Inflammatory Myopathies

4th year MBBS

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Consultant Rheumatologist

Case

- A 64 woman presents with erythematous itchy rash over back of hands & forehead. For 1 month she felt tired
- Tests: ESR 42, ALT & AST ↑. GGT & ALP normal
- Prescribed steroid cream
- Over next few weeks: can’t comb hair or rise from chair
- Rash now: forehead, eyes, anterior chest & upper back

- Nails: periungal erythema
- Power: reduced proximal muscle strength, cannot stand from chair
- Cannot raise head from supine position
- Facial muscles normal strength
- Bloods: CK 8000, ANA strongly positive

- Muscle biopsy: inflammatory infiltrate with myofiber necrosis & regeneration
- CT - CAP: mass in L ovary

Diagnosis??

Objectives

- Inflammatory myopathies
  - Epidemiology
  - Associations
  - Clinical features
  - Diagnosis & investigations
  - Pathology
  - Radiology
  - Overlap syndromes
  - Treatment
- Sjogren’s syndrome

Idiopathic inflammatory myopathies (IIM)

- Polymyositis
- Dermatomyositis
- Juvenile dermatomyositis
- Inclusion body myositis (IBM)

Epidemiology

- Rare diseases
- Annual incidence of PM/DM range from 1 to 9 cases/million/year
- Prevalence is 2–10 per 100 000
- PM is more frequent than DM
- Overlap syndromes with other autoimmune rheumatic diseases occur in 15–20%
- 4X more common in blacks than in Caucasians.
- F:M ratio 2:1
- Can occur at any age
  - PM 50 -60 years
  - DM :2 peaks—5 to 15 years & 45 to 65 years.
  - IBM >50

HLA asscociation

- DM: HLA-DRB1∗0301, DQB1∗0201
- JDM associated with HLA-DQA1*0501

Associations of IIM

- Inflammatory myopathies can occur in association with:
  1. Other autoimmune connective tissue diseases such as scleroderma, SLE, RA, SS, PAN.
  2. Malignancies
- Incidence of malignancy is higher in DM than in PM
- The most common tumors:
  - Ovary
  - Breast
  - Melanoma
  - Colon
- Treatment of Ca results in improvement of myositis

Clinical features of IIM

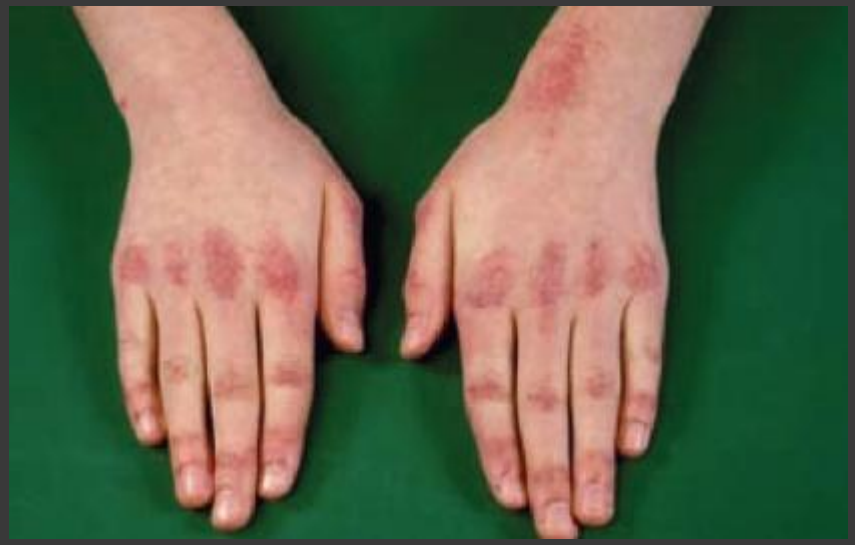
- Constitutional
- Muscle
- Skin
- Joint
- Lung
- Heart
- GI tract

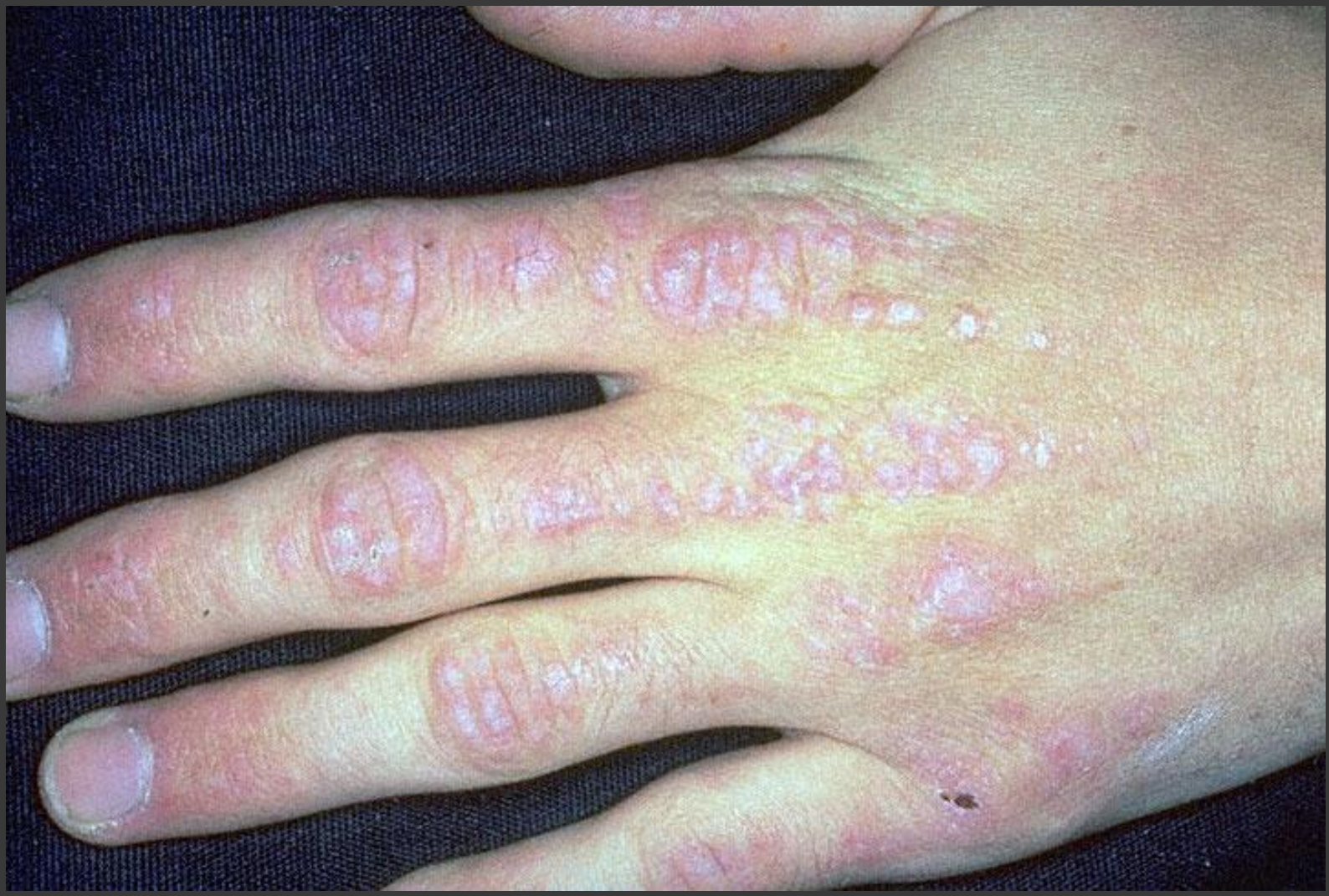
Constitutional

- Fatigue
- Fever
- Weight loss

Skin

- Gottron's papules
- 'V'-sign
- ‘Shawl'-sign
- Rash on the malar areas
- The heliotrope rash
- Periungual telangiectasia
- Nailfold capillaries changes
- 'mechanic's hands'

