A Classic Case of a Rare Autoantibody

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12-year-old Hispanic female

Progressive proximal muscle weakness

Difficulty standing from seated position

Falls

Softer voice

Dysphagia

Dyspnea

Rash

No past medical history, surgical history, family history, medications, drug allergies
Normal developmental history, unremarkable social history
Immunizations: up to date

Physical Examination

Heliotrope rash

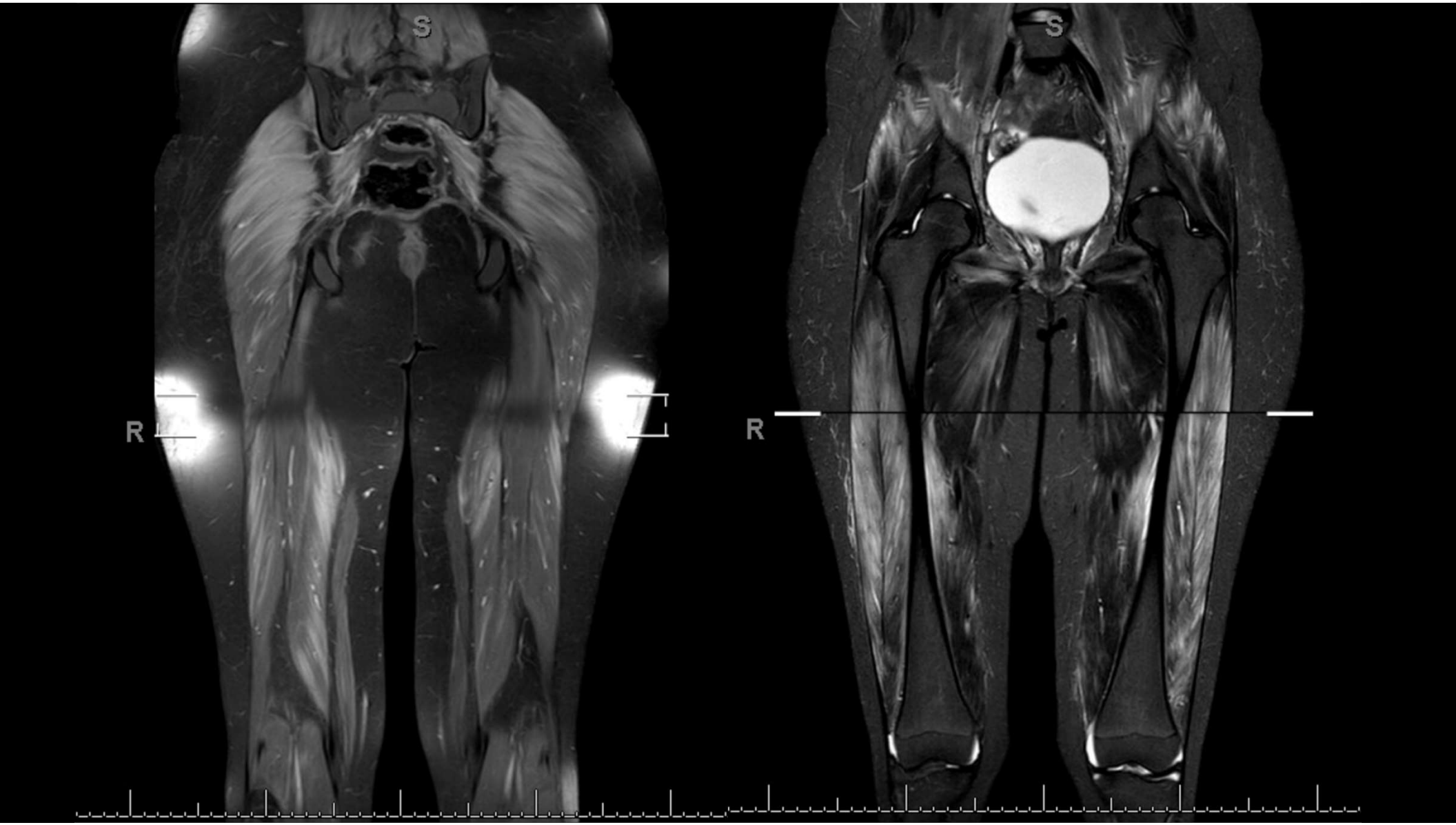
Gottron papules

Extensor erythema

Images courtesy of VisualDx

Evaluation

Labs	**Creatine kinase** (**CK**): 22,468 units/L **Aspartate aminotransferase AST**: 687 units/L **Alanine aminotransferase ALT**: 411 units/L
Autoimmune labs	Antinuclear antibody (**ANA**): negative **Double-stranded DNA antibody**: negative Myositis-specific antibodies: **PL-7 positive**
Imaging	MRI with/without contrast: **symmetric diffuse** increased signal intensity within **proximal muscles** of lower extremities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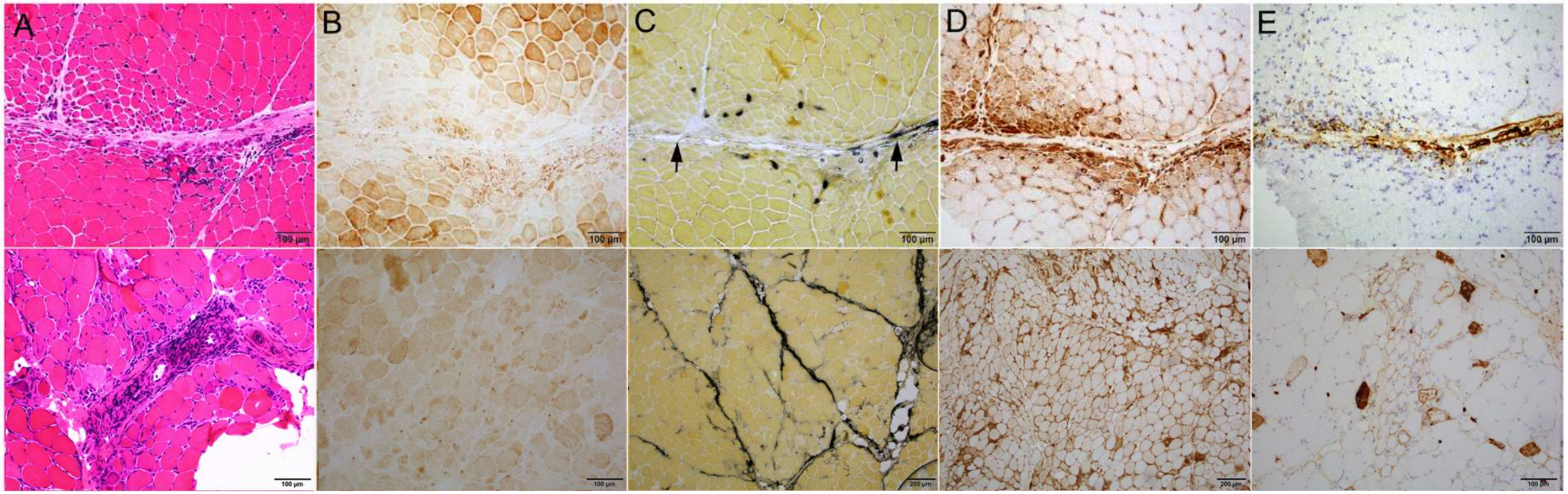
Juvenile Dermatomyositis (JDM)

- Symmetric proximal muscle weakness
- Elevated muscle enzymes
- Heliotrope rash
- Gottron papules
- Photosensitivity
- Capillaropathy
- Calcinosis

