscle Weakness

DERMATOMYOSITIS

Patient Initial Presentation

Patient Background

- **46-year-old Caucasian female**
- Complaints: Fatigue, progressive muscle weakness in proximal extremities (primarily in the arms and thighs)
- Duration: Past 4 weeks
- She felt tired and found it challenging to go about routine activities in the last few weeks.
- However, she did not report fever or weight loss.
- The weakness was profound and lately had increased to such an extent that she needed help for bathing and toileting.

Patient Initial Presentation

Patient Background

- **Additional Symptoms:**
- She recently noticed a slight change in her voice and mild dysphagia with solid foods.
- She also complained of worsening dyspnea on exertion and non-productive cough for the last two weeks, but not requiring supplementary oxygen.
- She denies any joint pain or swelling but has mild myalgias.
- She has developed several rashes in last 2-3 weeks.
- **Review of System:** She did not report Raynaud's, joint pain, and gastrointestinal symptoms; otherwise, the rest of the review of system was unrevealing.

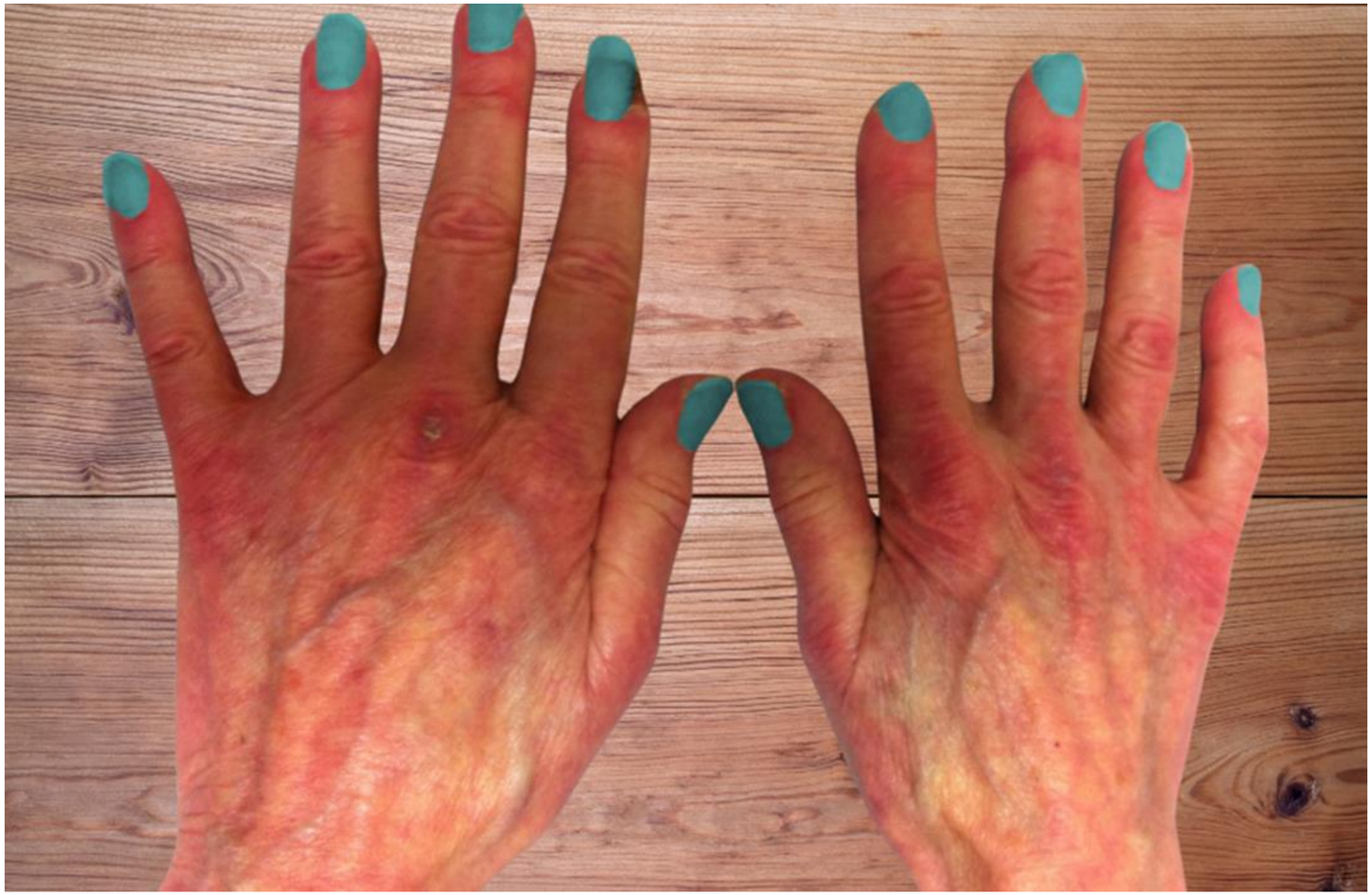
Physical Examination

Initial

- Rashes developed over 2-3 weeks
- Erythematous red papules with ulcer on the dorsum surface of the hands.
- Mild to moderate red rash on the upper chest, upper back
- Mild pink rash over both elbows with scales and a small area of redness
- Periungal erythema was observed with abnormal nail fold capillaries
- Rest of the body areas were free of rashes and there is no hair loss