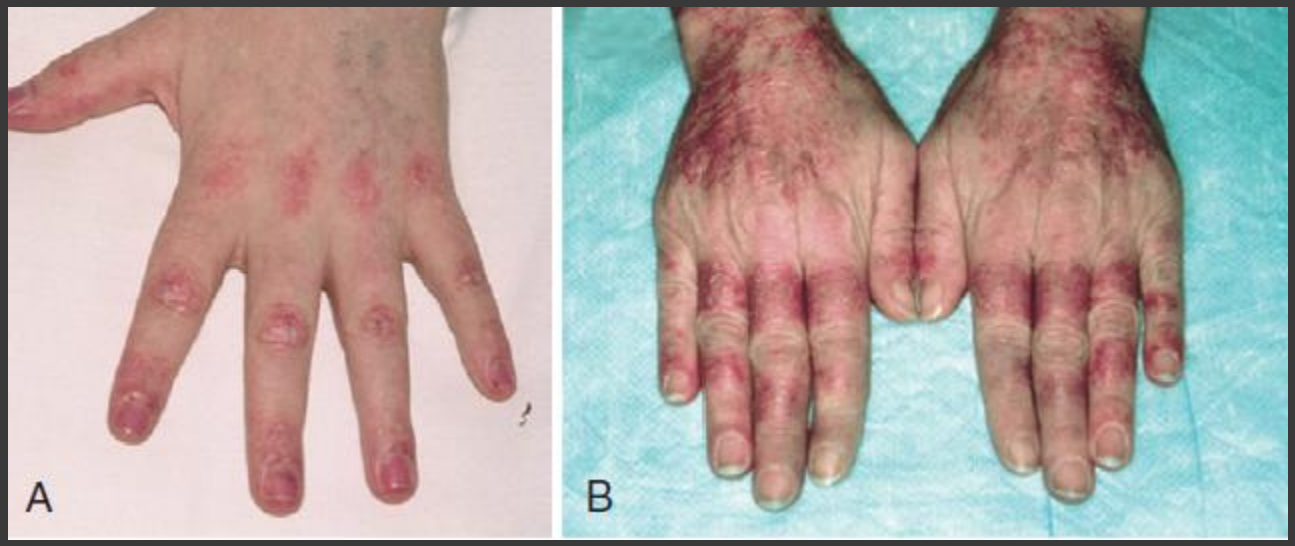


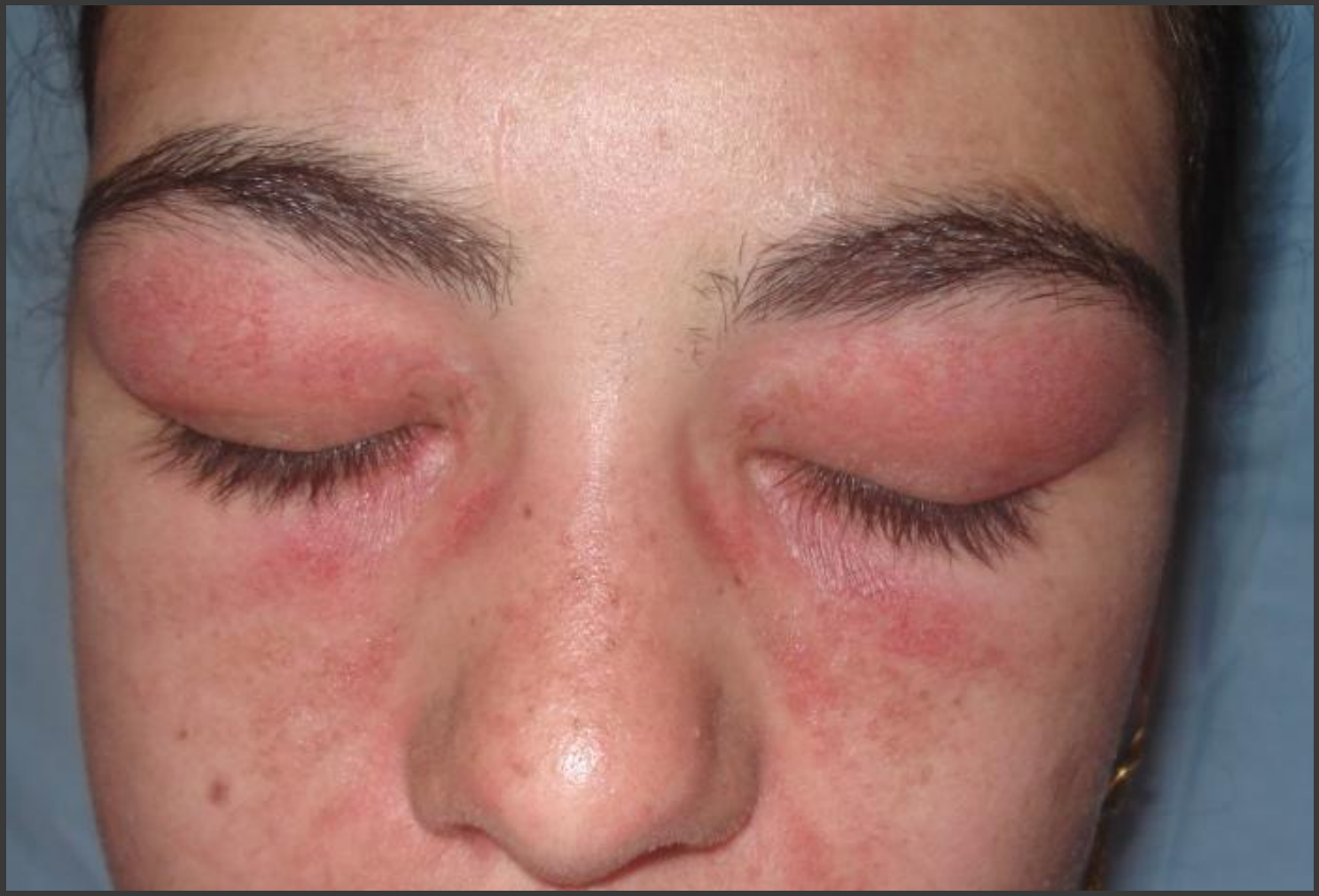


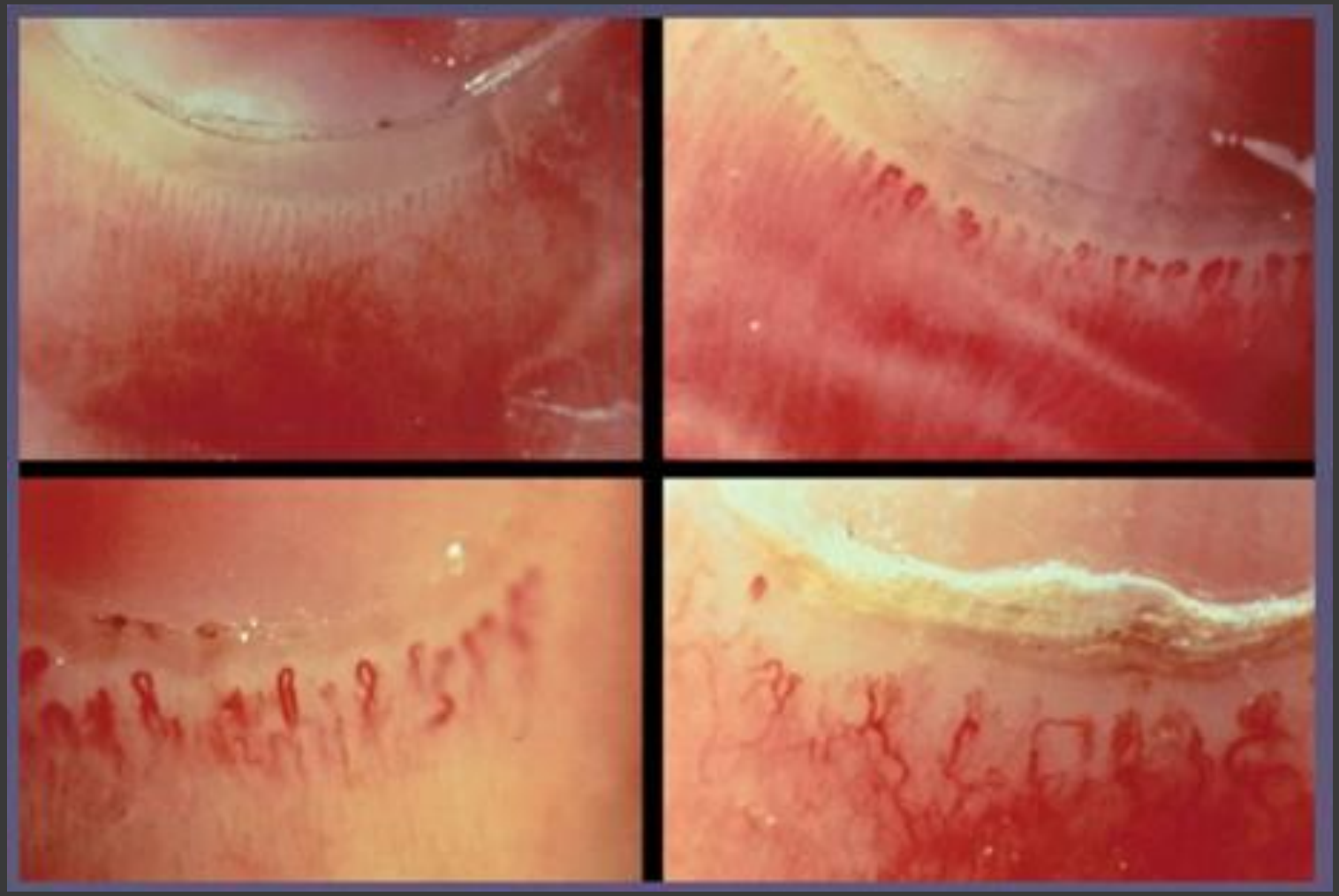
DM vs lupus

Dermatomyositis

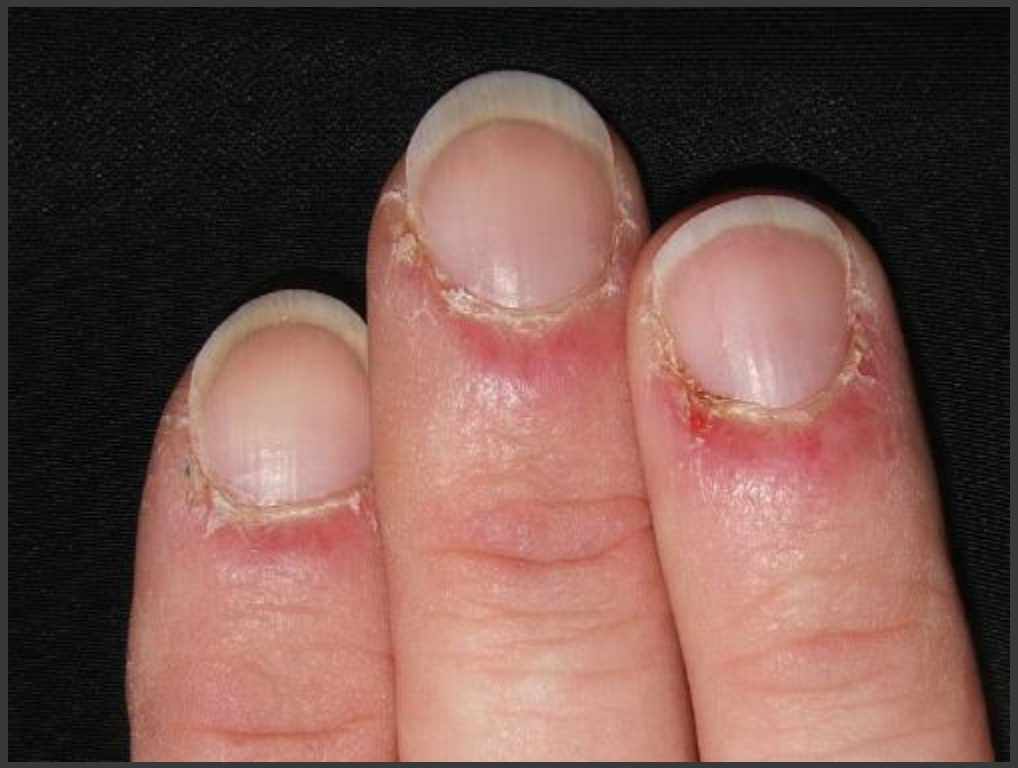
Lupus

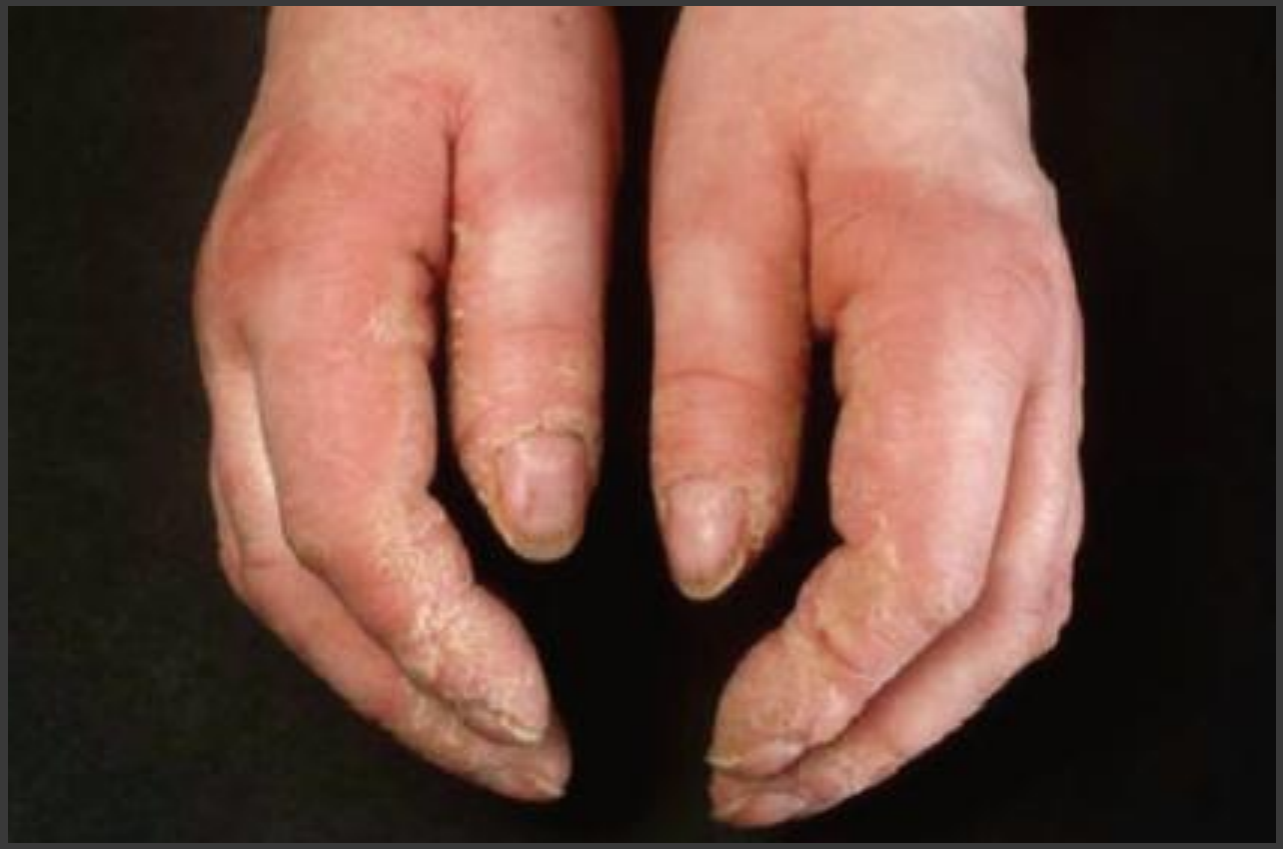


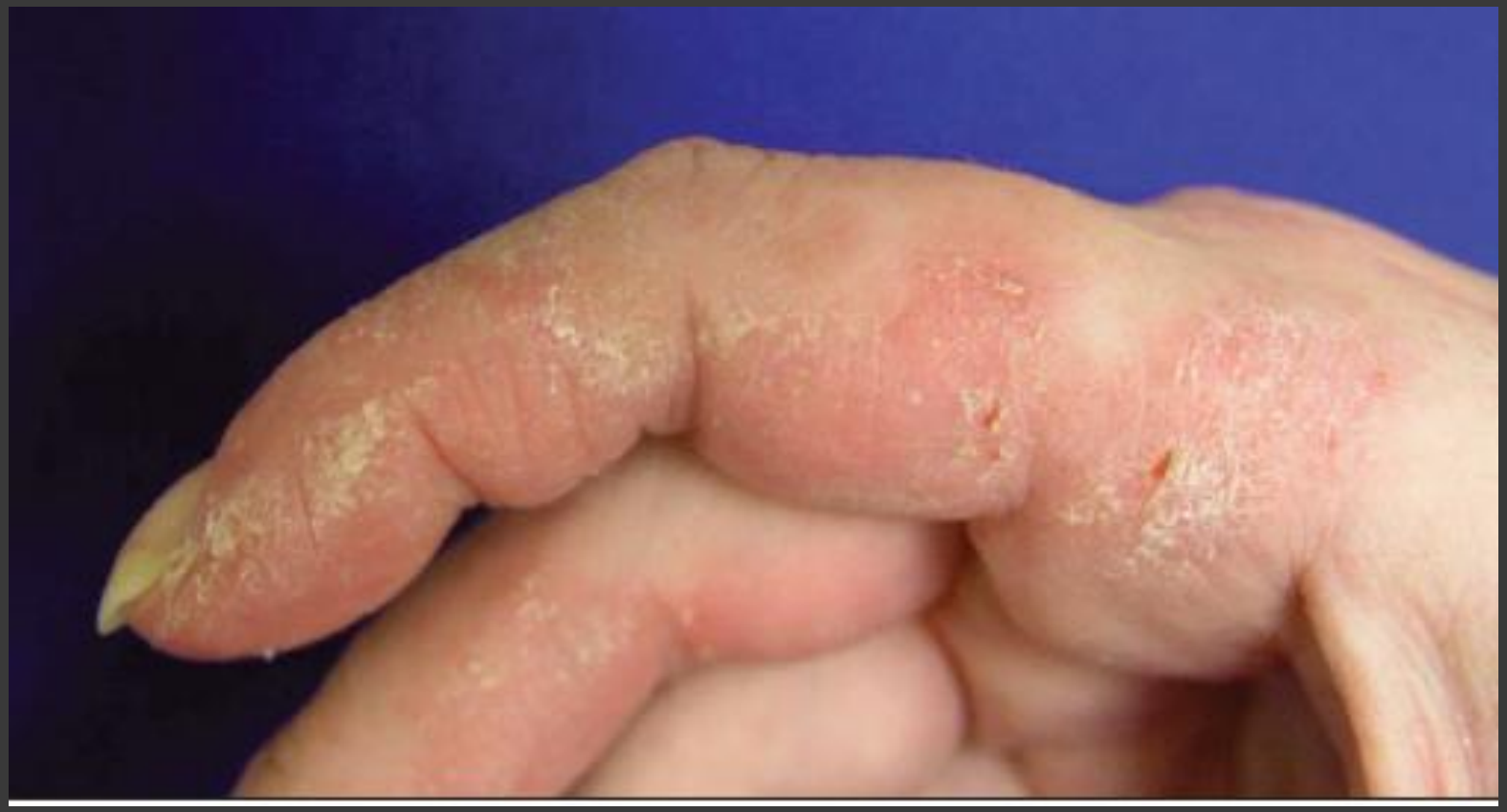




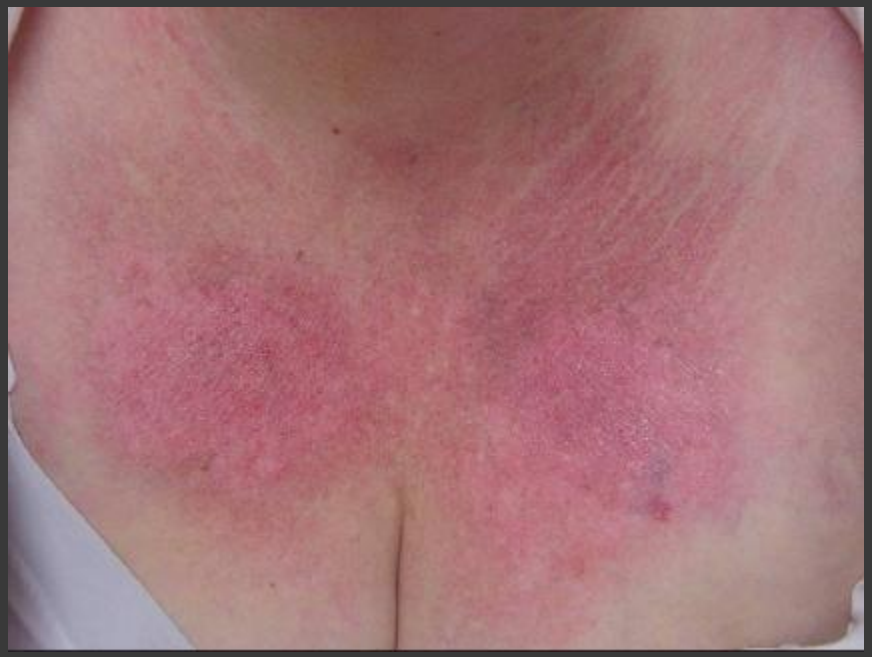
Cuticular overgrowth with periungual erythema and capillary dilatation