Rider LG & Nistala K *J Int Med*, 2016, **280**; 24–38

Myopathy in Dermatomyositis vs. Antisynthetase Syndrome



H&E | COX | Alkaline phosphatase | MHC-1 | C5b-9

Cai C et al. *Mod Pathol,* 2018

Antisynthetase Syndrome

Disease in children may be different than in adults

Interstitial lung disease

Pulmonary function test

Mechanic's hands

Myositis

Rash

Non-erosive arthritis

Raynaud phenomenon

Sicca syndrome

Constitutional symptoms

Anti-aminoacyl tRNA synthetases

- Jo-1, **PL-7**, PL-12, OJ, EJ, KS, Zo, Ha
- Rarer in JDM

Mahler M *Autoimm Rev*, 2014, **13**:367-371

Treatment

- Methylprednisolone IV pulsing
- Prednisone
- IV immunoglobulins
- Methotrexate
- Mycophenolate mofetil
- Abatacept

Summary

- **Juvenile dermatomyositis** presents with symmetric proximal muscle weakness, elevated muscle enzymes, heliotrope rash, Gottron papules, photosensitivity, capillaropathy, & calcinosis
- **Myositis-specific antibodies** are associated with different clinical phenotypes
- **Anti-PL-7** is an anti-aminoacyl tRNA synthetase, a key feature of **antisynthetase syndrome** in adults, and is very rare in children
- **Interstitial lung disease** is associated with anti-PL-7 antibody

A Boy with Arthritis and Ground Glass Opacities

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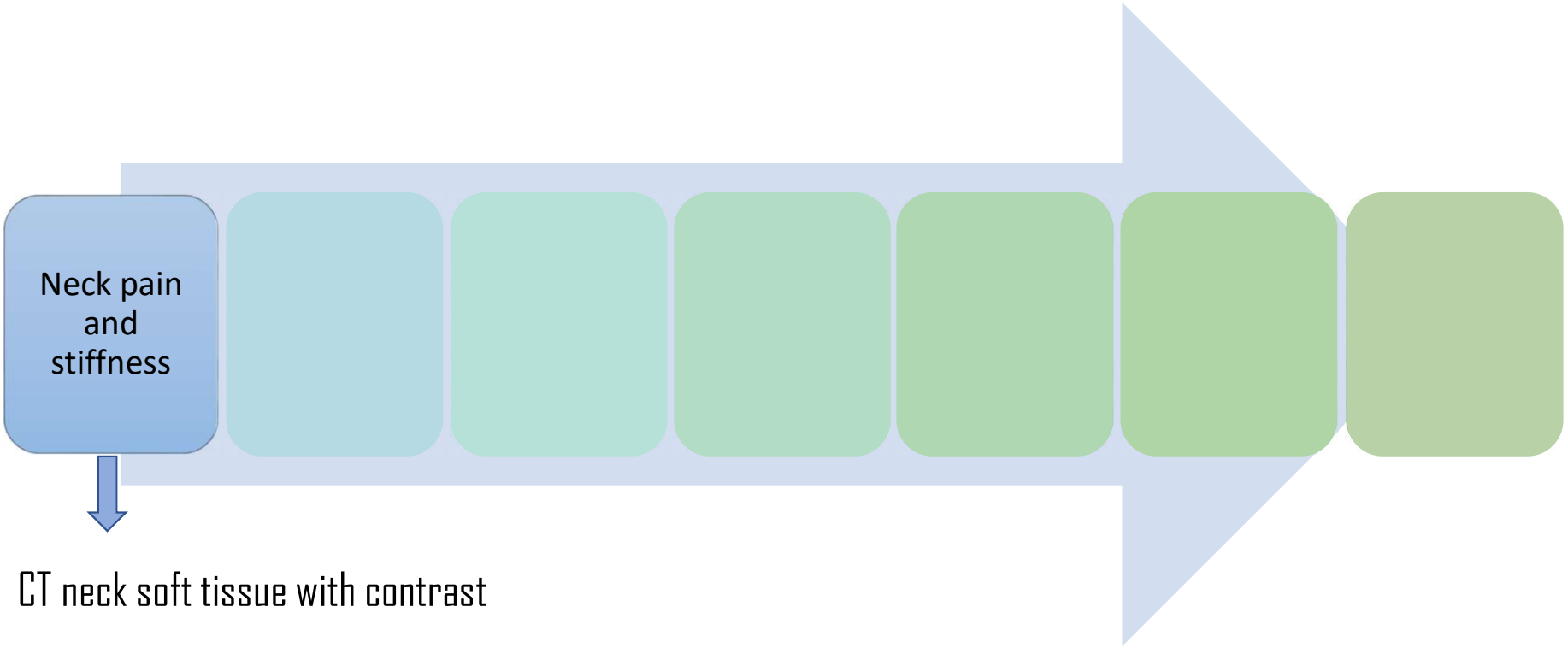
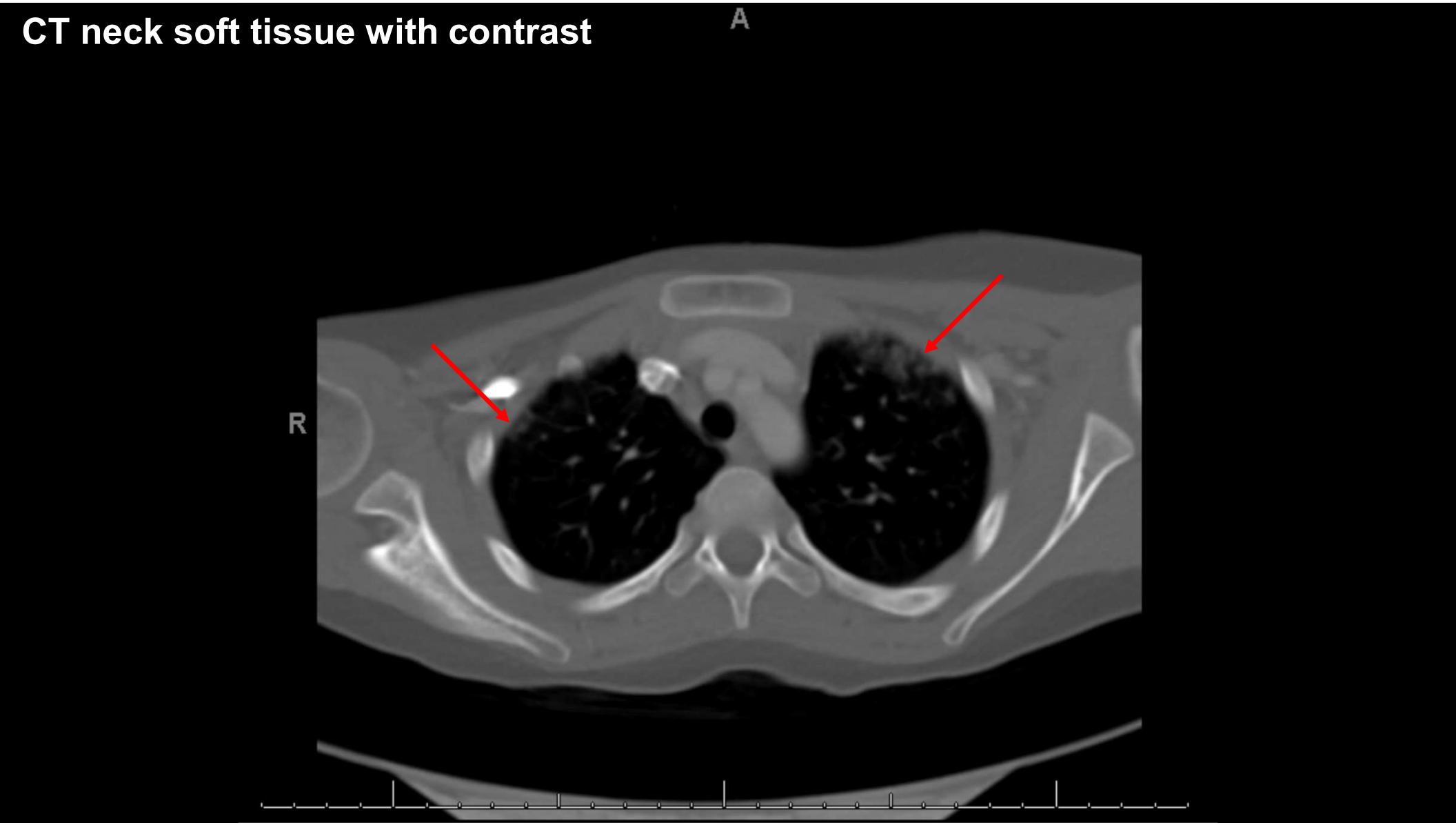
11-year-old Hispanic male