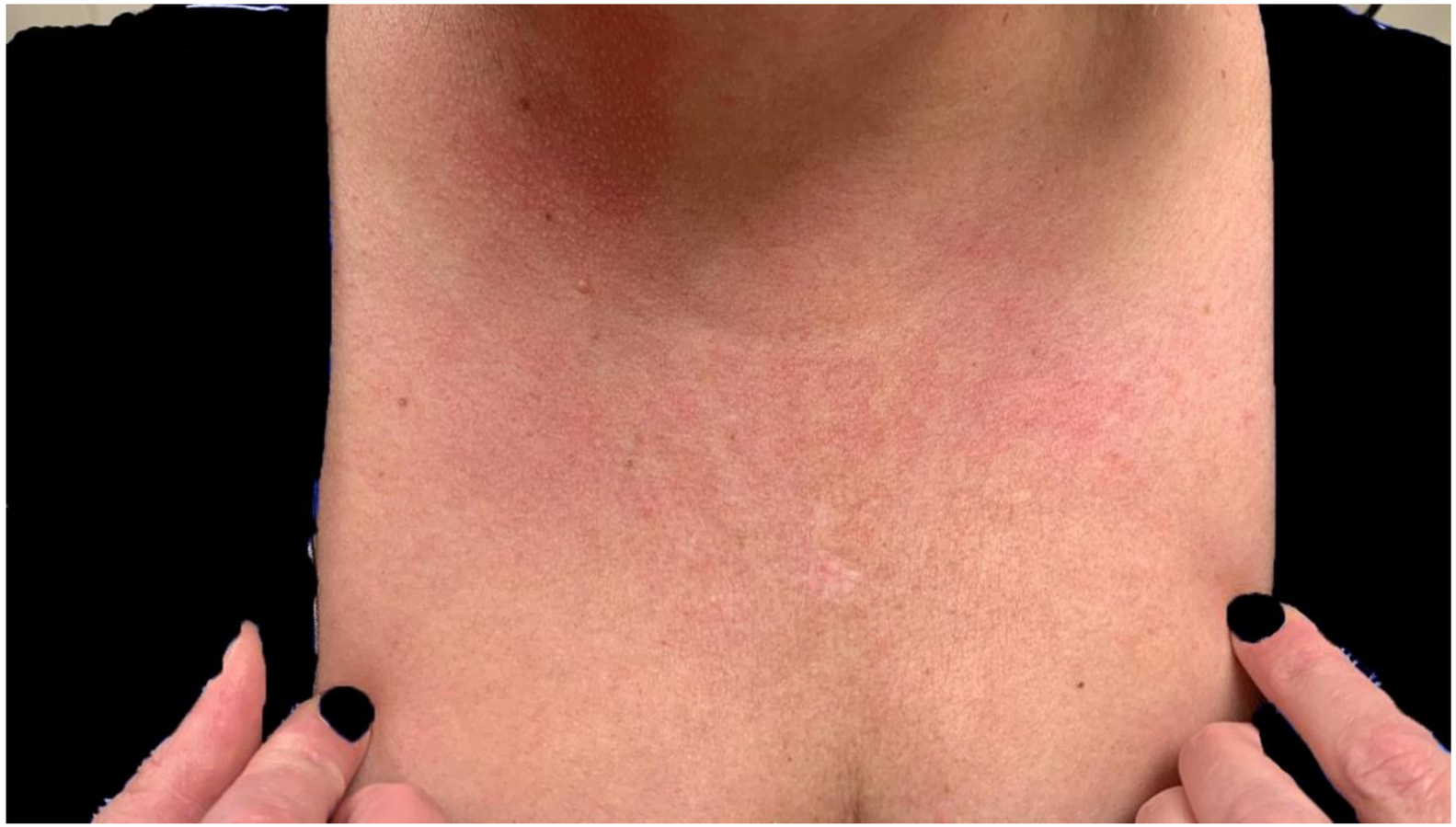
Case 1 Initial: Rash Images of Patient

Dorsum of Hand



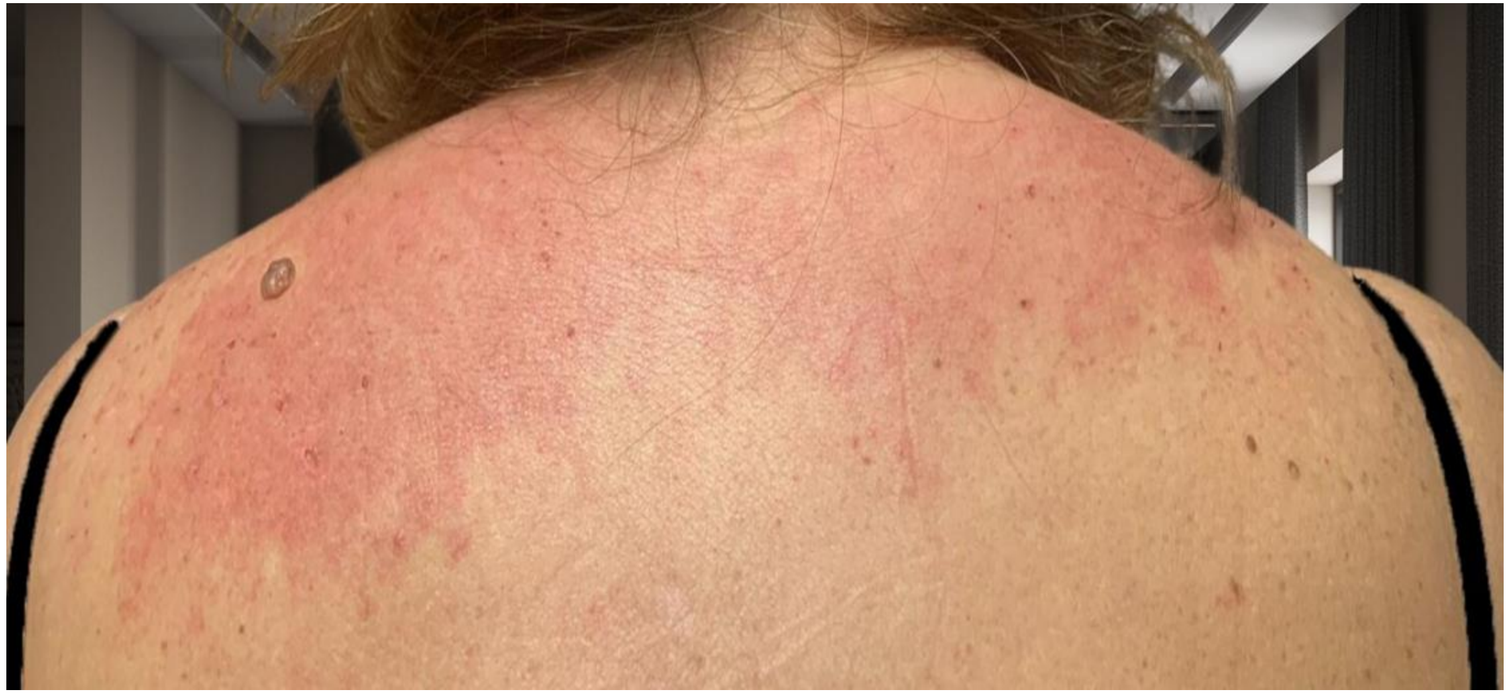
Case 1 Initial: Rash Images of Patient

Upper Chest (V area of neck)