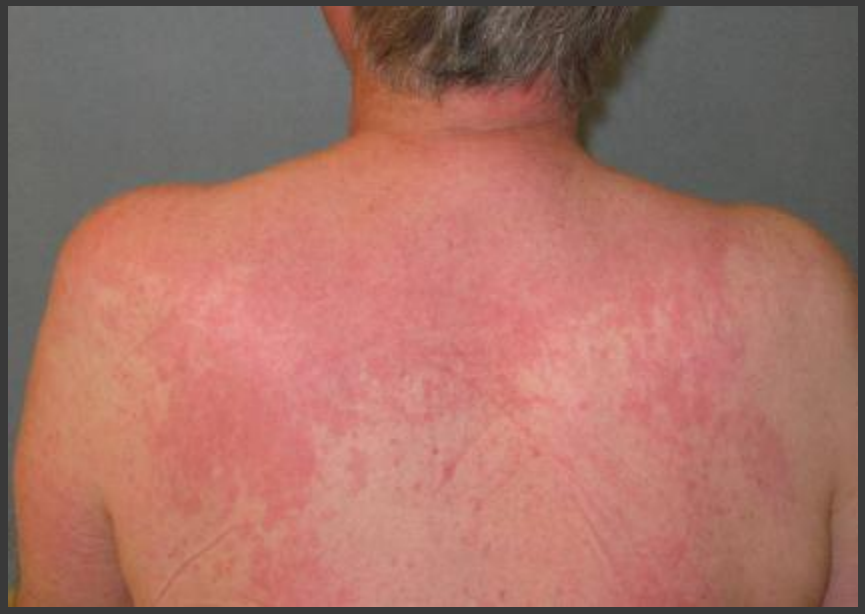




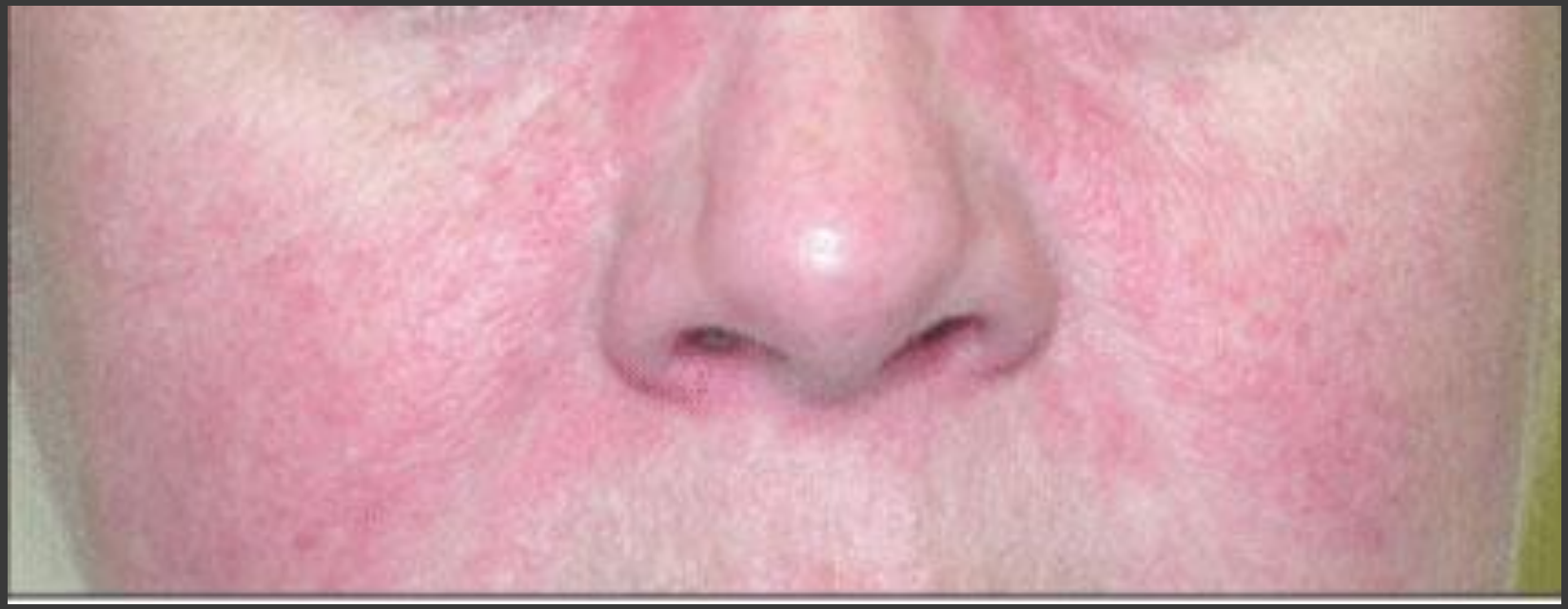
V sign

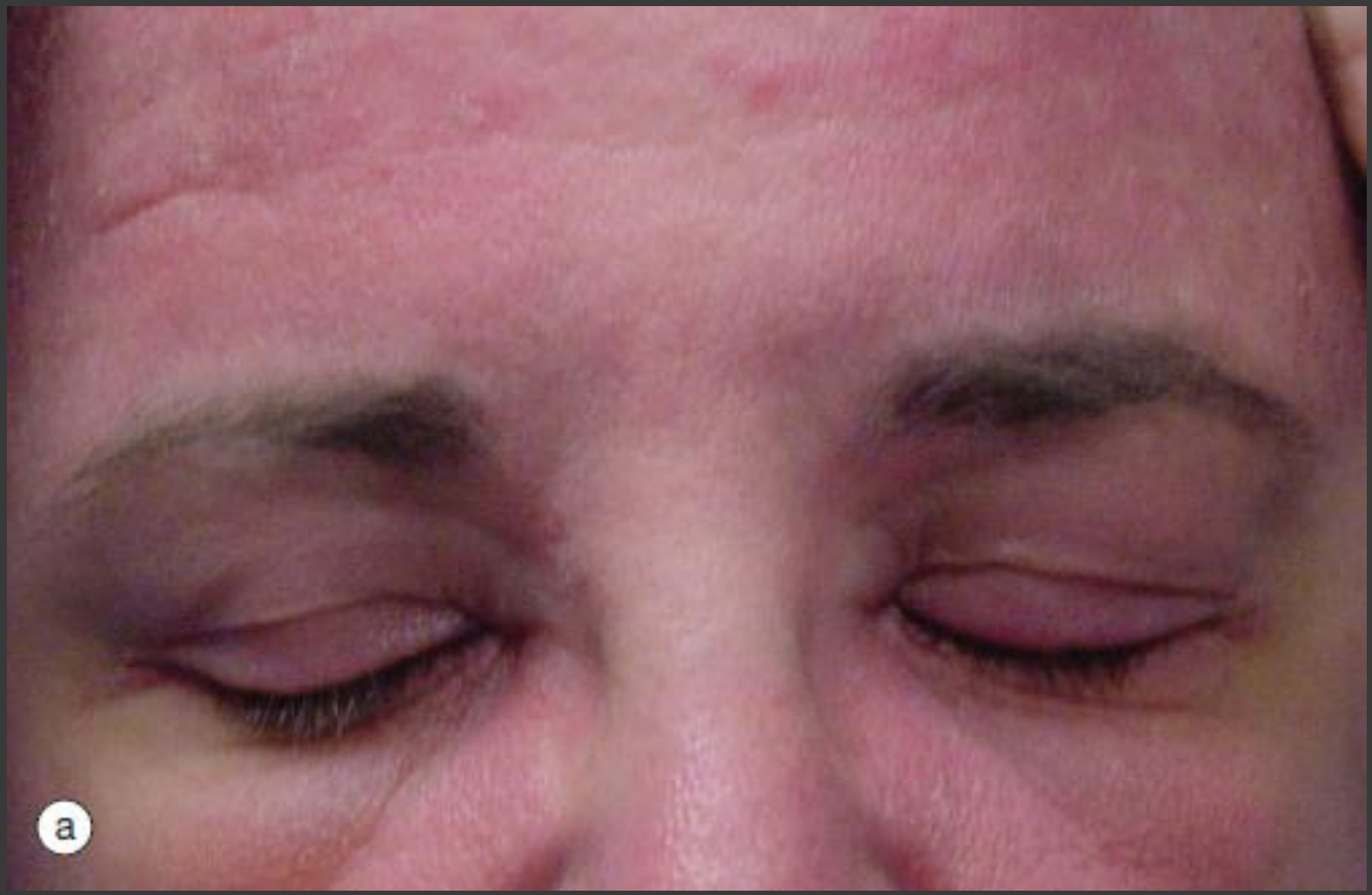


Shawl sign



Involvement of the nasolabial area and forehead distinguishes DM from SLE

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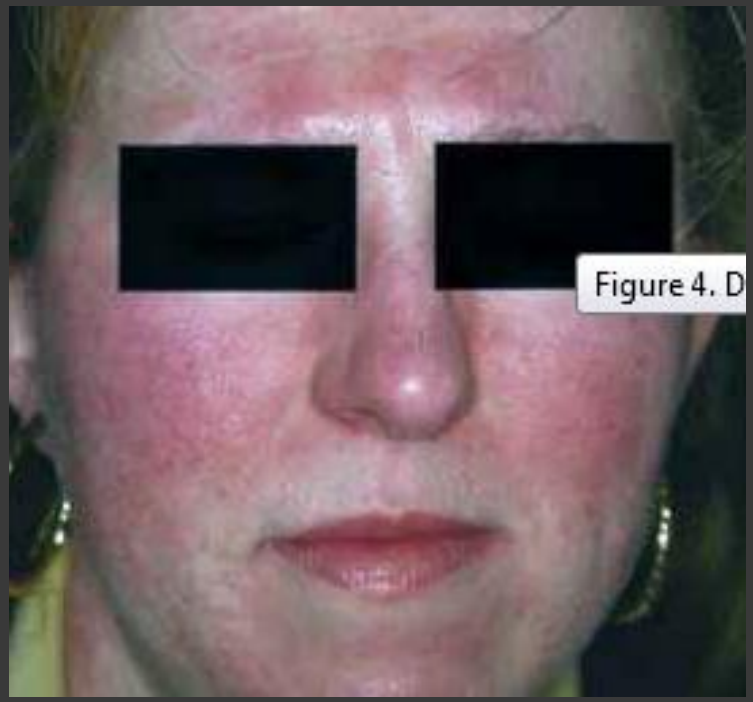
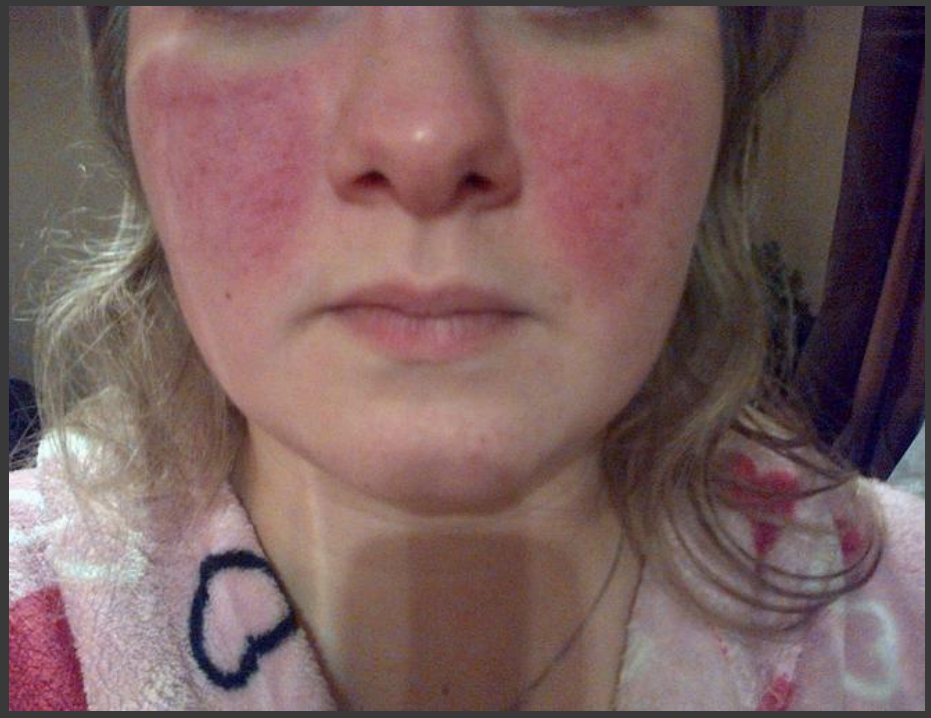
DM vs lupus