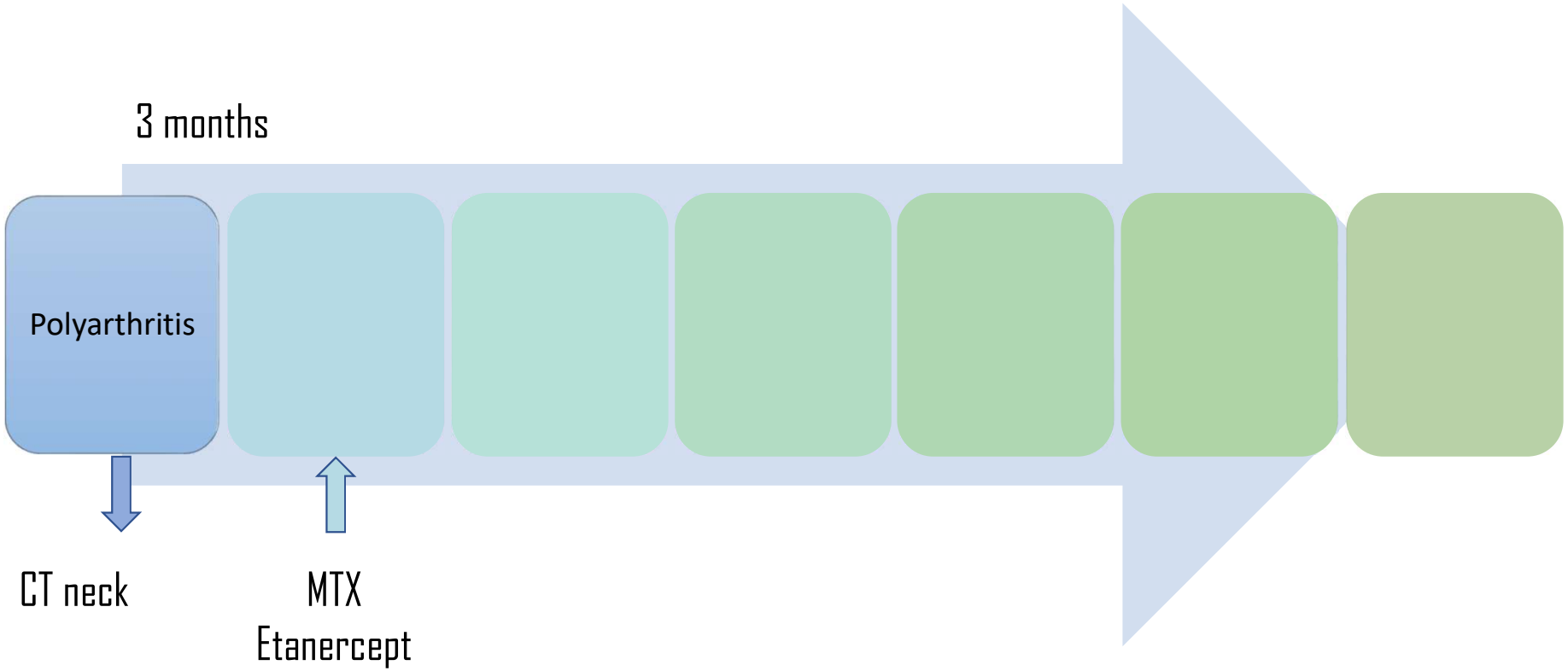


CT neck soft tissue with contrast

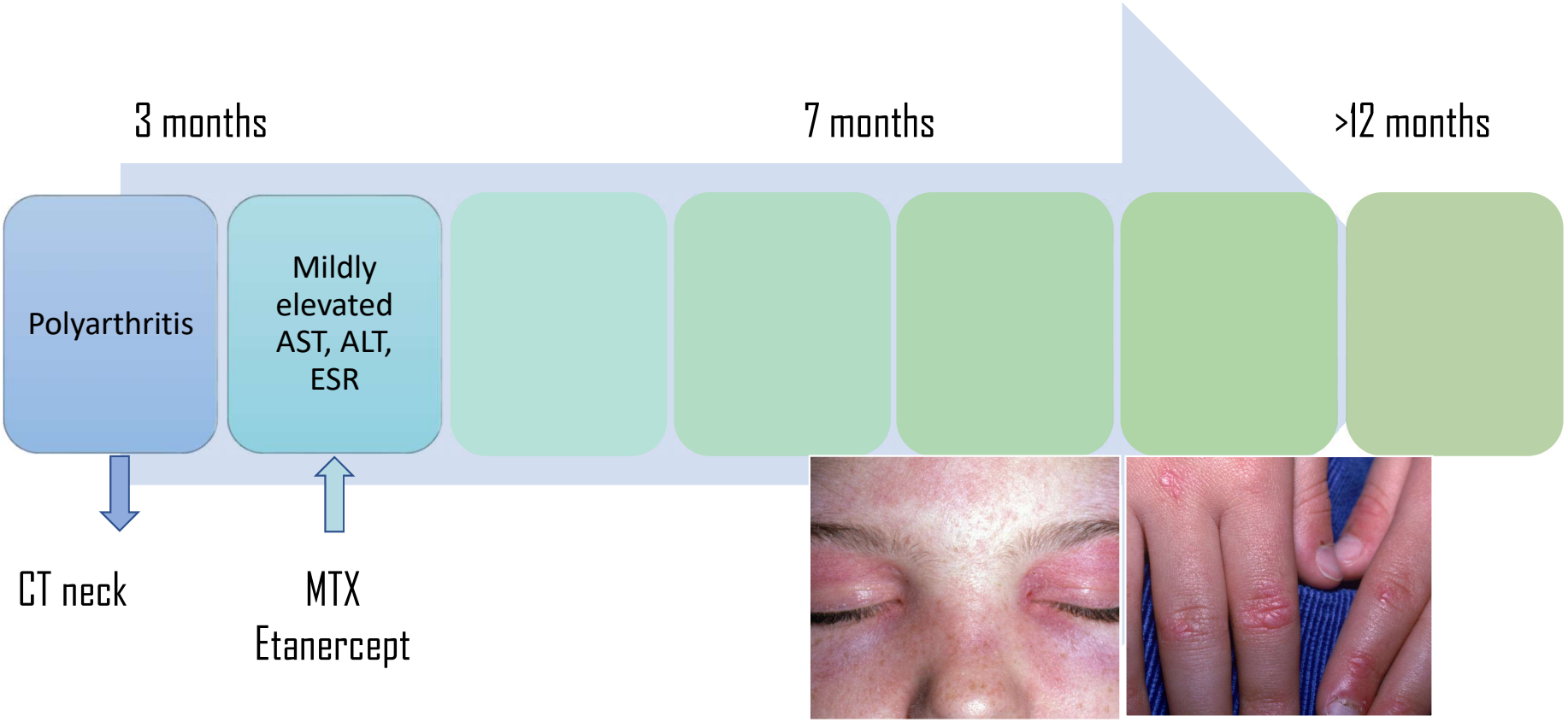
CT neck soft tissue with contrast



11-year-old Hispanic male



11-year-old Hispanic male



Evaluation

Imaging	MRI with/without contrast: **symmetric**, **patchy**, **diffuse** edema of **proximal muscles**
Muscle biopsy	**No inflammation or myopathic change**