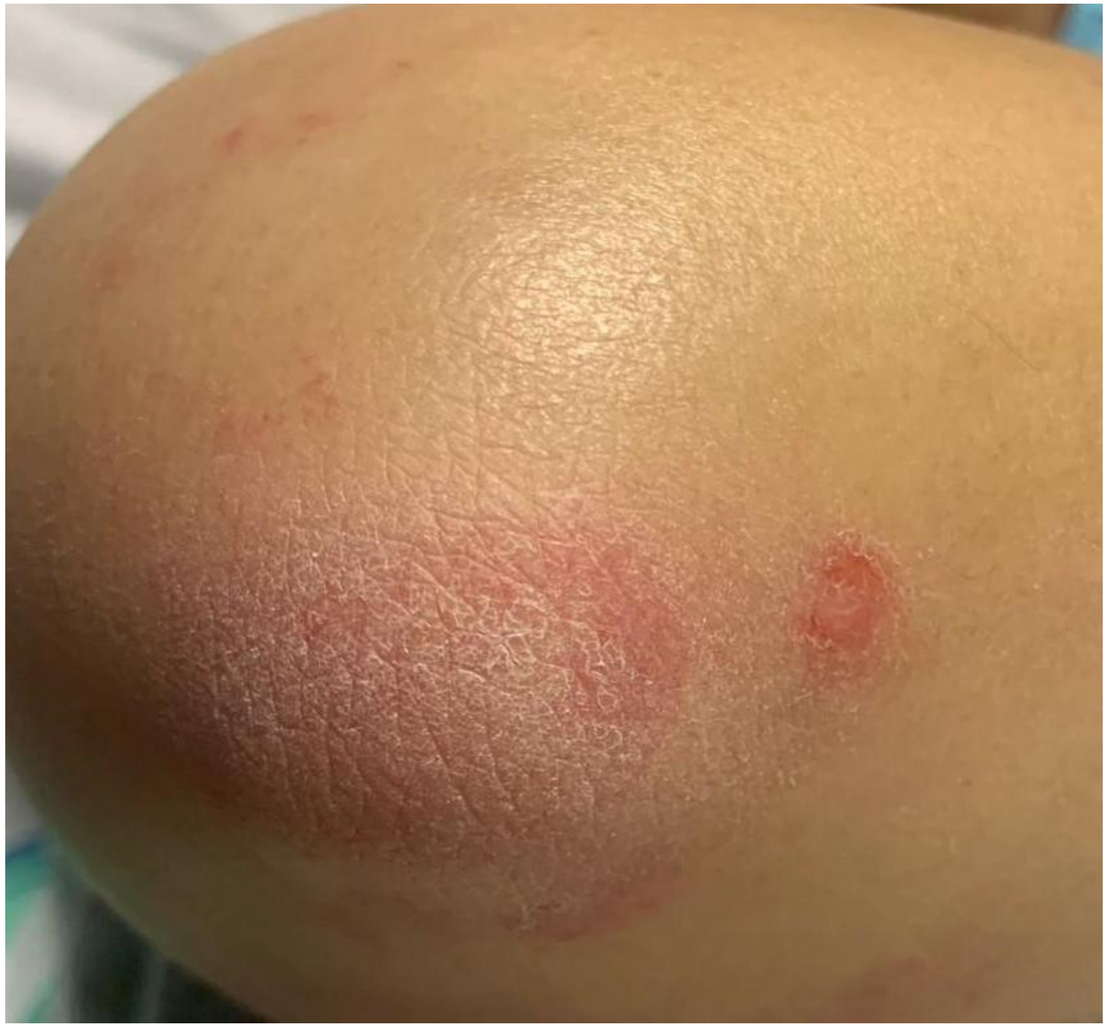
Case 1 Initial: Rash Images of Patient

Posterior Neck and upper back and shoulder



Case 1 Initial: Rash Images of Patient

Elbow



Case 1 Initial: Rash Images of Patient

Periungal rash

Case Study Questions

Investigators: please scan the QR code to access the presentation questions

https://www.surveymonkey.com/r/39TSJ82

Case 1 Initial Scoring

Myositis Disease Activity Assessment Tool MDAAT

Cutaneous Disease Activity	**(Absent)** ——— **(Maximum)** __ __ . __ cm __ __ . __ cm	**Examples of maximal score** - Ulceration to muscle, tendon or bone; - Extensive erythroderma

7. Erythematous rashes:

a. **with** secondary changes (e.g. accompanied by erosions, vesiculobullous change or necrosis)	0	1	2	3	4	NA
b. **without** secondary changes	0	1	2	3	4	NA

Q 1. Based on the patient presentation specifically rashes, what should be the Cutaneous Disease Activity (0-10 cm VAS) and score for 7 a/b.

a. 4 cm (VAS) and 4 for 7a
b. 2 cm (VAS) and 4 for 7a
c. 6 cm (VAS) and 3 for 7b
d. 4 cm (VAS) and 4 for 7b
e. 2 cm (VAS) and 4 for 7b

Case 1 Initial Scoring

Myositis Disease Activity Assessment Tool MDAAT

Cutaneous Disease Activity	**(Absent)** ——— **(Maximum)** __ __ . __ cm __ __ . __ cm	**Examples of maximal score** - Ulceration to muscle, tendon or bone; - Extensive erythroderma

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Q 1. Based on the patient presentation specifically rashes, what should be the Cutaneous Disease Activity (0-10 cm VAS) and score for 7 a/b.

a. 4 cm (VAS) and 4 for 7a
b. 2 cm (VAS) and 4 for 7a
c. 6 cm (VAS) and 3 for 7b
d. 4 cm (VAS) and 4 for 7b
e. 2 cm (VAS) and 4 for 7b

Physical Examination

MMT-8

- Profound proximal bilateral symmetric muscle weakness with the patient:
- She had full range of motion against the gravity in deltoid and iliopsoas but unable to sustain (hold) it beyond 2-3 seconds bilaterally
- Able to hold against only mild pressure by the examiner in gluteus medius and maximus bilaterally
- Able to hold against only mild to moderate pressure in neck flexor
- Able to moderate to strong pressure in neck extensors, biceps, triceps, quadriceps and hamstring bilaterally
- The rest of the muscle showed no significant abnormalities

Case 1 Initial Scoring

MMT-8

Q 2. Based on the patient presentation specifically manual muscle testing, what should be the score for bilateral deltoid on Kendall scale (0-10)

a. 2
b. 3
c. 4
d. 5
e. 6

Case 1 Initial Scoring

MMT-8

Q 2. Based on the patient presentation specifically manual muscle testing, what should be the score for bilateral deltoid on Kendall scale (0-10)

a. 2
b. 3
c. 4
d. 5
e. 6

MMT-8 grading using Kendall scale (0-10)

	Function of the muscle	Grade	
		Kendall	MRC
No Movement	No contractions felt in the muscle	0	0
	Tendon becomes prominent or feeble contractions felt but no visible movement	T=Trace (score as 0)	1
Test Movement	Gravity Eliminated (Movement in horizontal plane)		
	Moves through partial range of motion	1	2-
	Moves through complete range of motion	2	2
	Anti-Gravity Position		
	Moves through partial range of motion	3	2+
Test holding of Position	Gradual release from test position	4	3-
	Holds test position (no added pressure)	5	3
	Hold test position against slight pressure	6	3+
	Holds test position against slight to moderate pressure	7	4-
	Holds test position against moderate pressure	8	4
	Holds test position against moderate to strong pressure	9	4+
	Holds test position against strong pressure	10	5

Investigators can use MRC scale (0-5) to evaluate patient and then convert it to Kendall (0-10) scale for scoring/recording.

Reference: Florence P. Kendall et al. 1993

MRC, Aids to examination of peripheral nervous systems 1976

Manual Muscle Testing-8 (MMT-8)

Muscle Groups	Right (0-10)	Left (0-10)	Axial (0-10)
Axial Muscle			
Neck flexor	X	X	7
Proximal Muscles			
Deltoid	4	4	X
Biceps	9	9	X
Gluteus Medius	6	6	X
Gluteus Maximus	6	6	X
Quadriceps	9	9	X
Distal Muscles			
Wrist extensor	10	10	X
Ankle dorsiflexion	10	10	X
Total Score	0-54	0-54	0-7

MMT-8 score = 115/ 150

Physical Examination

Other

- There was a bilateral late inspiratory crackle sound in the lung bases upon auscultation.
- No other significant findings on examination.