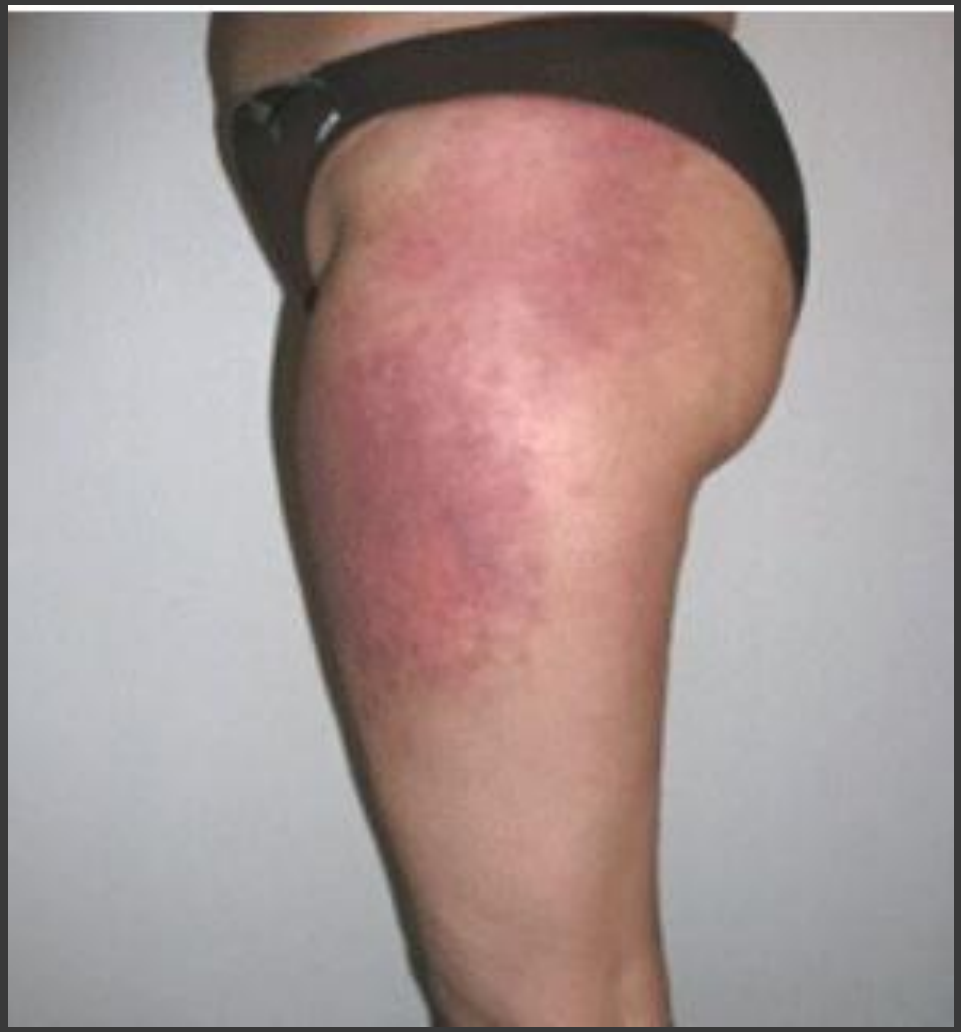
DM



Lupus

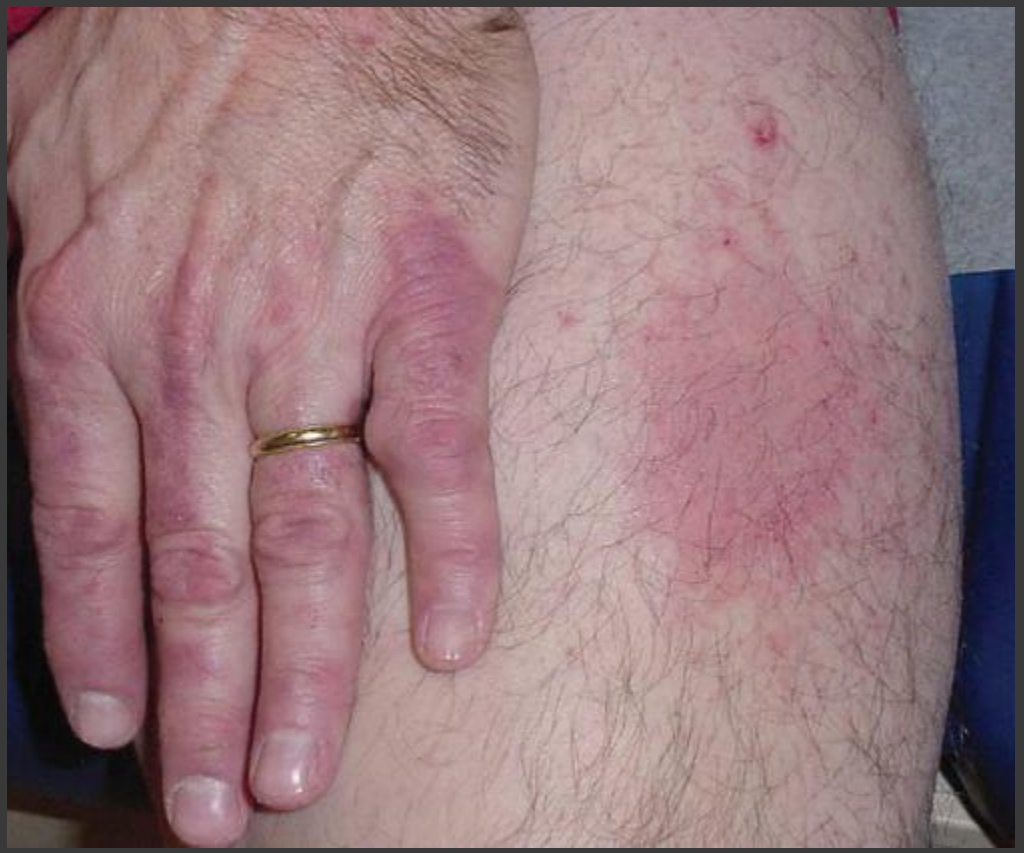


holster sign

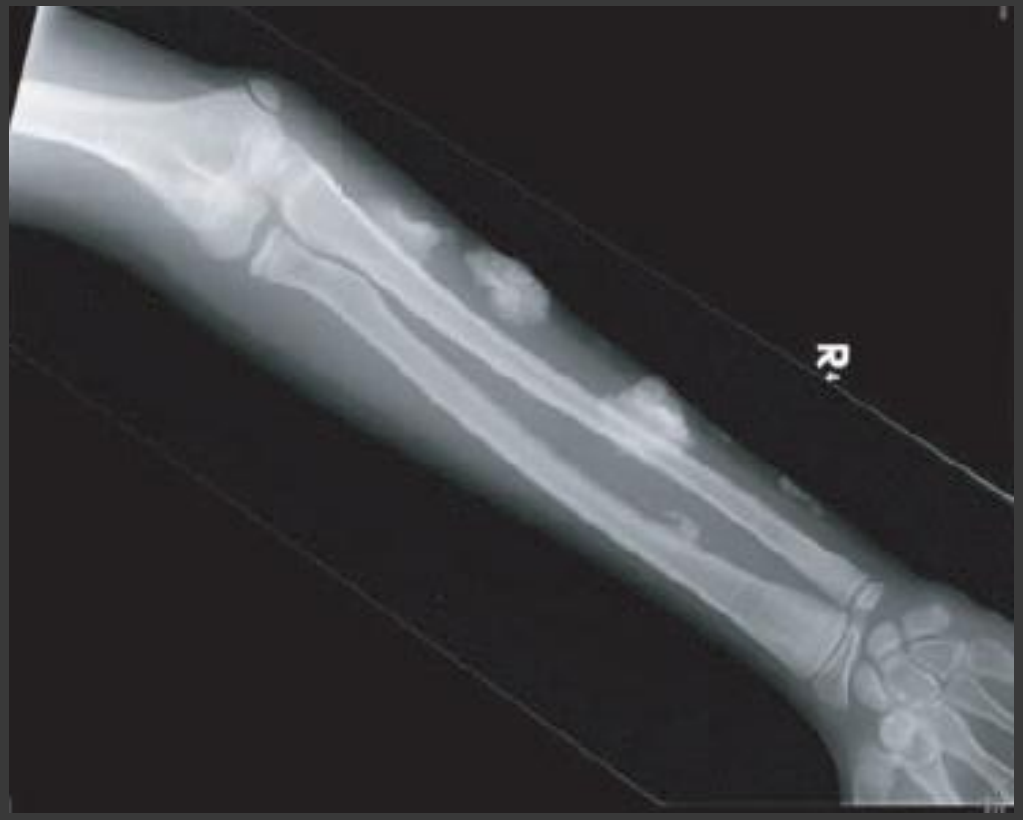


lateral surface of the thighs and hips

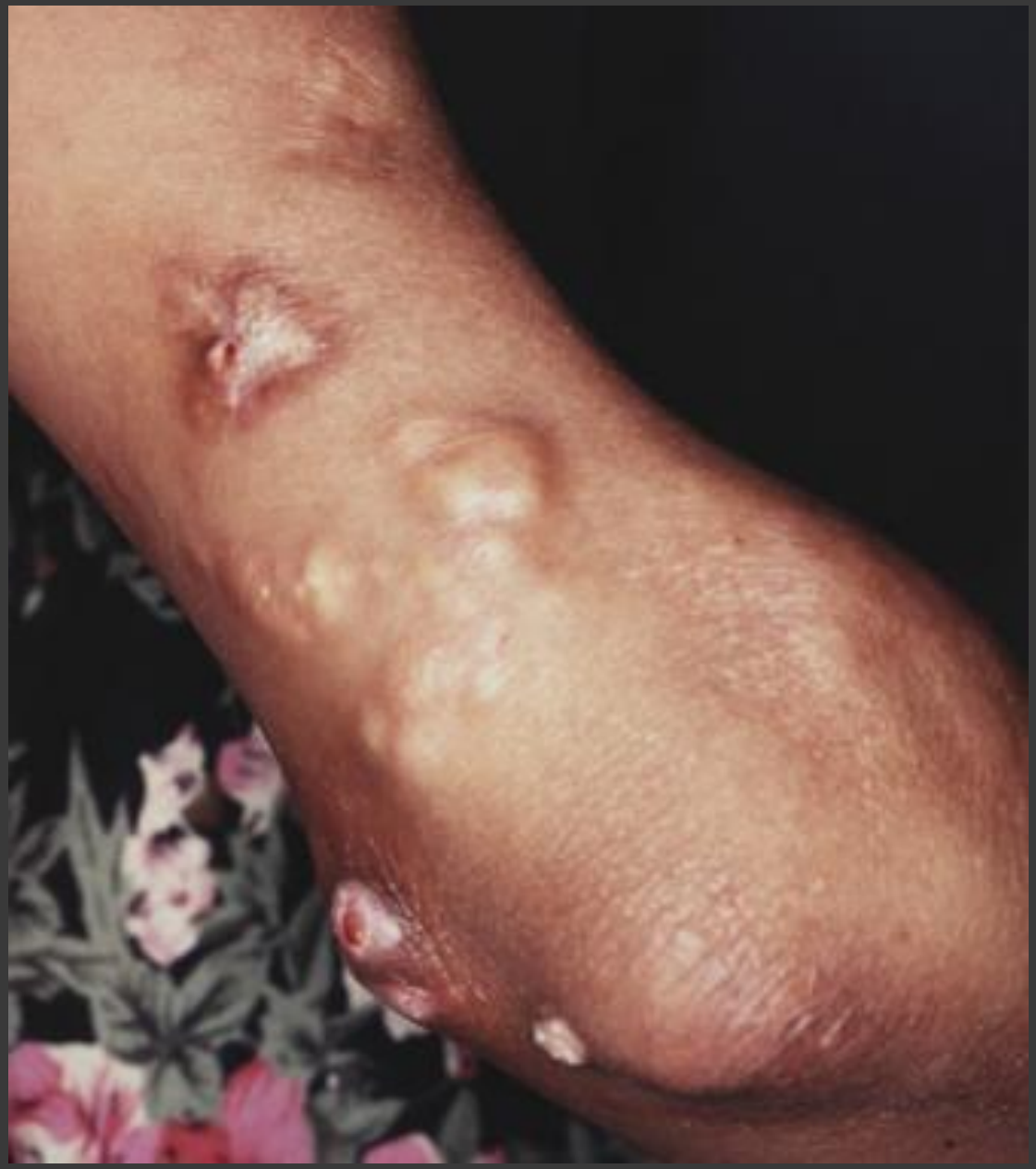
Holster sign erythema & Gottron erythema.

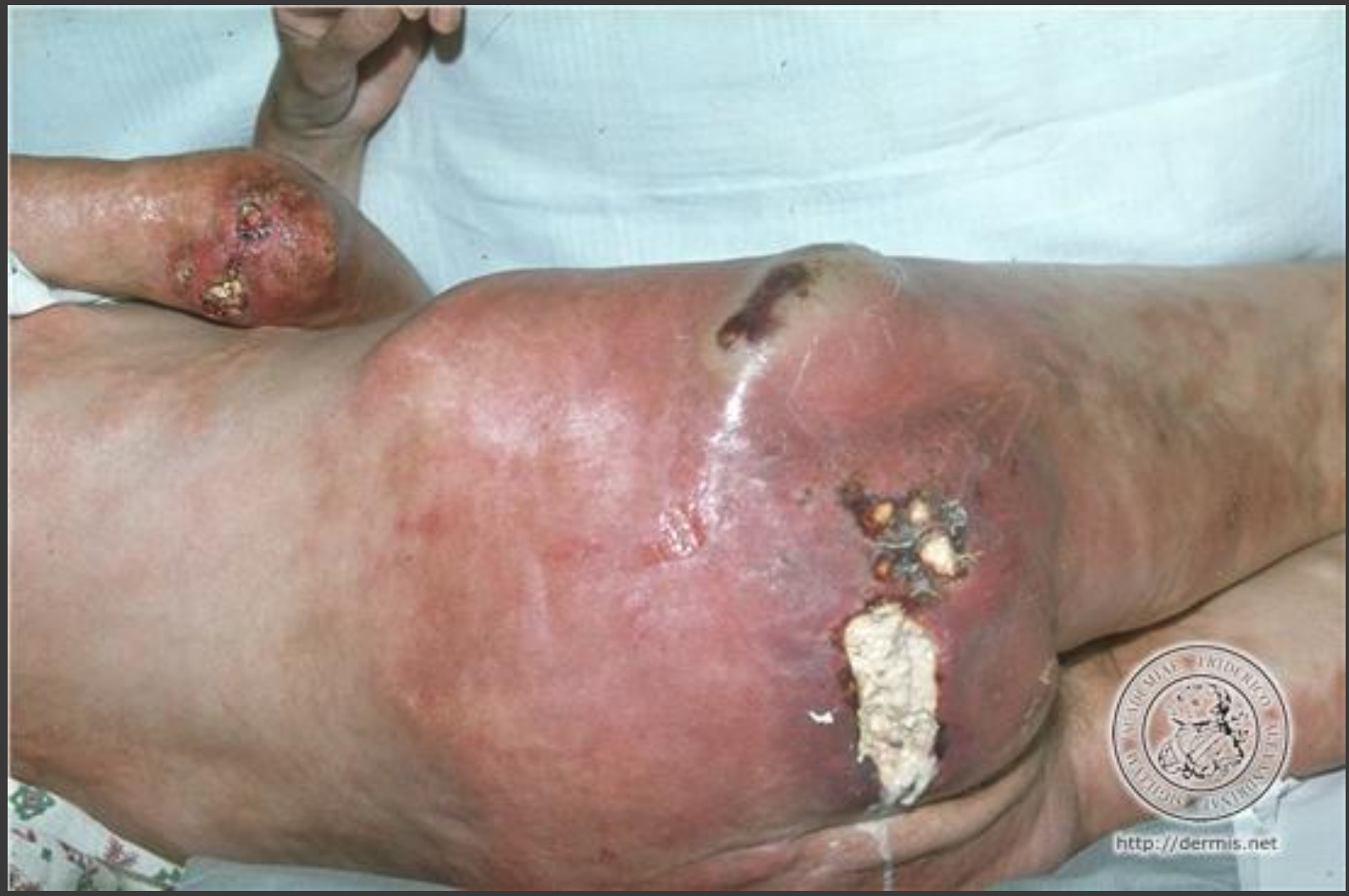


Calcinosis



Soft tissue calcification, which can be disabling, occurs most commonly in chronic, childhood-onset DM




http://dermis.net

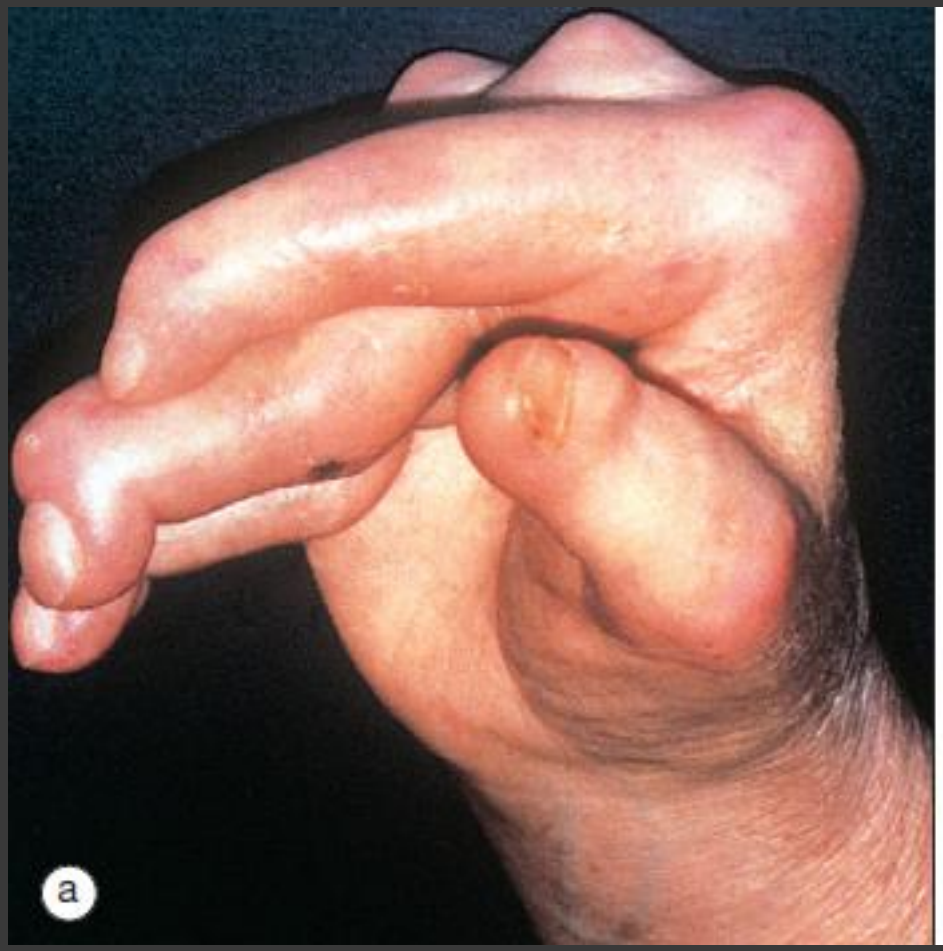
Muscle

- Weakness:
  - Insidious onset over 3-6 months
  - Symmetrical
  - Affects the large proximal muscles around the shoulders, hips, thighs, trunk, and neck.
  - Difficulty standing from a chair, getting out of a car, climbing stairs, raising the head off the pillow or combing hair.
  - No pain
  - There may be impairment of chewing or dysphagia.
  - Weakness of neck flexors
  - Early morning stiffness

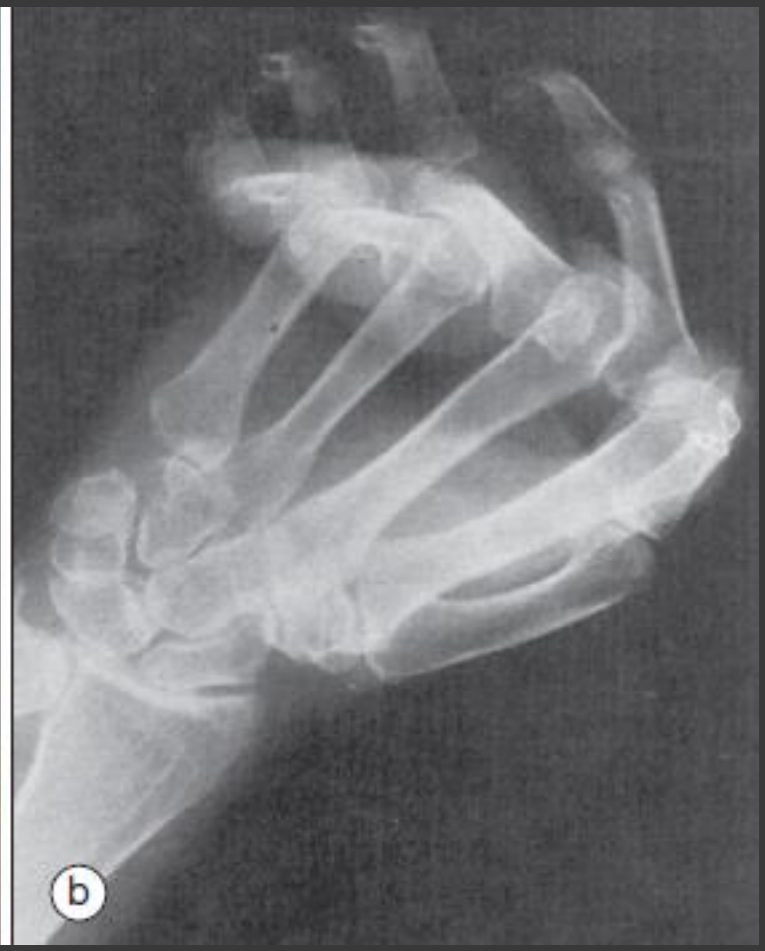
Joints

- Arthralgia
- Arthritis
- Rheumatoid-like
- Generally mild

Deforming arthropathy of polymyositis.