Evaluation

Labs

CK: normal

AST: 66 (ref: 9-47 units/L)

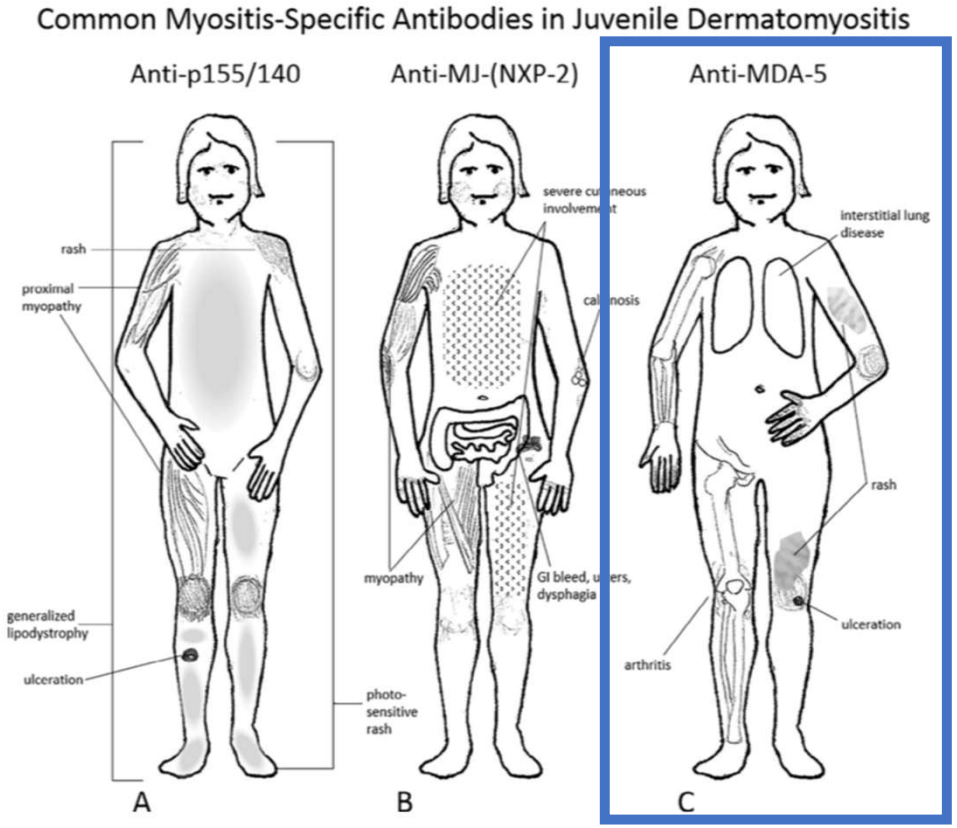
ALT: normal

Aldolase: 8.8 (ref: 1.5-7.4 units/L)

Autoimmune labs

ANA, **rheumatoid factor**, **HLA-B27**: negative

Myositis-specific Abs: **MDA-5 positive**



Interstitial lung disease

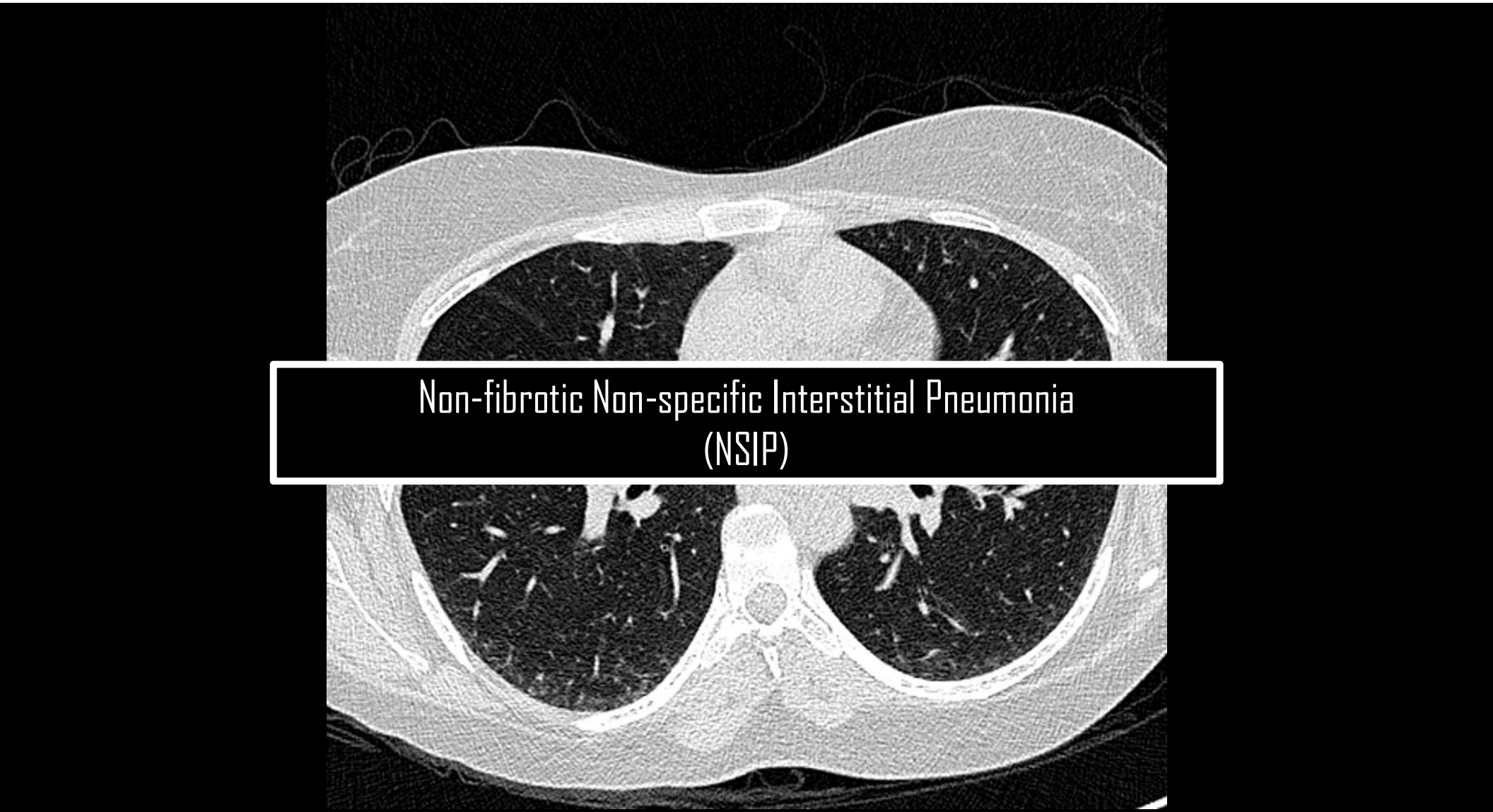
Ulcerations & rash

Arthritis

Milder myositis

Figure 2. Phenotypes associated with the 3 most common MSAs in children with myositis: anti-p155/140, anti-MJ, and anti-MDA-5. **A,** Anti-p155/140, present in 18%-30% of idiopathic juvenile inflammatory myopathies display an extensive photosensitive rash which ulcerates, a chronic disease course and generalized lipodystrophy. **B,** 15%-23% of children positive for anti-MJ (nuclear matrix protein 2 in the United Kingdom) may have disease onset at a younger age, have dysphonia, muscle cramps, atrophy and contractures, with increased weakness, and they are more likely to develop calcifications and gastrointestinal symptoms; their rash often spares the truncal area. **C,** Anti-MDA-5 is increased in the Japanese population (33%) vs the United Kingdom (6%) and is associated with inflammatory lung disease, oral and cutaneous ulcers, arthritis and a milder form of muscle involvement. Adapted with permission from Rider et al.[40] *GI*, gastrointestinal.