Laboratory and Imaging Findings

Diagnostic Findings

- Laboratory Investigations showed elevated CK (900 IU/L) and ferritin (1010 mcg/L).
- HRCT of the chest was suggestive of Interstitial Lung Disease (ILD) with bi-basal ground-glass opacities and linear reticulations suggestive of moderate Non-Specific Interstitial Pneumonia (NSIP) involving 25-50% of the lung fields scanned.
- EMG also showed evidence of myopathy; however, a muscle biopsy was not performed.

Case 1 Initial Scoring

Myositis Disease Activity Assessment Tool (MDAAT)

Pulmonary Disease Activity	(Absent) ——— (Maximum) __ __ . __ cm __ __ . __ cm	Examples of maximal score: Active interstitial lung disease or respiratory muscle weakness requiring ventilatory support					
17. Respiratory muscle weakness **without** interstitial lung disease (ILD):							
a. Dyspnea at rest		0	1	2	3	4	NA
b. Dyspnea on exertion		0	1	2	3	4	NA
18. **Active reversible ILD** (i.e. not just ventilatory abnormalities due to pulmonary fibrosis): *Read glossary for scoring pulmonary function tests and score each item below (a,b and c).*							
a. Dyspnea or cough due to ILD		0	1	2	3	4	NA
b. Parenchymal abnormalities on chest x-ray or high resolution CT scan (HRCT) and/or ground glass shadowing on HRCT		0	1	2	3	4	NA
c. Pulmonary Function Tests: ≥ 10% change in FVC or DLCO		0	1	2	3	4	NA

Q 3. Based on the patient presentation specifically lung findings, what should be the score for 17 b (dyspnea on exertion) and 18 a (Dyspnea or cough due to ILD)

a. 0 and 4
b. 0 and 3
c. 4 and 4
d. 3 and 0
e. 4 and 0

Case 1 Initial Scoring

Myositis Disease Activity Assessment Tool (MDAAT)

Pulmonary Disease Activity	(Absent) ——— (Maximum) __ __ . __ cm __ __ . __ cm	Examples of maximal score: Active interstitial lung disease or respiratory muscle weakness requiring ventilatory support					
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b. Parenchymal abnormalities on chest x-ray or high resolution CT scan (HRCT) and/or ground glass shadowing on HRCT		0	1	2	3	4	NA
c. Pulmonary Function Tests: ≥ 10% change in FVC or DLCO		0	1	2	3	4	NA

Q 3. Based on the patient presentation specifically lung findings, what should be the score for 17 b (dyspnea on exertion) and 18 a (Dyspnea or cough due to ILD)

a. 0 and 4

b. 0 and 3

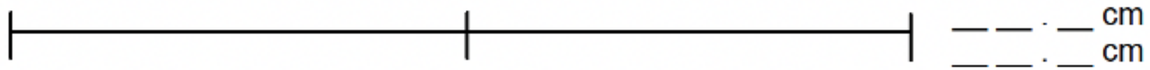
c. 4 and 4

d. 3 and 0

e. 4 and 0

Case 1 Initial Scoring

Myositis Disease Activity Assessment Tool (MDAAT)

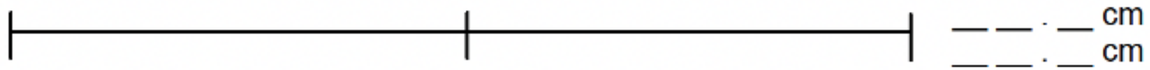
Extramuscular Global Assessment [Core Set Measure for RIM Study]	**(Absent)** **(Maximum)**  __ __ . __ cm __ __ . __ cm	Overall evaluation for disease activity in all extramuscular systems **(EXCLUDING MUSCLE DISEASE ACTIVITY)**

Q 4. Based on the patient presentation, what should be the score for Extra-muscular global disease activity ?

a. 2
b. 3
c. 4.5
d. 7
e. 8

Case 1 Initial Scoring

Myositis Disease Activity Assessment Tool (MDAAT)

Extramuscular Global Assessment [Core Set Measure for RIM Study]	**(Absent)** **(Maximum)**  __ __ . __ cm __ __ . __ cm	Overall evaluation for disease activity in all extramuscular systems **(EXCLUDING MUSCLE DISEASE ACTIVITY)**

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b. 3
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e. 8

Case 1 Initial Scoring

Myositis Disease Activity Assessment Tool (MDAAT)

Global Disease Activity	**(Absent)** **(Maximum)**  __ __ . __ cm __ __ . __ cm	Overall evaluation for the disease activity in ALL systems including muscle

Q 5. Based on the patient presentation, what should be the score for global disease activity ?

a. 3
b. 10
c. 5
d. 6
e. 7

Case 1 Initial Scoring

Myositis Disease Activity Assessment Tool (MDAAT)

Global Disease Activity	**(Absent)** — **(Maximum)**  __ __ . __ cm __ __ . __ cm	Overall evaluation for the disease activity in ALL systems including muscle

Q 5. Based on the patient presentation, what should be the score for global disease activity ?

a. 3
b. 10
c. 5
d. 6
e. 7

Case 1 Initial Scoring

Physician Global Disease Activity

Disease Activity is defined as potentially reversible pathology or physiology resulting from the myositis. Clinical findings known or suspected to be due to another disease process should not be considered in this evaluation. The global assessment of disease activity is to be judged from all the information available to you today including the subject's appearance, history, physical examination, diagnostic laboratory testing and your resultant medical therapy.

Please rate your global (overall) disease activity assessment by drawing a vertical mark on the 10-cm line below according to the following scale:

- left end of line = no evidence of disease activity,
- midpoint of line = moderate disease activity, and
- right end of line = extremely active or severe disease activity.

No evidence of disease activity

Extremely active or severe disease activity

Q 6. Based on the patient presentation, what should be the score for global disease activity ?

a. 3
b. 7
c. 5
d. 6
e. 10

Case 1 Initial Scoring

Physician Global Disease Activity

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No evidence of disease activity

Extremely active or severe disease activity

Q 6. Based on the patient presentation, what should be the score for global disease activity ?

a. 3
b. 7
c. 5
d. 6
e. 10

Diagnosis and Treatment

Diagnostic Findings

- The patient tested positive for anti-MDA5 antibodies.
- Therefore, cyclosporine, mycophenolate, and steroids were commenced for rapidly progressive ILD.

Follow-Up Visit (1 Month)

One Month Follow-Up and Management

- She was followed up after 1 month and had moderate improvement in her muscle weakness.
- MMT-8 improved a lot, as well as her myalgia, and fatigue.
- She is able to carry out her daily activities with minimal support; however, her dyspnea and cough remained the same.
- Dysphonia and dysphagia have improved but yet not completely normal.
- Cutaneous rashes have started to heal but were still bothersome.
- She has no other new complaints.