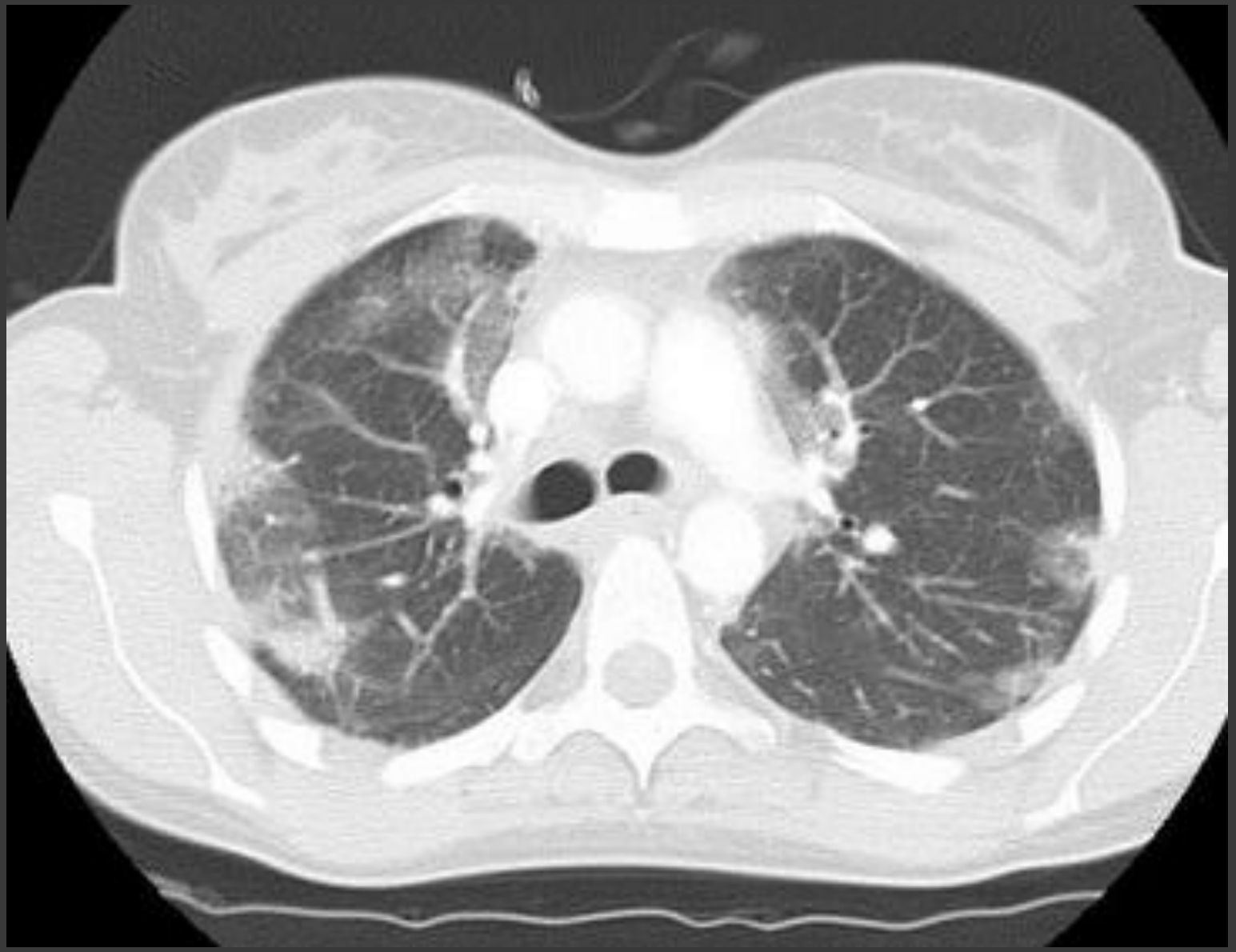
Rheumatoid-like deformities of the hand in a patient with anti-Jo-1 autoantibody.

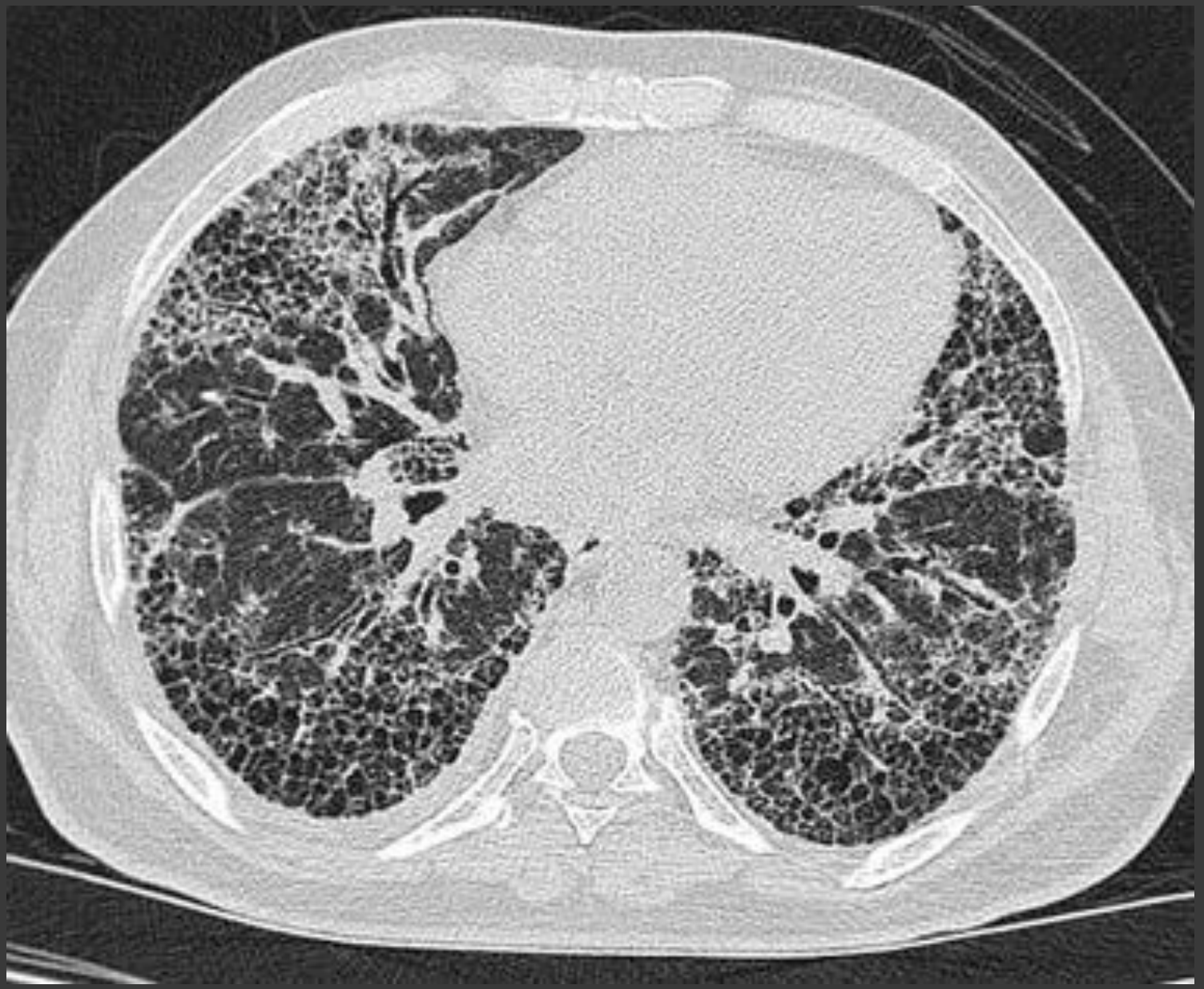


Radiograph hand, showing numerous subluxations but minimal bony erosive changes.

Lung

- Respiratory muscle weakness
- Interstitial lung disease





Heart

- Arrhythmias
- Myocarditis
- Pericardial effusions

GI tract

- Swallowing problems (upper dysphagia)
- If severe, aspiration of oral contents leads to chemical pneumonitis

Diagnosis

Diagnosis

- Muscle enzymes
- EMG
- Muscle biopsy
- Autoantibodies: JO-1, Mi-2, SRP
- MRI

Muscle enzymes

- CK, AST, ALT, LDH, aldolase
- There is a correlation between CK level and disease activity
- There is correlation between anti-Jo-1 titre and disease activity
- ESR & CRP do not correlate with disease activity or response to treatment

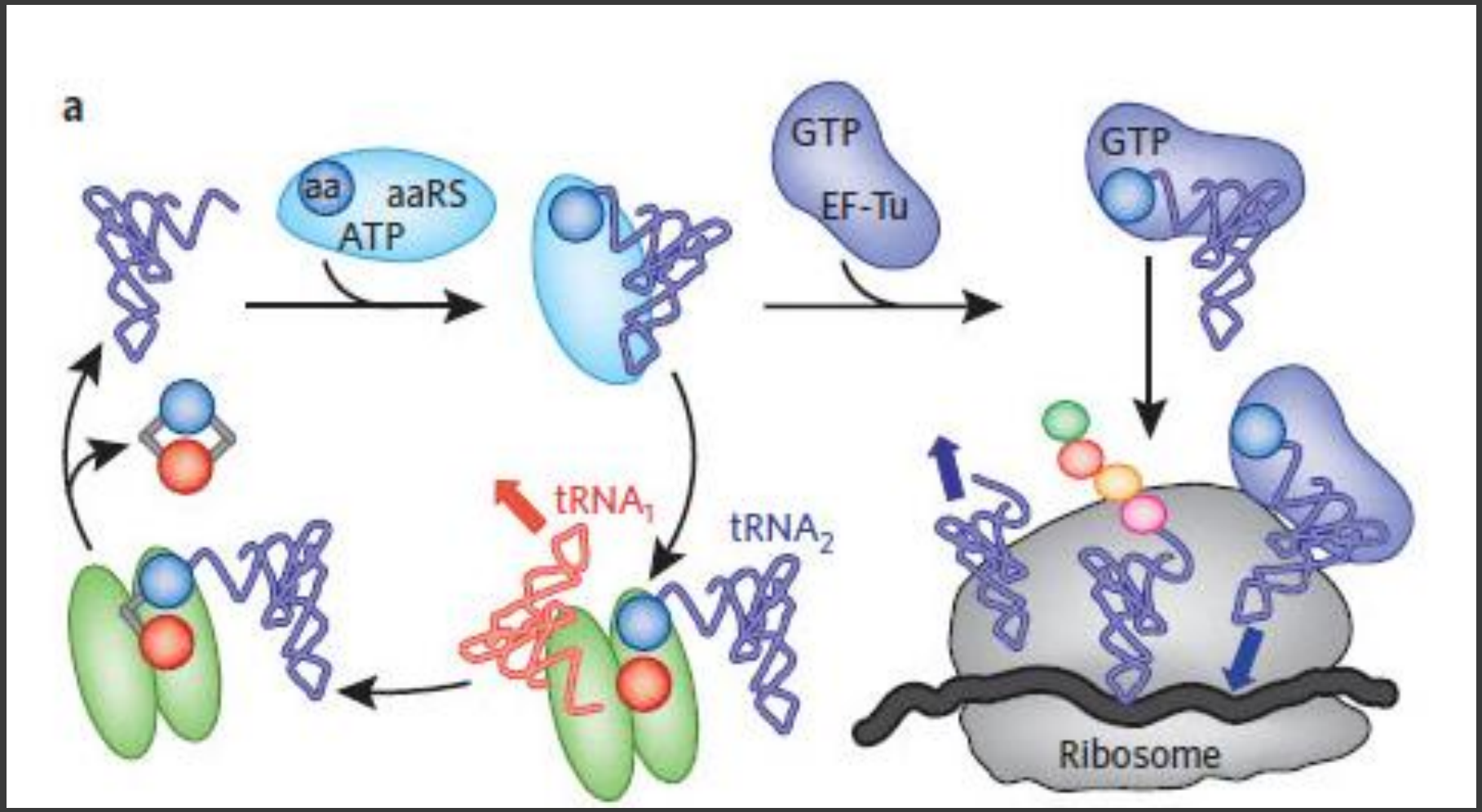
Causes of raised CK

- **1.** Strenuous exercise
- **2.** Muscle trauma
  - **(a)** Injury
  - **(b)** EMG
  - **(c)** Surgery
- **3.** Diseases affecting muscle
  - **(a)** Myositis
  - **(b)** Metabolic
  - **(c)** Dystrophies
  - **(d)** Myocardial infarction
  - **(e)** Rhabdomyolysis
- **4.** Drugs
  - colchicine, steroids , statins
- **5.** Endocrine and metabolic abnormalities
  - **(a)** Hypothyroidism
  - **(b)** Hypokalaemia
- **6.** Normal
  - **(a)** Ethnic group
  - **(b)** Increased muscle mass
  - **(c)** Technical artefact

Autoantibodies

– **Myositis-specific antibodies :**

- Antisynthetase
  - –Jo-1: Histidyl-tRNA synthetase
- SRP: Signal recognition particle
- Mi-2: Nucleosome remodelling complex


a
aa
aaRS
ATP
GTP
EF-Tu
GTP
tRNA1
tRNA2
Ribosome

Anti-synthetase syndrome

- 25% of PM and DM patients have antibodies to an aminoacyl-tRNA synthetase (JO-1)

- **Clinical features:**
  - PM/DM
  - ILD
  - Arthritis
  - Raynaud's phenomenon
  - Fever
  - mechanic's hands.

Anti-SRP

- Polymyositis
- cardiac involvement
- resistance to treatment.