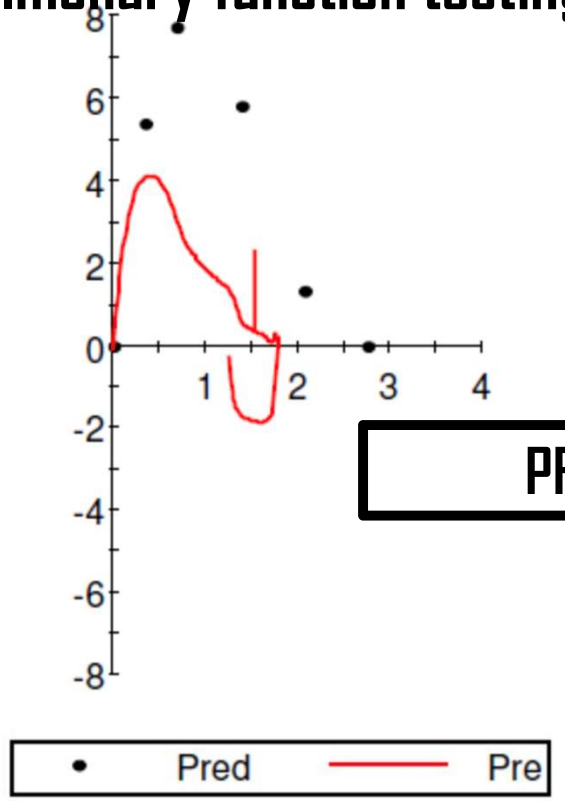
Pachman, L. M. and A. M. Khojah (2018). *J Pediatr* 195: 16-27.

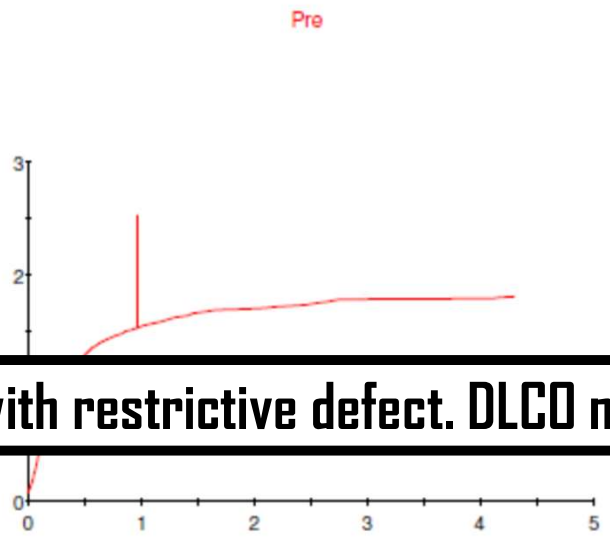


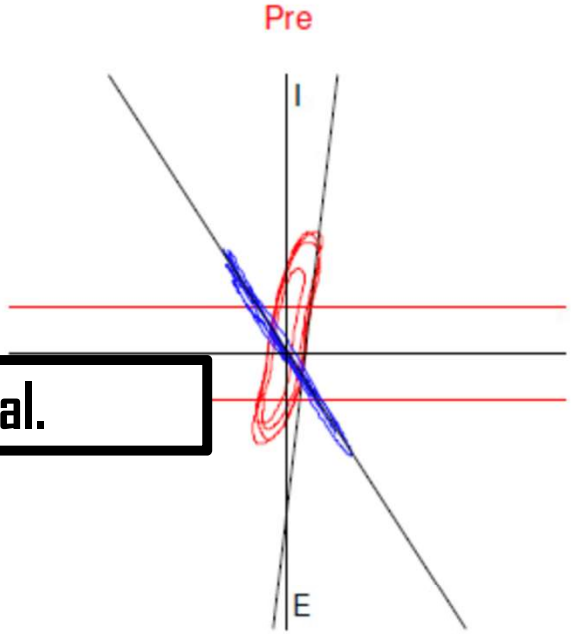
Non-fibrotic Non-specific Interstitial Pneumonia (NSIP)

Case courtesy of Dr Hani Salam, Radiopaedia.org, rID: 13432

Pulmonary function testing







PFTs with restrictive defect. DLCO normal.

Interpretation: Test values are likely affected by patient coughing. Spirometry demonstrates decreased FVC and FEV1 consistent with restrictive defect. Body plethysmography shows a decreased total lung capacity, supporting the restrictive defect. DLCO corrected for hemoglobin and ventilation is normal.

Interstitial lung disease in inflammatory myopathy

- 3 patterns of presentation
  - Acute and rapidly progressive
  - **Subacute or chronic**
  - Chronic progressive fibrosing

- Severity of lung disease not correlated with severity of myositis

- Disease monitoring
  - PFTs, high-resolution CT chest, 6-minute walk testing, patient-reported

Oddis C, et al. *Curr Rheumatol Rev* 2010 May; 6(2): 108–119

Treatment

- Methotrexate, etanercept
- Corticosteroid: IV pulsing and oral
- Abatacept
- NSIP → Mycophenolate mofetil
- Rituximab
- IVIG
- Tocilizumab
- Worsening ILD → Cyclophosphamide

Summary

- Consider **juvenile dermatomyositis** (JDM) in a patient presenting with arthritis, mild transaminitis, and mild weakness, especially if they develop rash

- **Anti-MDA-5** is associated with arthritis, milder myositis, skin ulceration and rash, and interstitial lung disease in JDM

- **Interstitial lung disease** in inflammatory myopathies can be rapidly progressive, chronic, or chronic progressive fibrosing