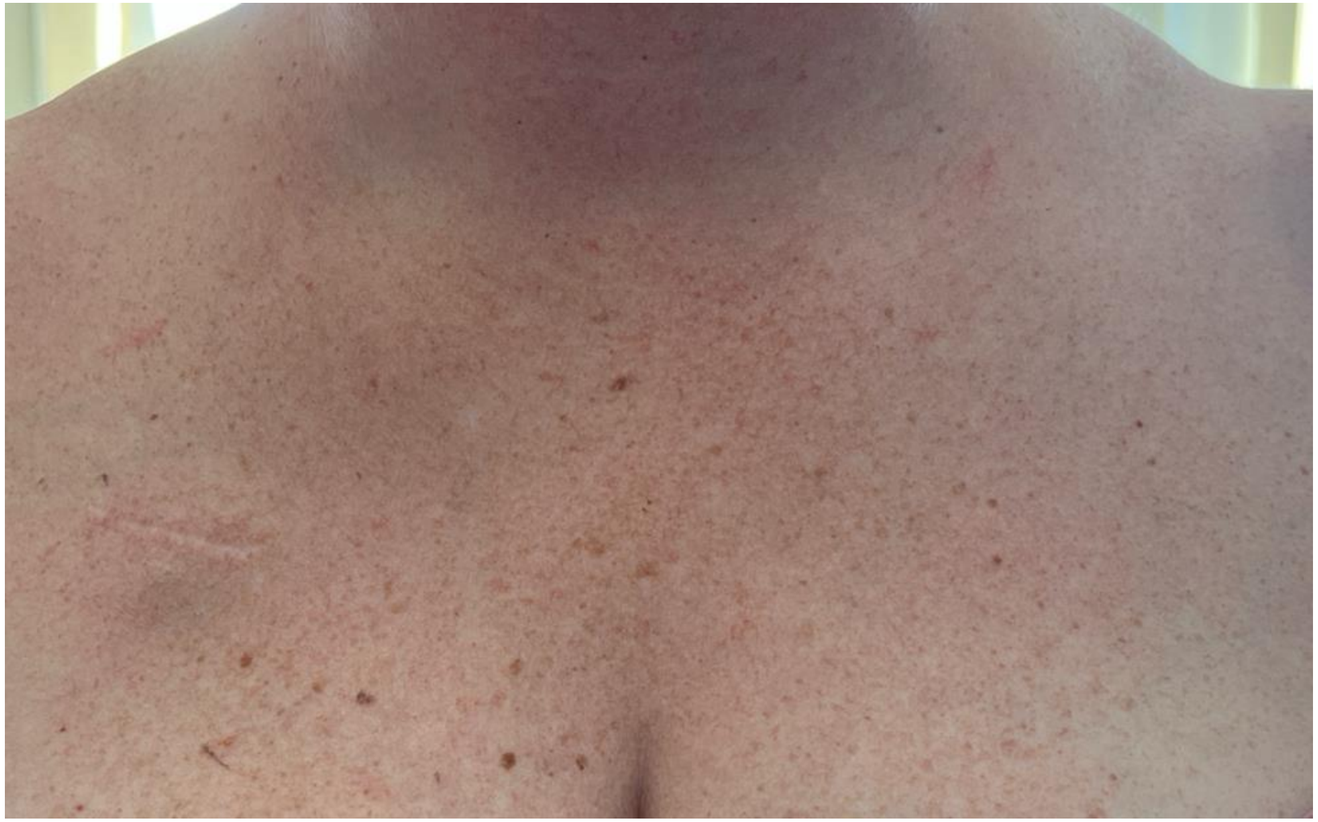
Physical Examination

Follow Up Skin Exam

- On examination, all rashes have significantly improved but present, with mild pink rash on the upper chest and upper back.
- Mild pink non-palpable rash on back of her hands with no ulcerations, but no rash on elbows or knees.
- Periungal erythema has resolved.
- She does endorse new diffuse alopecia in the last month.

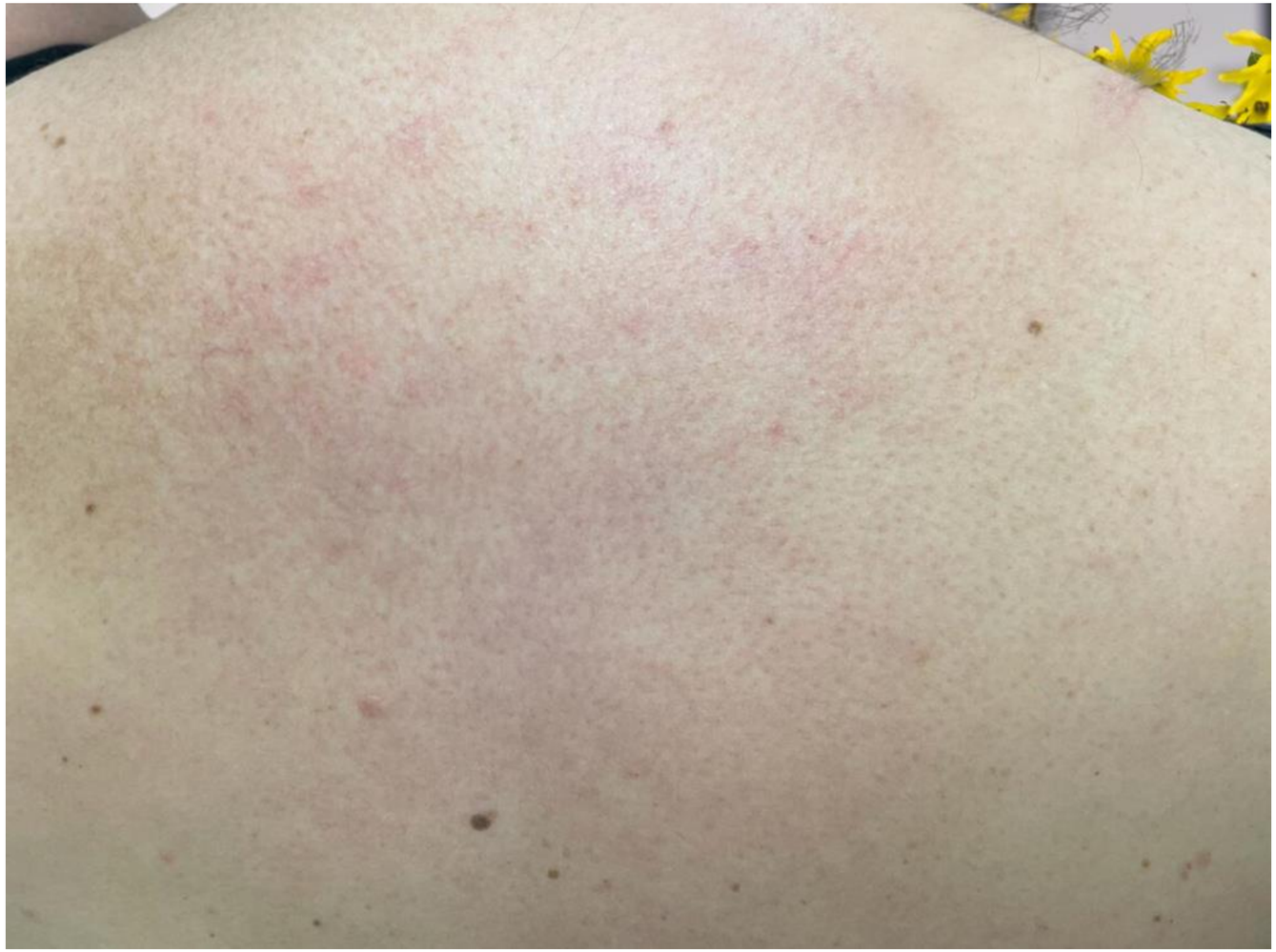
Case 1 Follow Up: Rash Images of Patient