Anti-Mi-2

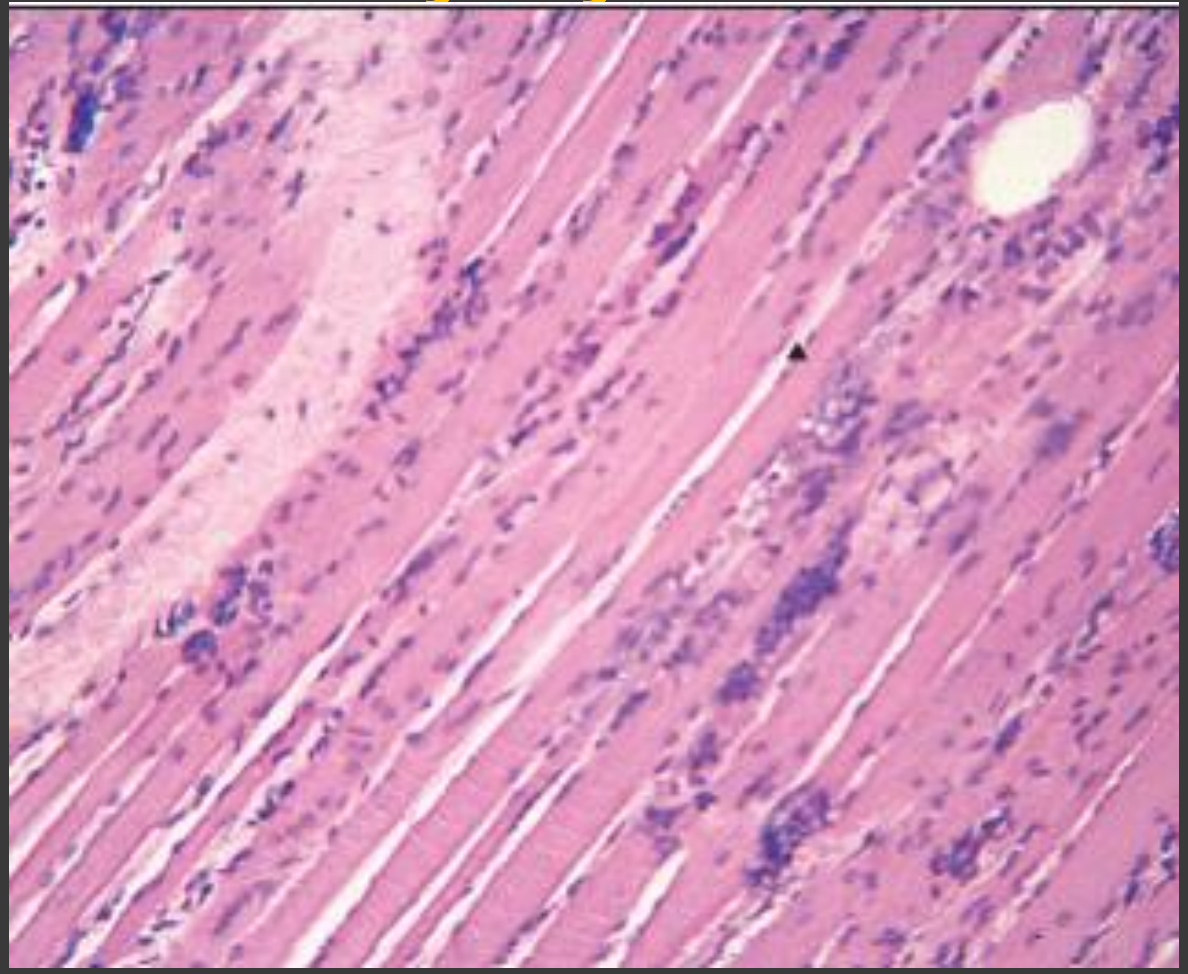
- DM with V sign or shawl sign.
- Good prognosis.

Pathology

- **PM: Cell-mediated**
  - cellular immune attack on muscle fibres is a prominent pathogenetic process in PM. CD8+ T-cells are abundant in the **endomysial** areas
- **DM: humoral**
  - There is intense B-cell and CD4+ T-cell infiltrate in the **perivascular** area, suggesting a local humoral response

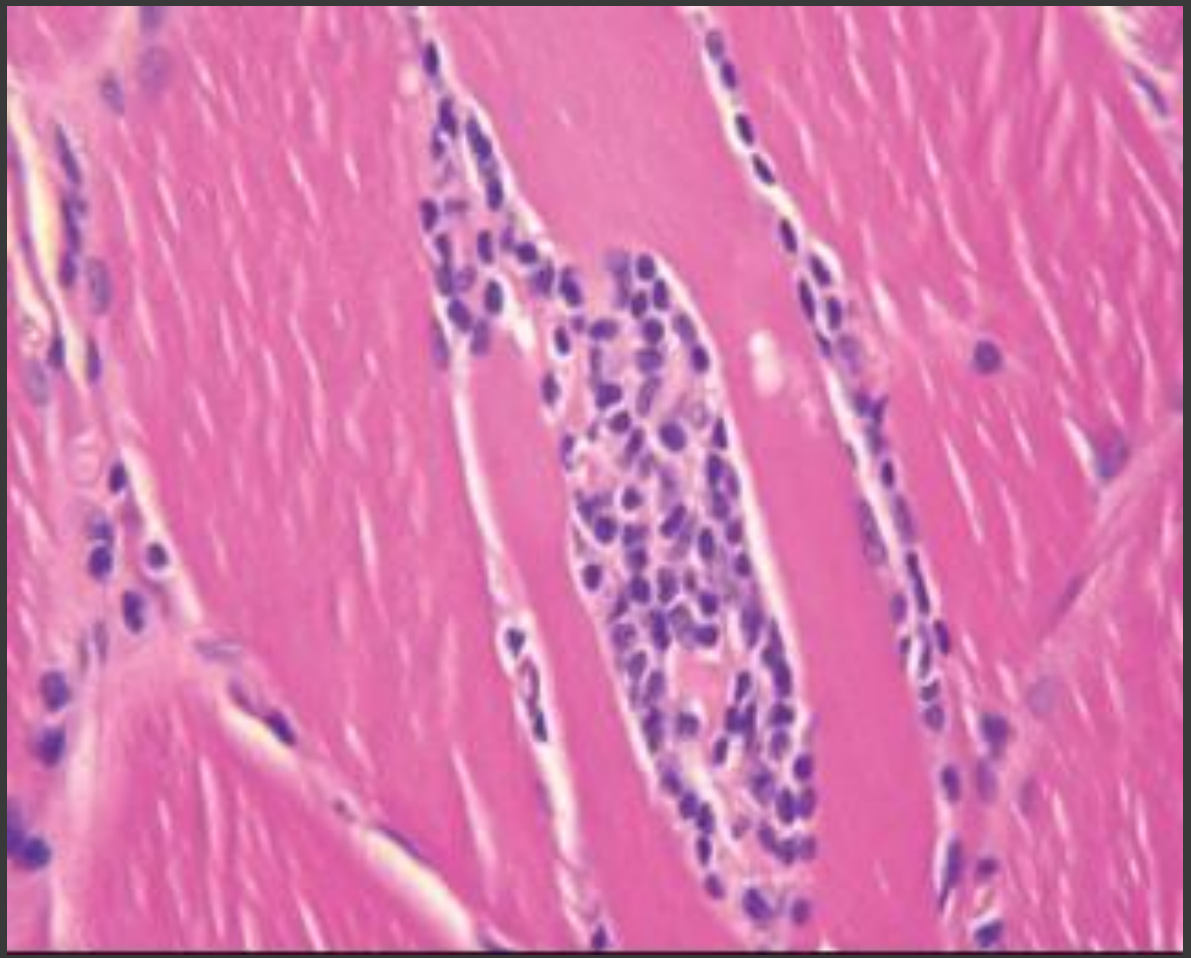
- In PM, inflammatory infiltrates more often predominate in the **endomysial** area around the muscle fibres

Polymyositis

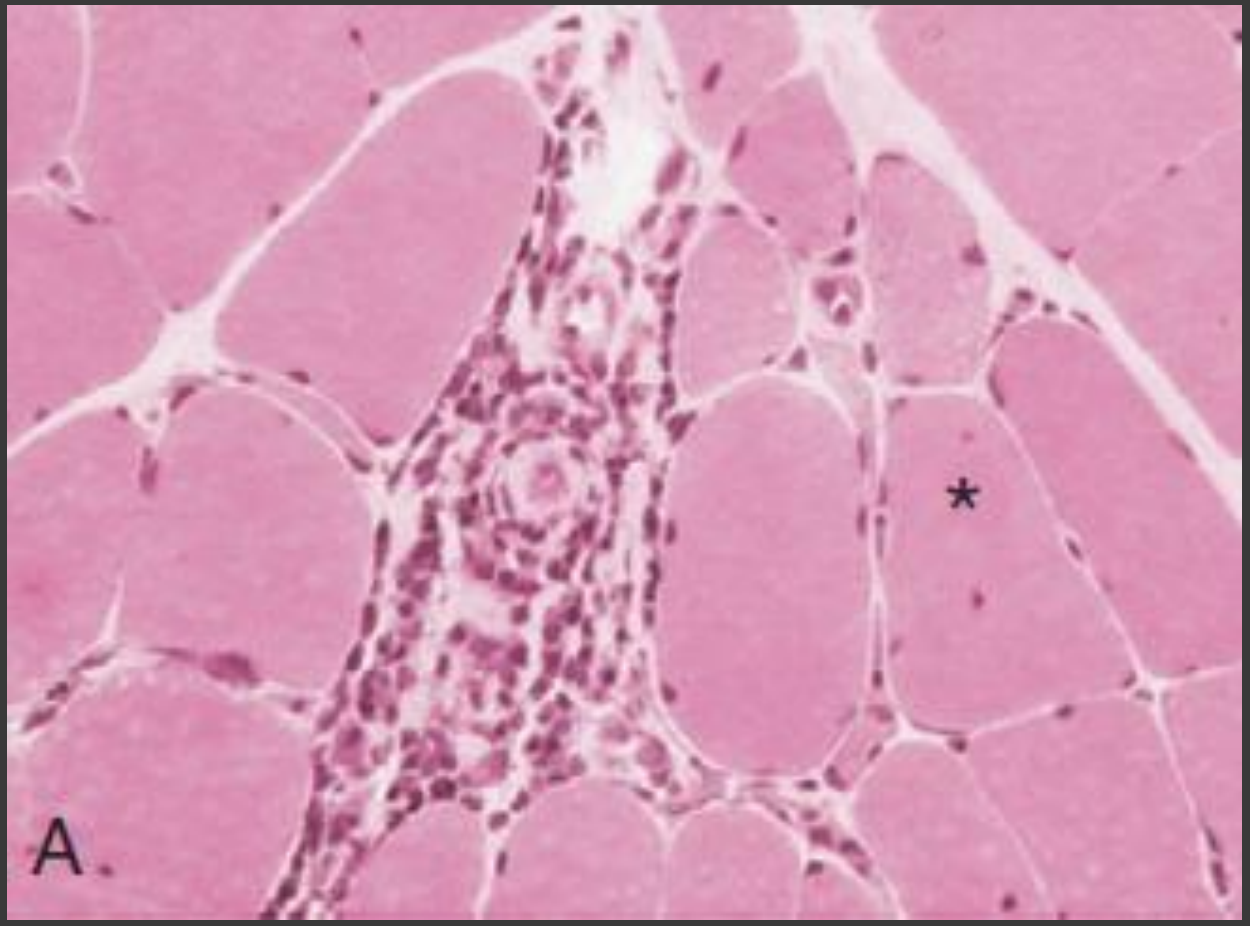


The arrow indicates an area of degeneration and necrosis of myofibers in association with interstitial lymphocytic and histiocytic cellular infiltration