References

- Cai C et al. *Mod Pathol,* 2018
- Mahler M *Autoimm Rev* , 2014, **13**:367-371
- Oddis C, et al. *Curr Rheumatol Rev* 2010 May; **6**(2): 108–119
- Pachman, LM & Khojah AM *J Pediatr*; 2018, **195**: 16-27
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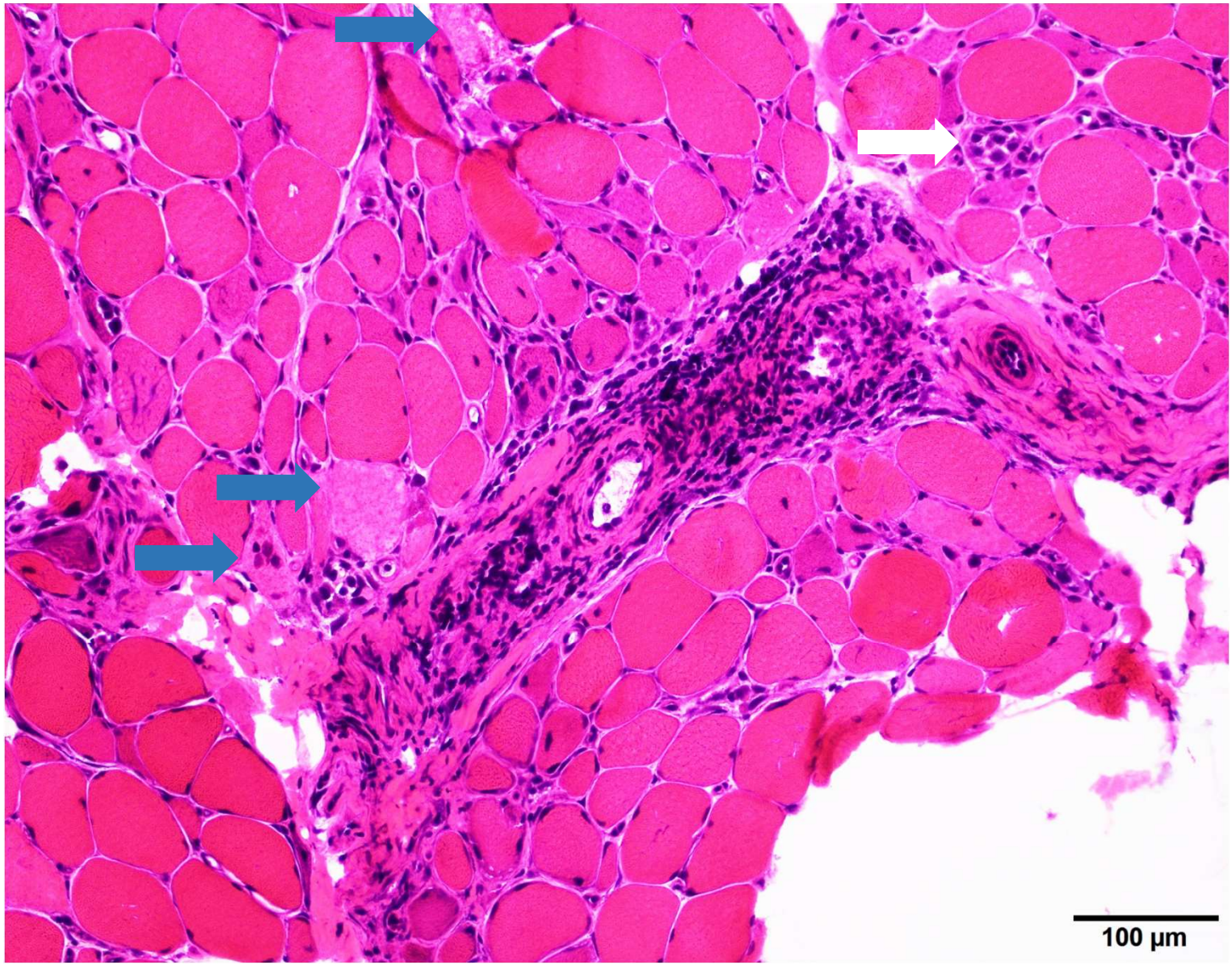