Upper Chest



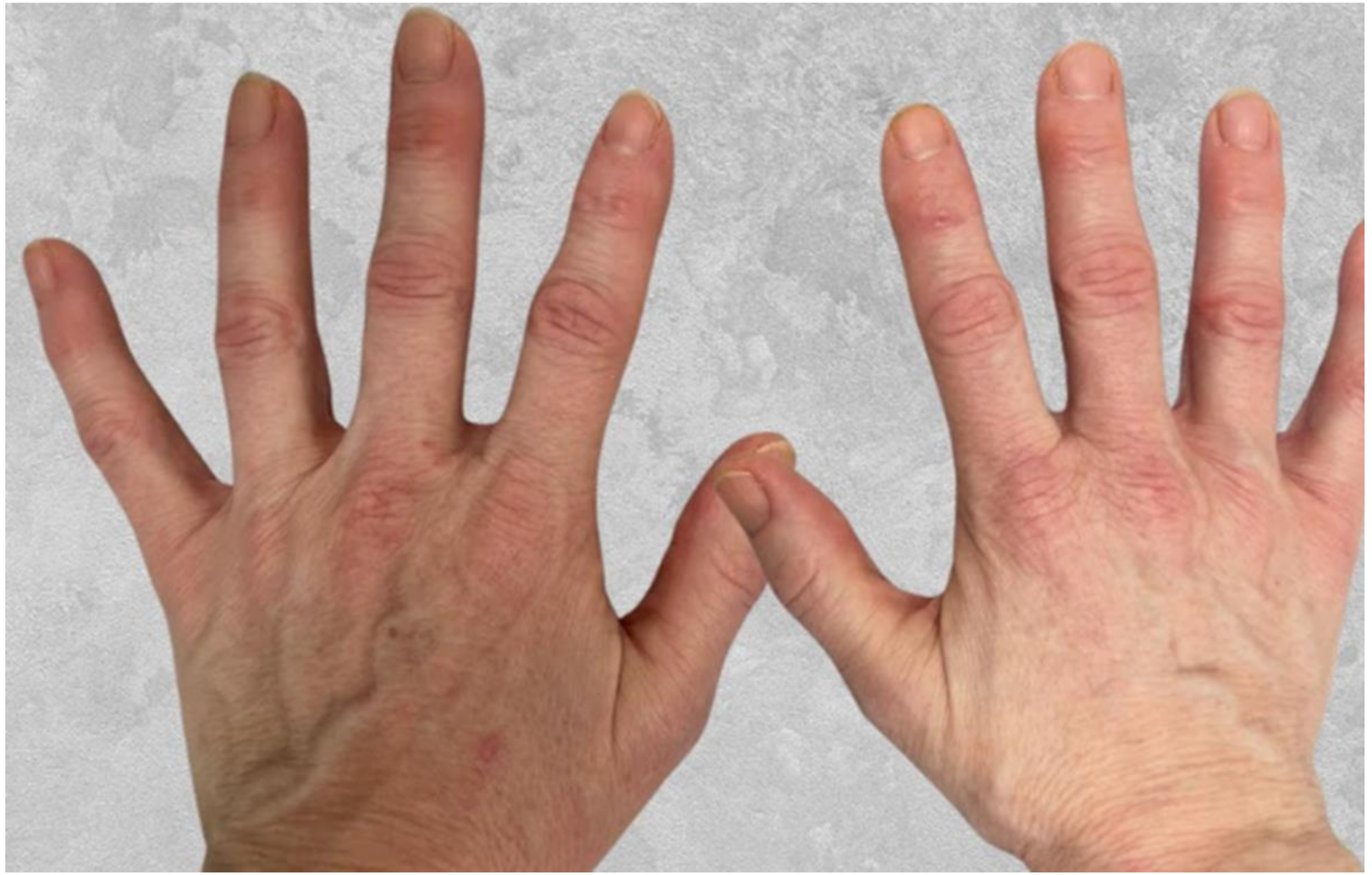
Case 1 Follow Up: Rash Images of Patient

Upper back and neck



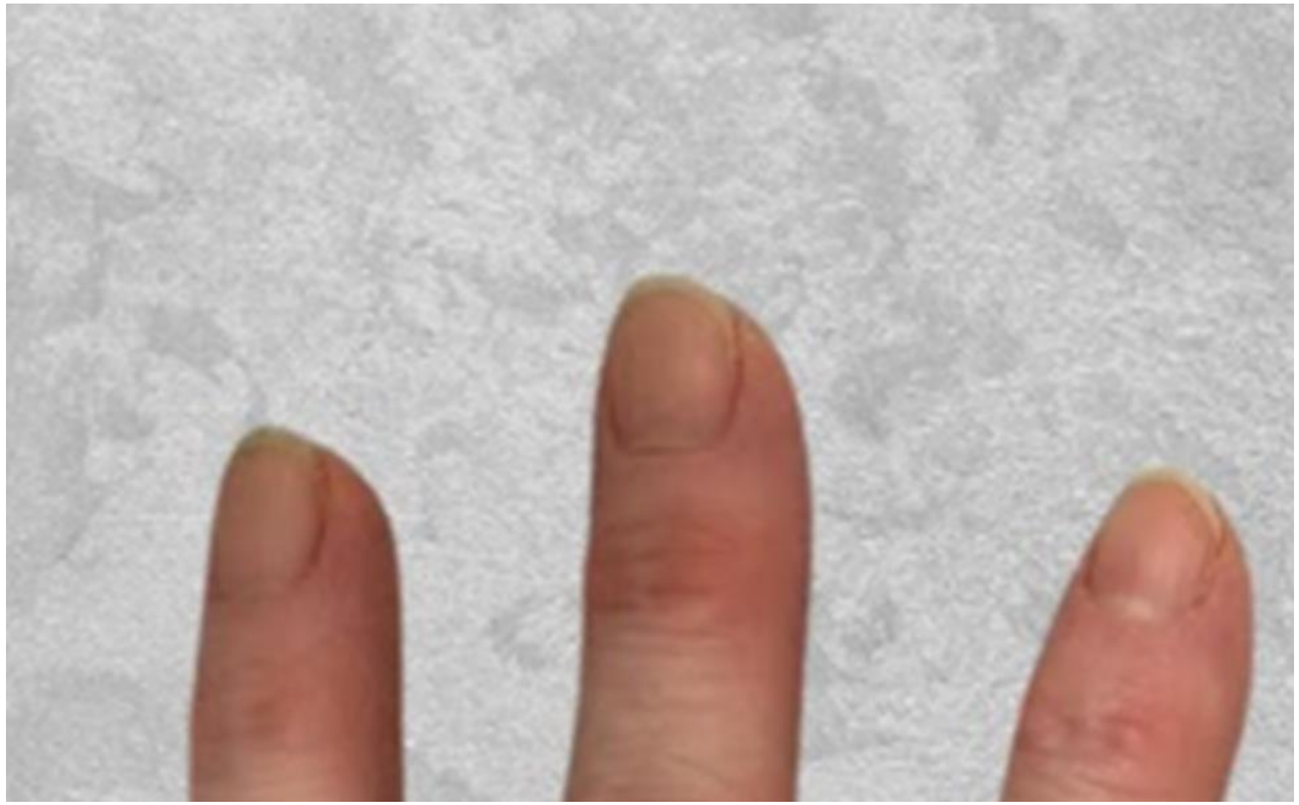
Case 1 Follow Up: Rash Images of Patient