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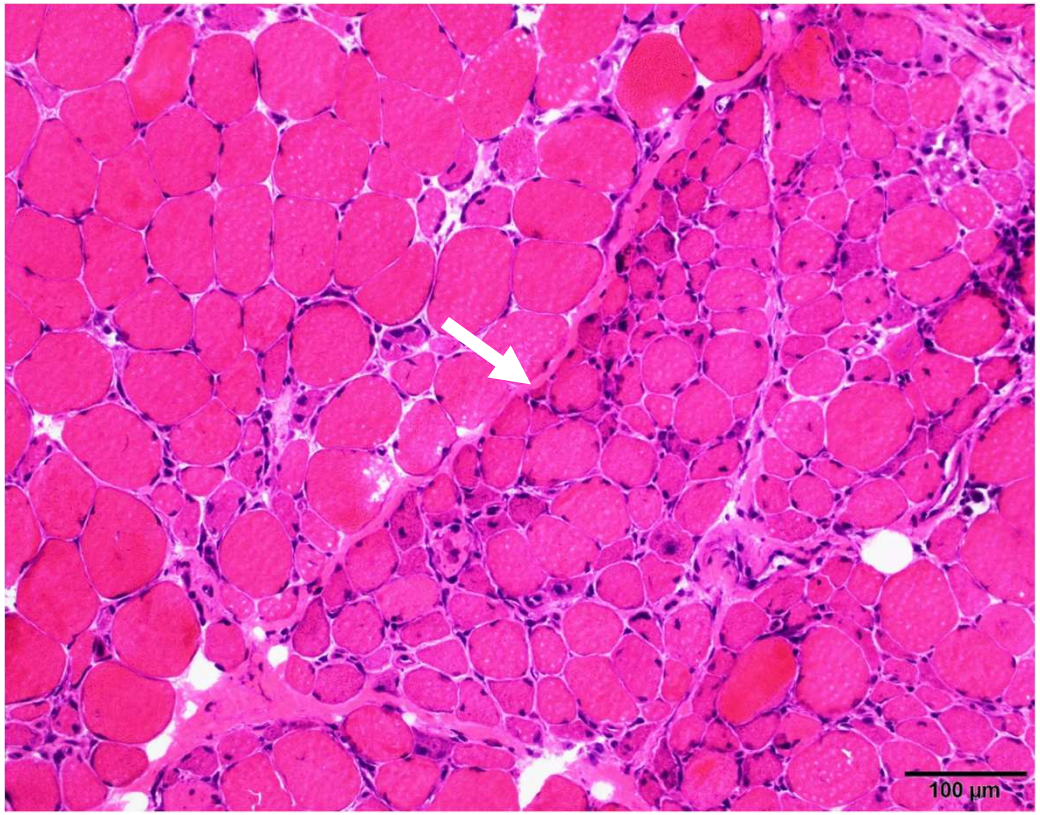
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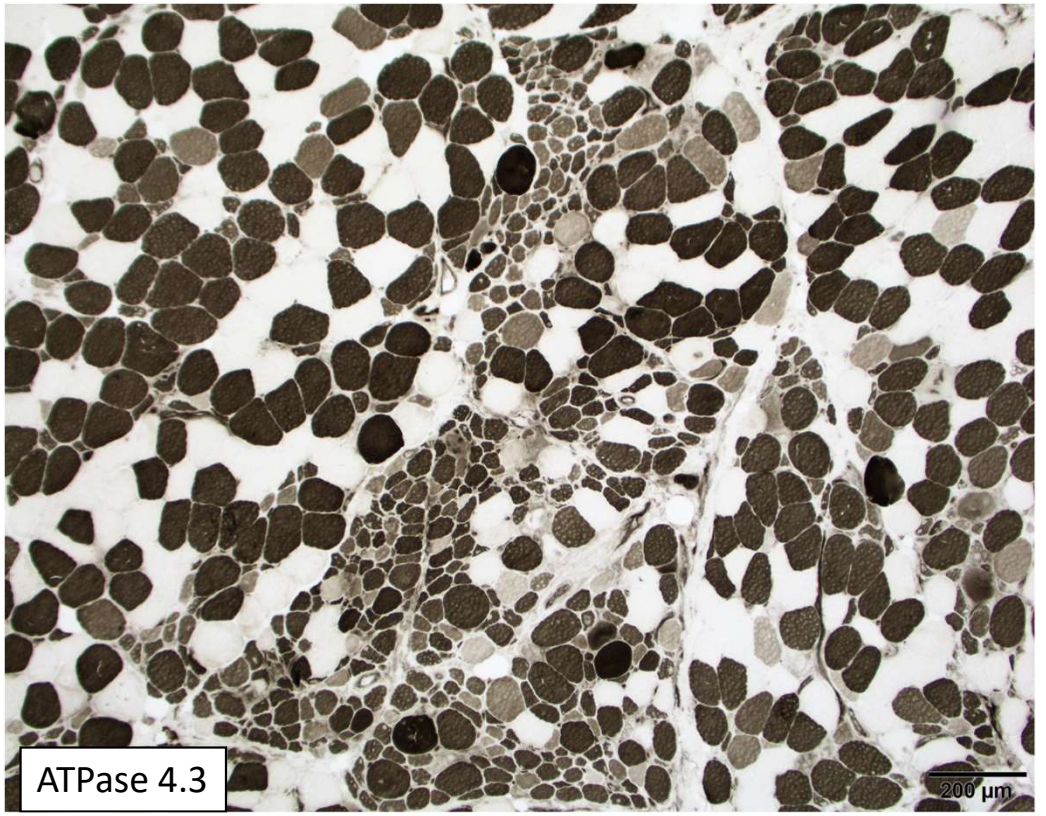
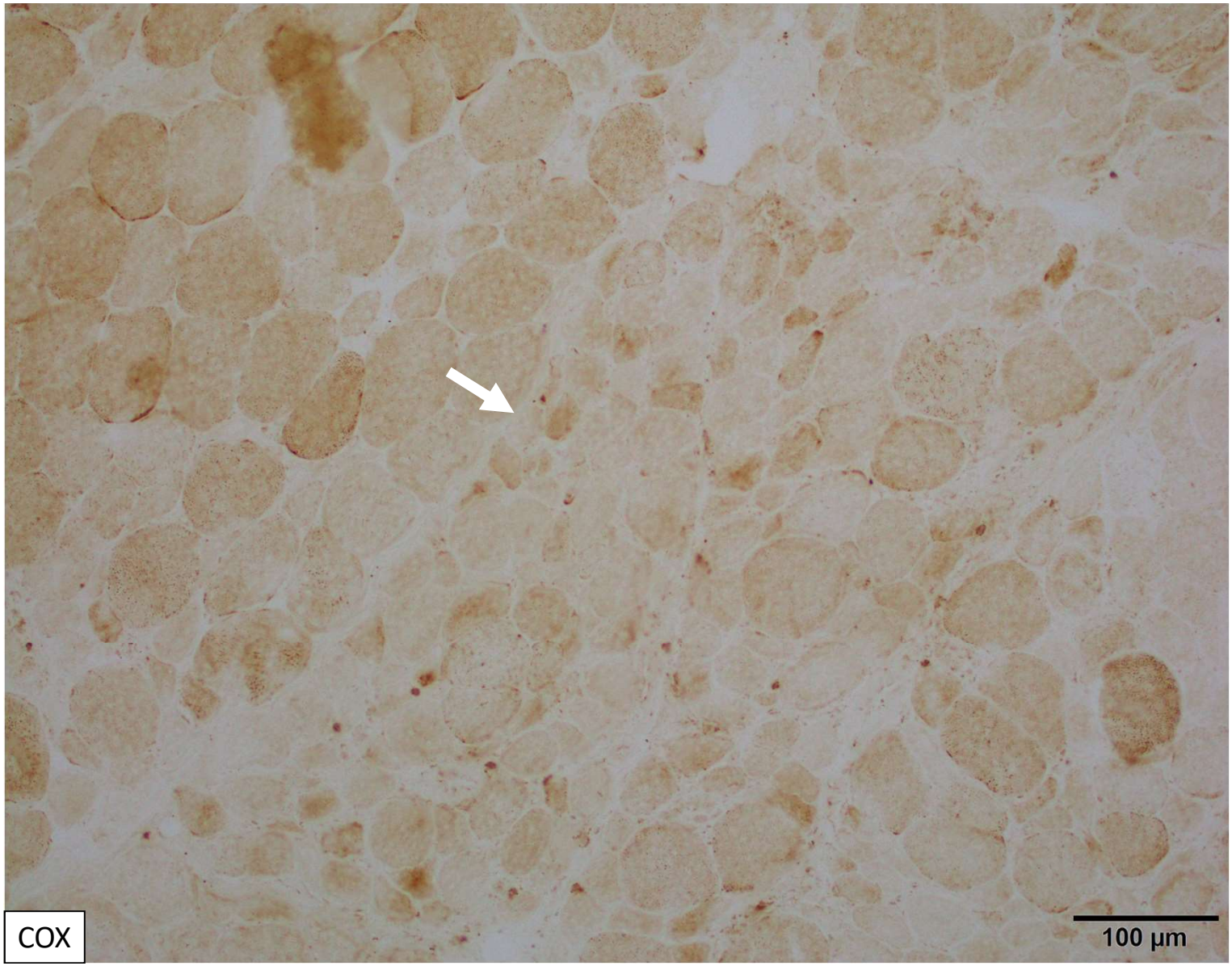
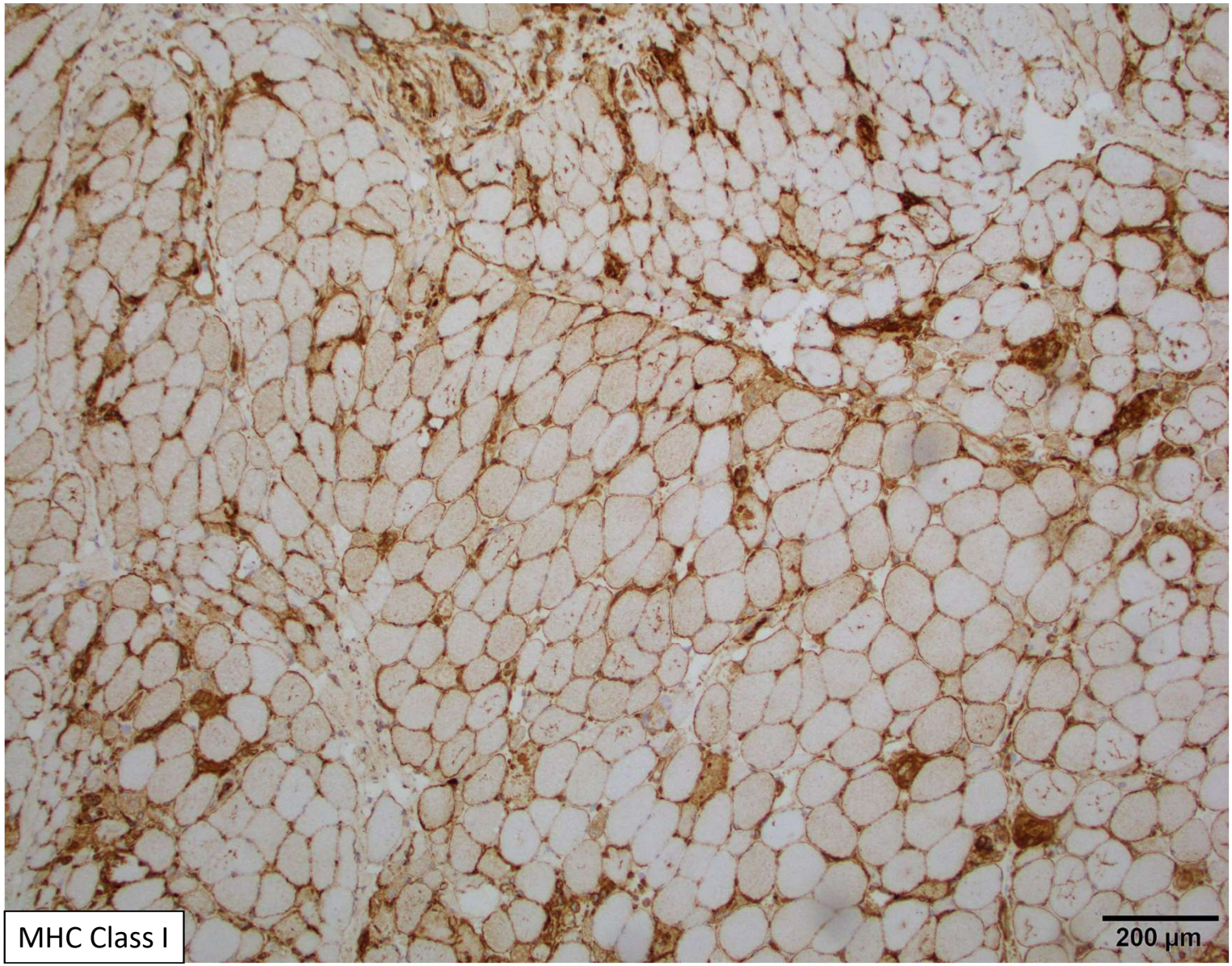
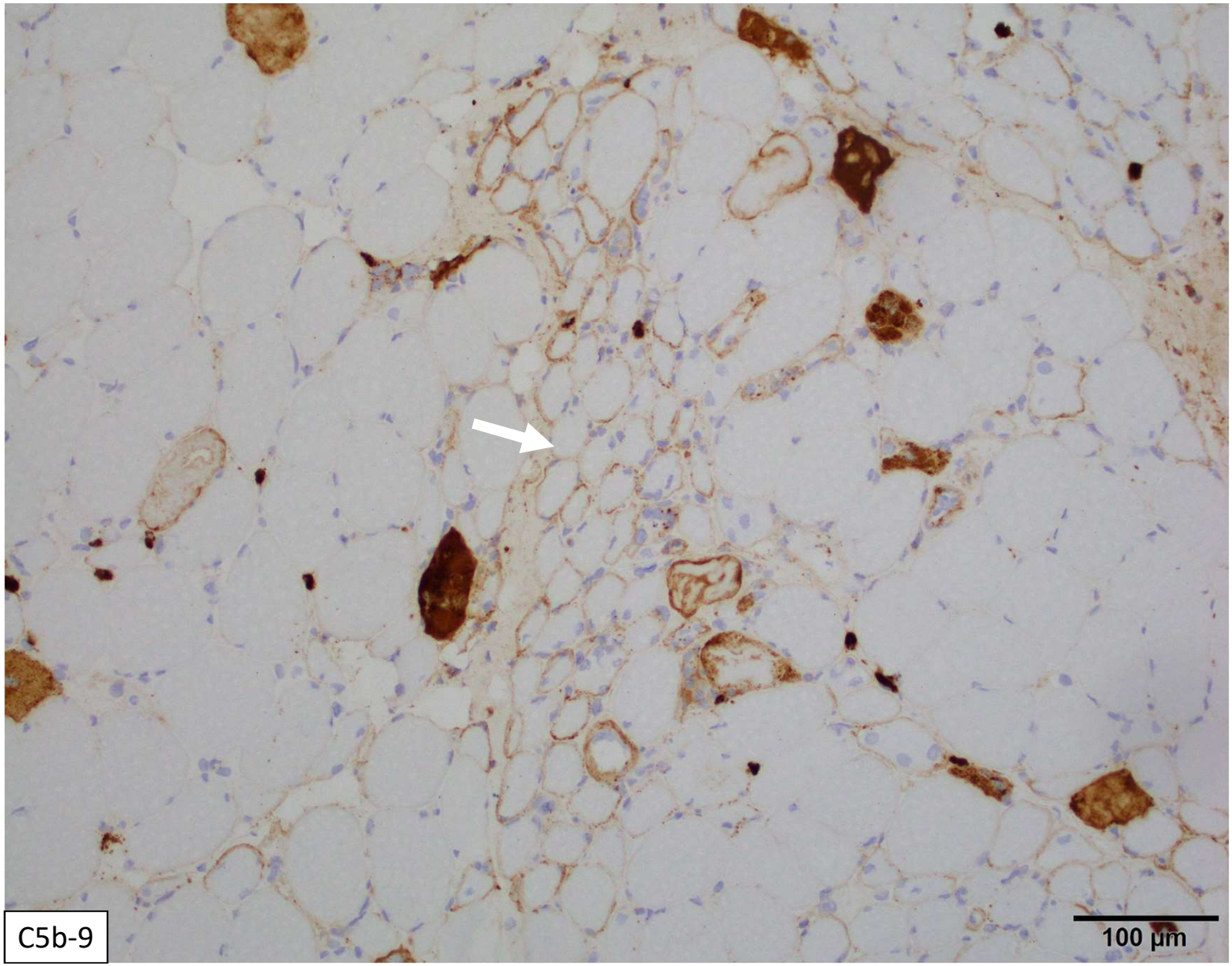