Dorsum of Hand



Case 1 Follow Up: Rash Images of Patient

Periungal Changes



Physical Examination

MMT-8

- Patient is able to hold against gravity with mild to moderate pressure in iliopsoas and deltoid.
- Moderate pressure in gluteus medius and maximus and neck flexors
- Strong pressure in neck extensors
- Rest of the muscle examination shows no weakness.

Case 1 Follow up Scoring

MMT-8

Q 7. Based on the patient presentation specifically manual muscle testing, what should be the score for neck flexion on Kendall scale (0-10)

a. 5
b. 6
c. 7
d. 8
e. 9

Case 1 Follow up Scoring

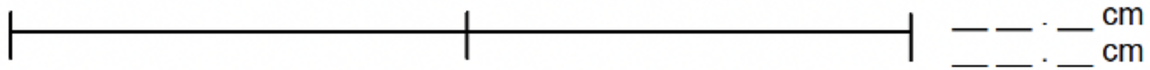
MMT-8

Q 7. Based on the patient presentation specifically manual muscle testing, what should be the score for neck flexion on Kendall scale (0-10)

a. 5
b. 6
c. 7
d. 8
e. 9

Case 1 Follow up Scoring

Myositis Disease Activity Assessment Tool (MDAAT)

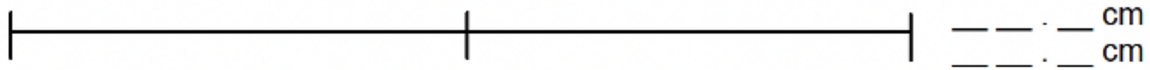
Extramuscular Global Assessment [Core Set Measure for RIM Study]	**(Absent)** **(Maximum)**  __ __ . __ cm __ __ . __ cm	Overall evaluation for disease activity in all extramuscular systems **(EXCLUDING MUSCLE DISEASE ACTIVITY)**

Q 8. Based on the patient presentation, what should be the score for Extra-muscular global disease activity ?

a. 2
b. 3
c. 4
d. 7
e. 8

Case 1 Follow up Scoring

Myositis Disease Activity Assessment Tool (MDAAT)

Extramuscular Global Assessment [Core Set Measure for RIM Study]	**(Absent)** **(Maximum)**  __ __ . __ cm __ __ . __ cm	Overall evaluation for disease activity in all extramuscular systems **(EXCLUDING MUSCLE DISEASE ACTIVITY)**

Q 8. Based on the patient presentation, what should be the score for Extra-muscular global disease activity ?

a. 2
b. 3
c. 4
d. 7
e. 8

Case 1 Follow up Scoring

Myositis Disease Activity Assessment Tool (MDAAT)

Global Disease Activity	**(Absent)** **(Maximum)**  __ __ . __ cm __ __ . __ cm	Overall evaluation for the disease activity in ALL systems including muscle

Q 9. Based on the patient presentation, what should be the score for global disease activity ?

a. 3
b. 7
c. 5
d. 4
e. 8

Case 1 Follow up Scoring

Myositis Disease Activity Assessment Tool (MDAAT)

Global Disease Activity	**(Absent)** **(Maximum)**  __ __ . __ cm __ __ . __ cm	Overall evaluation for the disease activity in ALL systems including muscle

Q 9. Based on the patient presentation, what should be the score for global disease activity ?

a. 3
b. 7
c. 5
d. 4
e. 8

Case 1 Follow up Scoring

Physician Global Disease Activity

Disease Activity is defined as potentially reversible pathology or physiology resulting from the myositis. Clinical findings known or suspected to be due to another disease process should not be considered in this evaluation. The global assessment of disease activity is to be judged from all the information available to you today including the subject's appearance, history, physical examination, diagnostic laboratory testing and your resultant medical therapy.

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- midpoint of line = moderate disease activity, and
- right end of line = extremely active or severe disease activity.

No evidence of disease activity

Extremely active or severe disease activity

Q 10. Based on the patient presentation, what should be the score for global disease activity ?

a. 3
b. 7
c. 5
d. 4
e. 8

Case 1 Follow up Scoring

Physician Global Disease Activity

Disease Activity is defined as potentially reversible pathology or physiology resulting from the myositis. Clinical findings known or suspected to be due to another disease process should not be considered in this evaluation. The global assessment of disease activity is to be judged from all the information available to you today including the subject's appearance, history, physical examination, diagnostic laboratory testing and your resultant medical therapy.

Please rate your global (overall) disease activity assessment by drawing a vertical mark on the 10-cm line below according to the following scale:

- left end of line = no evidence of disease activity,
- midpoint of line = moderate disease activity, and
- right end of line = extremely active or severe disease activity.

No evidence of disease activity

Extremely active or severe disease activity

Q 10. Based on the patient presentation, what should be the score for global disease activity ?

a. 3
b. 7
c. 5
d. 4
e. 8

THANK YOU

Extra-Slides

Case 1 Initial Scoring

Myositis Disease Activity Assessment Tool MDAAT

Constitutional Disease Activity	**(Absent)** — **(Maximum)** __ __ . __ cm __ __ . __ cm	**Examples of maximal score** Severe fatigue or malaise resulting in being bed bound and an inability to perform self -care

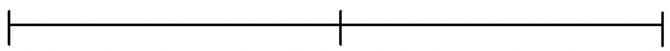
1.	Pyrexia – documented fever > 38° Celsius	0	1	2	3	4	NA
2.	Weight loss – unintentional > 5%	0	1	2	3	4	NA
3.	Fatigue/malaise/lethargy	0	1	2	3	4	NA

Cutaneous Disease Activity	**(Absent)** — **(Maximum)** __ __ . __ cm __ __ . __ cm	**Examples of maximal score** - Ulceration to muscle, tendon or bone; - Extensive erythroderma

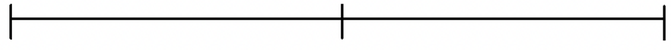
4.	Cutaneous ulceration	0	1	2	3	4	NA
5.	Erythroderma	0	1	2	3	4	NA
6.	Panniculitis	0	1	2	3	4	NA
7.	Erythematous rashes:						
	a. **with** secondary changes (e.g. accompanied by erosions, vesiculobullous change or necrosis)	0	1	2	3	4	NA
	b. **without** secondary changes	0	1	2	3	4	NA
8.	Heliotrope rash	0	1	2	3	4	NA
9.	Gottron's papules/sign	0	1	2	3	4	NA
10.	Periungual capillary changes	0	1	2	3	4	NA
11.	Alopecia:						
	a. Diffuse hair loss	0	1	2	3	4	NA
	b. Focal, patchy with erythema	0	1	2	3	4	NA
12.	Mechanics hands	0	1	2	3	4	NA

Case 1 Initial Scoring

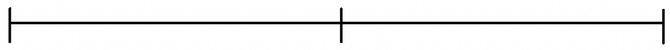
Myositis Disease Activity Assessment Tool MDAAT

Skeletal Disease Activity	**(Absent)** — **(Maximum)**  __ __ . __ cm __ __ . __ cm	**Examples of maximal score** Severe arthritis with extreme loss of function (bedridden, inability for self care)

13. Arthritis:						
a. Severe active polyarthritis	0	1	2	3	4	NA
b. Moderately active arthritis	0	1	2	3	4	NA
c. Mild arthritis	0	1	2	3	4	NA
14. Arthralgia	0	1	2	3	4	NA

Gastrointestinal Disease Activity	**(Absent)** — **(Maximum)**  __ __ . __ cm __ __ . __ cm	**Examples of maximal score** Major abdominal crisis requiring surgery or intensive care

15. Dysphagia:						
a. Moderate/severe dysphagia	0	1	2	3	4	NA
b. Mild dysphagia	0	1	2	3	4	NA
16. Abdominal pain related to the myositis disease process:						
a. Severe	0	1	2	3	4	NA
b. Moderate	0	1	2	3	4	NA
c. Mild	0	1	2	3	4	NA

Pulmonary Disease Activity	**(Absent)** — **(Maximum)**  __ __ . __ cm __ __ . __ cm	**Examples of maximal score** Active interstitial lung disease or respiratory muscle weakness requiring ventilatory support

17. Respiratory muscle weakness **without** interstitial lung disease (ILD):						
a. Dyspnea at rest	0	1	2	3	4	NA
b. Dyspnea on exertion	0	1	2	3	4	NA
18. **Active reversible ILD** (i.e. not just ventilatory abnormalities due to pulmonary fibrosis): *Read glossary for scoring pulmonary function tests and score each item below (a,b and c).*						
a. Dyspnea or cough due to ILD	0	1	2	3	4	NA
b. Parenchymal abnormalities on chest x-ray or high resolution CT scan (HRCT) and/or ground glass shadowing on HRCT	0	1	2	3	4	NA
c. Pulmonary Function Tests: ≥ 10% change in FVC or DLCO	0	1	2	3	4	NA
19. Dysphonia:						
a. Moderate to severe	0	1	2	3	4	NA
b. Mild	0	1	2	3	4	NA

Case 1 Initial Scoring

Myositis Disease Activity Assessment Tool MDAAT

Cardiovascular Disease Activity	**(Absent)** ——— **(Maximum)** __ __ . __ cm __ __ . __ cm	**Examples of maximal score** Myocarditis, pericarditis or severe arrhythmia requiring intensive care unit

20. Pericarditis	0	1	2	3	4	NA
21. Myocarditis	0	1	2	3	4	NA
22. Arrhythmia:						
a. Severe arrhythmia	0	1	2	3	4	NA
b. Other arrhythmia, except sinus tachycardia	0	1	2	3	4	NA
23. Sinus tachycardia	0	1	2	3	4	NA

Other Disease Activity	**(Absent)** ——— **(Maximum)** __ __ . __ cm __ __ . __ cm	**Examples of maximal score** Extreme disease activity with major impact on function

24. Specify:_____	0	1	2	3	4	NA

Extramuscular Global Assessment **[Core Set Measure for RIM Study]**	**(Absent)** ——— **(Maximum)** __ __ . __ cm __ __ . __ cm	Overall evaluation for disease activity in all extramuscular systems **(EXCLUDING MUSCLE DISEASE ACTIVITY)**

Muscle Disease Activity	**(Absent)** ——— **(Maximum)** __ __ . __ cm __ __ . __ cm	**Examples of maximal score** Severe muscle weakness resulting in being bed bound and an inability to perform self care

25. Myositis:						
a. Severe muscle inflammation	0	1	2	3	4	NA
b. Moderate muscle inflammation	0	1	2	3	4	NA
c. Mild muscle inflammation	0	1	2	3	4	NA
26. Myalgia	0	1	2	3	4	NA

Global Disease Activity	**(Absent)** ——— **(Maximum)** __ __ . __ cm __ __ . __ cm	Overall evaluation for the disease activity in ALL systems including muscle

Case 1 Initial Scoring

Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI)

Case 1 Presentation: Initial

Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI)

Select the score in each anatomical location that describes the most severely affected dermatomyositis-associated skin lesion

Activity ⟷ **Damage** ⟷

EXTENT ↕

Anatomical Location	Erythema	Scale	Erosion/ Ulceration	Poikiloderma (Dyspigmentation or Telangiectasia)	Calcinosis	Anatomical Location
	0-absent 1-pink; faint erythema 2-red 3-dark red	0-absent 1-scale 2-crust; lichenification	0-absent 1-present	0-absent 1-present	0-absent 1-present	
Scalp						Scalp
Malar Area						Malar Area
Periorbital						Periorbital
Rest of the face						Rest of the face
V-area neck (frontal)						V-area neck (frontal)
Posterior Neck						Posterior Neck
Upper Back & Shoulders						Upper Back & Shoulders
Rest of Back & Buttocks						Rest of Back & Buttocks
Abdomen						Abdomen
Lateral Upper Thigh						Lateral Upper Thigh
Rest of Leg & Feet						Rest of Leg & Feet
Arm						Arm
Mechanic's Hand						Mechanic's Hand
Dorsum of Hands (not over joints)						Dorsum of Hands (not over joints)
Gottron's - Not on Hands						Gottron's - Not on Hands

Case 1 Initial Scoring

Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI)

Gottron's – Hands

Examine the patient's hands and double score if papules a present		Ulceration		Examine patient's hands and score if damage is present	
0-absent 1-pink; faint erythema 2-red erythema 3-dark red				0-absent 1-dyspigmentation 2-scarring	

Penungual

Periungual changes (examine)					
0-absent 1-pink; red erythema/microscopic telangiectasias 2-visible telangiectasias					

Alopecia

Recent Hair loss (within last 30 days as reported by the patient)					
0-absent 1-present					

Total Activity Score
(For the activity score, please add up the scores of the left side, i.e. Erythema, Scale, Excoriation, Ulceration, Gottron's, Periungual, Alopecia)

Total Damage Score
(For the damage score, add up the scores of the right side, i.e. Poikioloderma, Calcinosis)