ATPase 4.3
200 µm


COX
100 µm


Alkaline phosphatase
200 µm


MHC Class I
200 µm


C5b-9
100 µm

Myositis autoantibodies

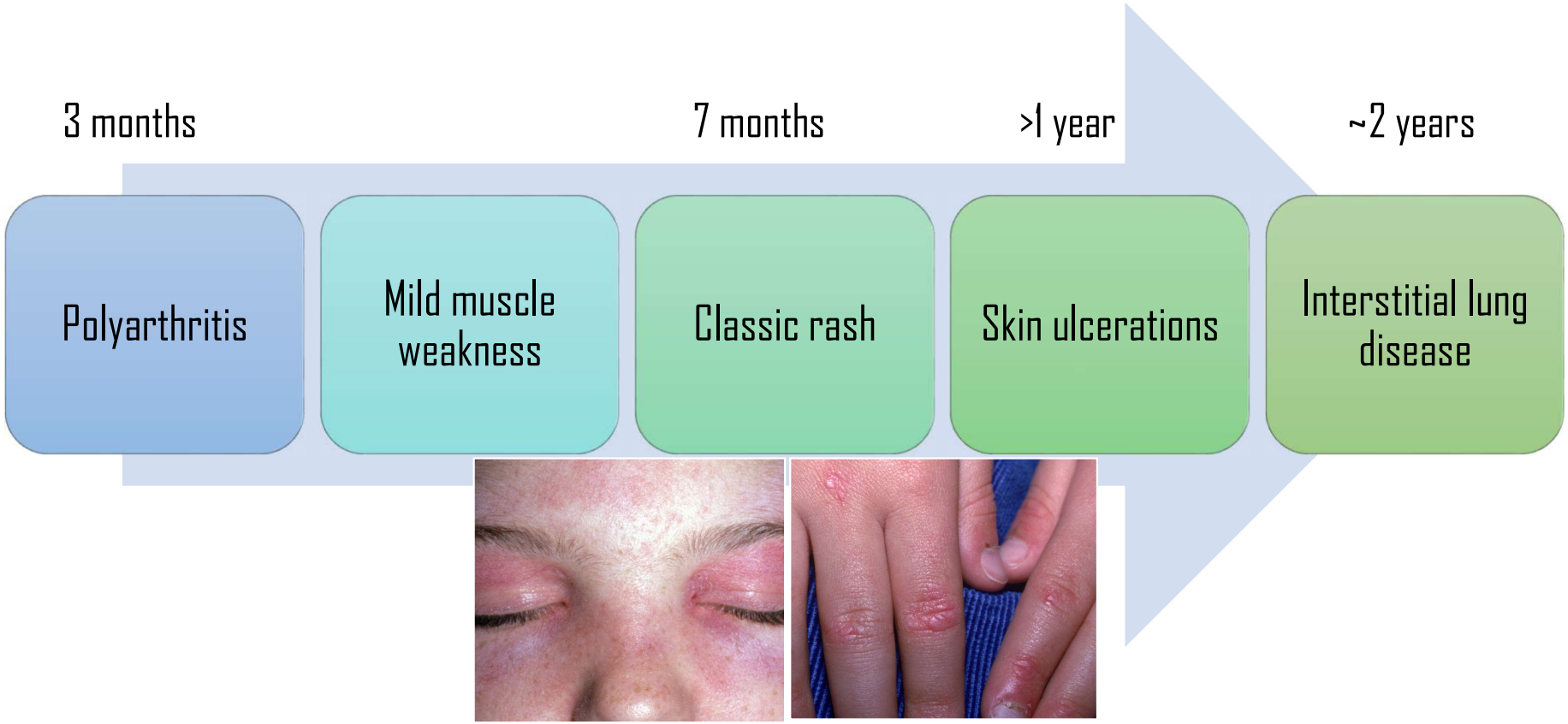
- Two classes of **myositis autoantibodies**
  - Myositis-specific antibodies (MSAs)
  - Myositis-associated autoantibodies (MAAs)
    - In patients with myositis overlap syndromes

- **70%** of patients with juvenile idiopathic inflammatory myopathies (JIIMs) have at least one myositis autoantibody

- **54%** of U.S. patients and 51% of U.K. patients with juvenile dermatomyositis (JDM) have at least one MSA.

Pachman, L. M. and A. M. Khojah (2018). *J Pediatr* 195: 16-27.
Rider, L. G. and K. Nistala (2018). *J of Int Med* 280(1): 24-38.

Summary


3 months
7 months
>1 year
~2 years
Polyarthritis
Mild muscle weakness
Classic rash
Skin ulcerations
Interstitial lung disease