Polymyositis



lymphocytic invasion of non-necrotic myofiber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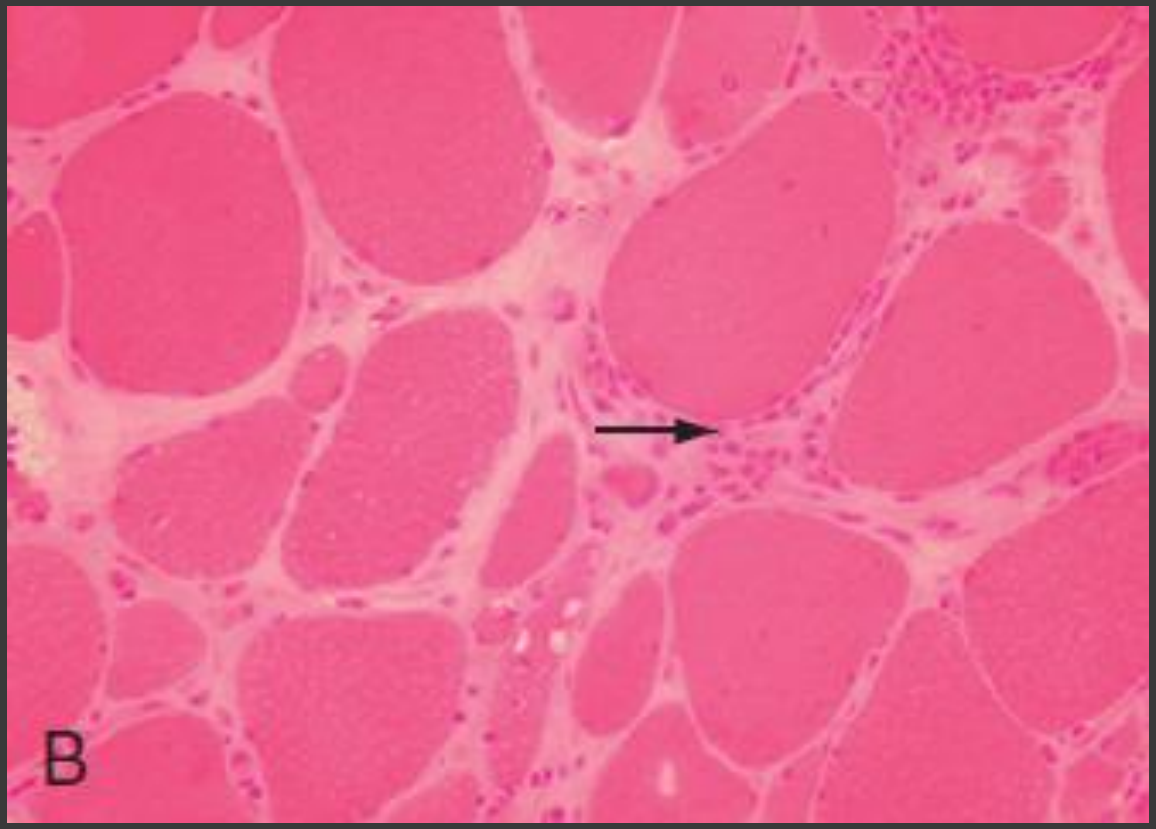
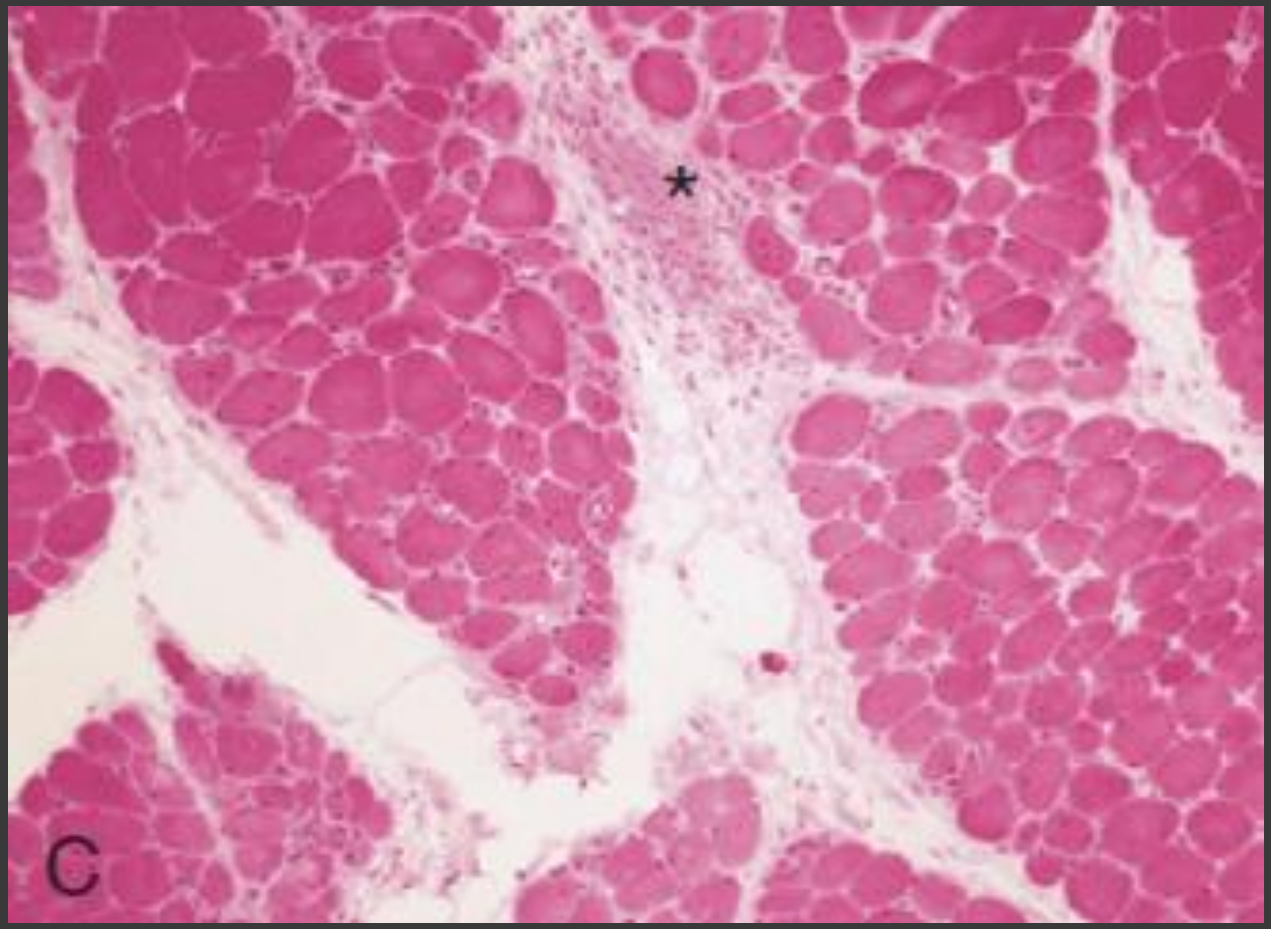
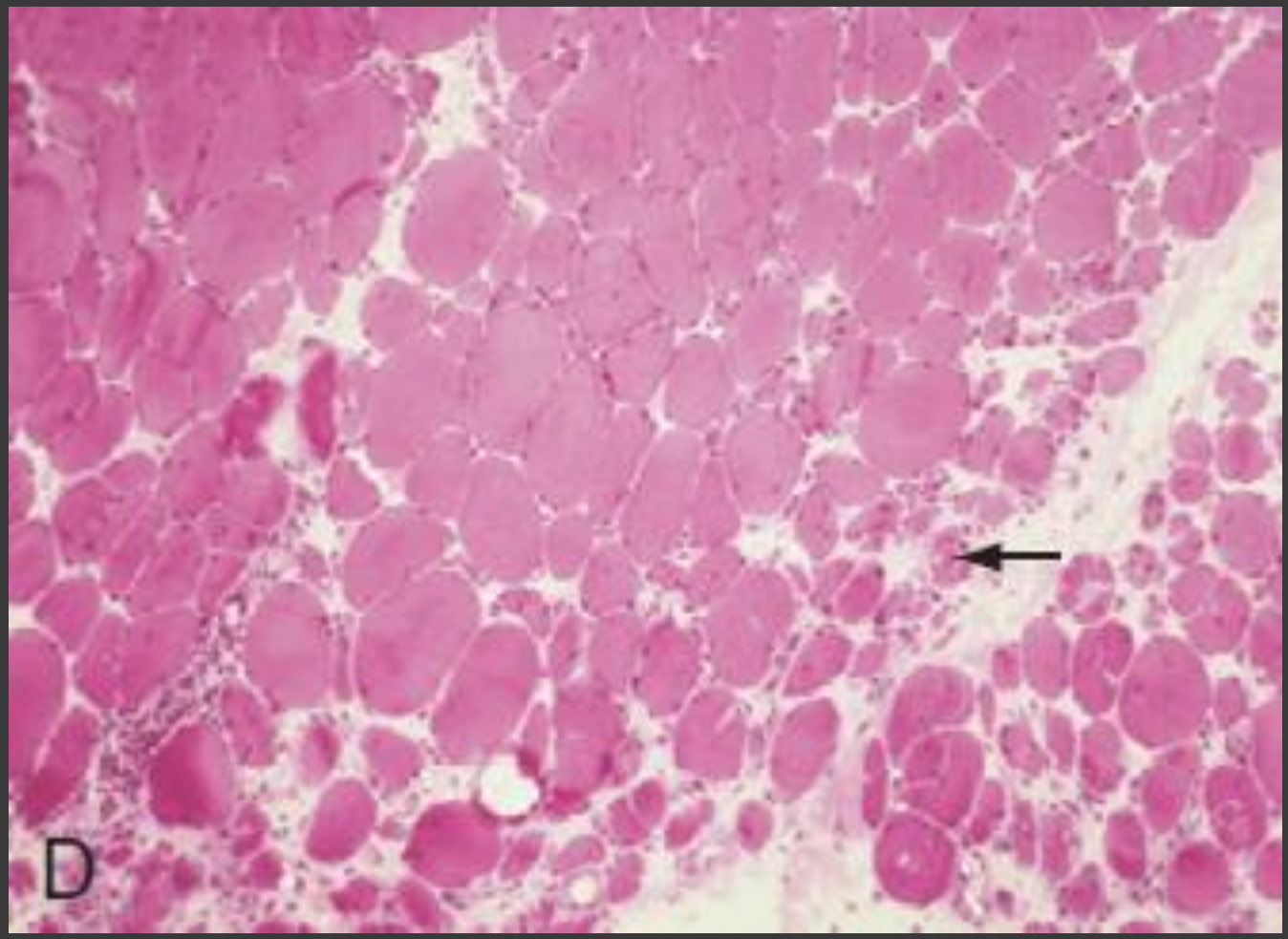


endomysial distribution
inflammatory cellular infiltrates CD8+ T cells and macrophages

- In DM, infiltration predominates in the **perimysial** area (around the fascicles) and around small blood vessels

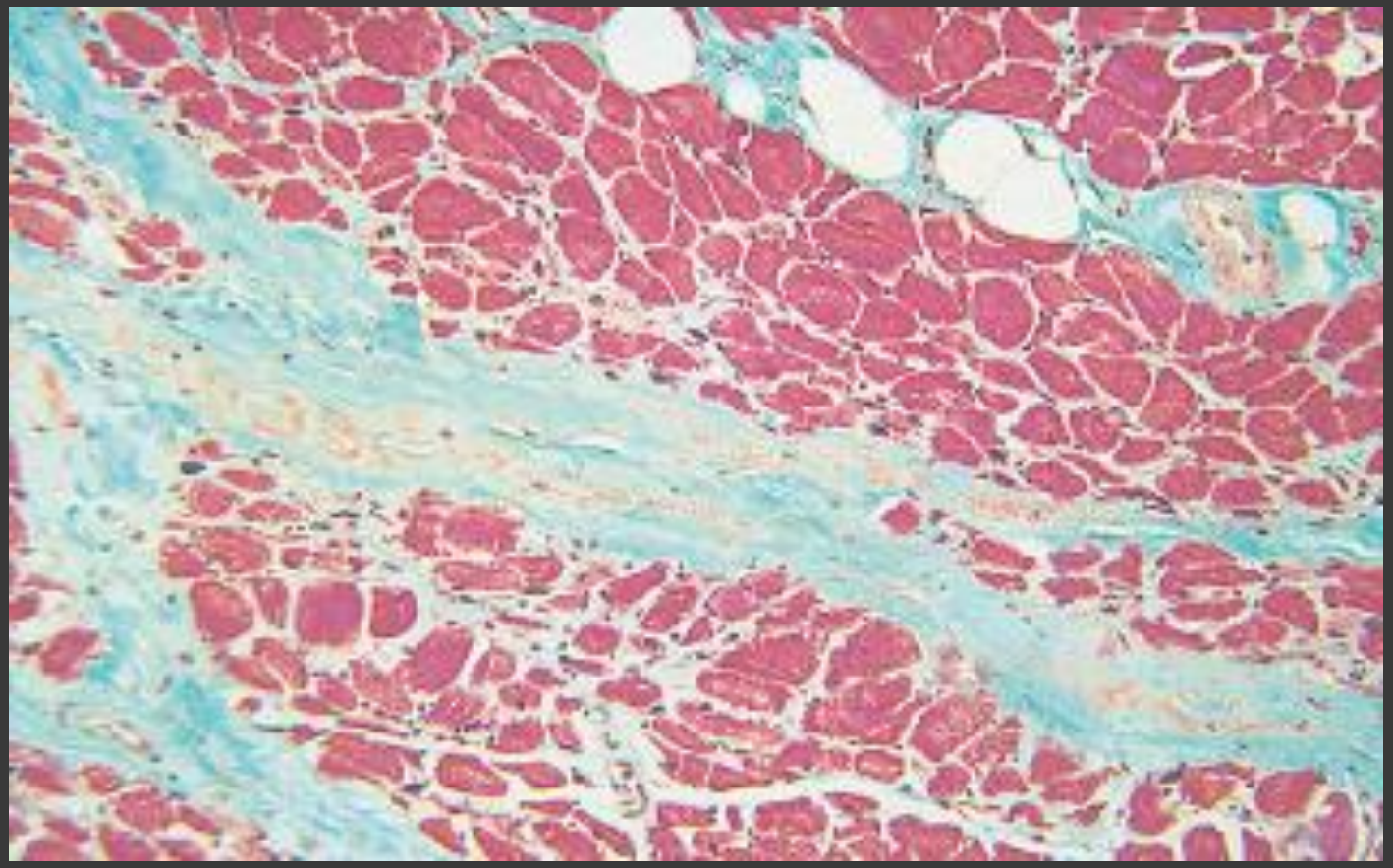


perimysial
largely made up of CD4+ T cells, macrophages, and dendritic cells



Perifascicular atrophy

dermatomyositis

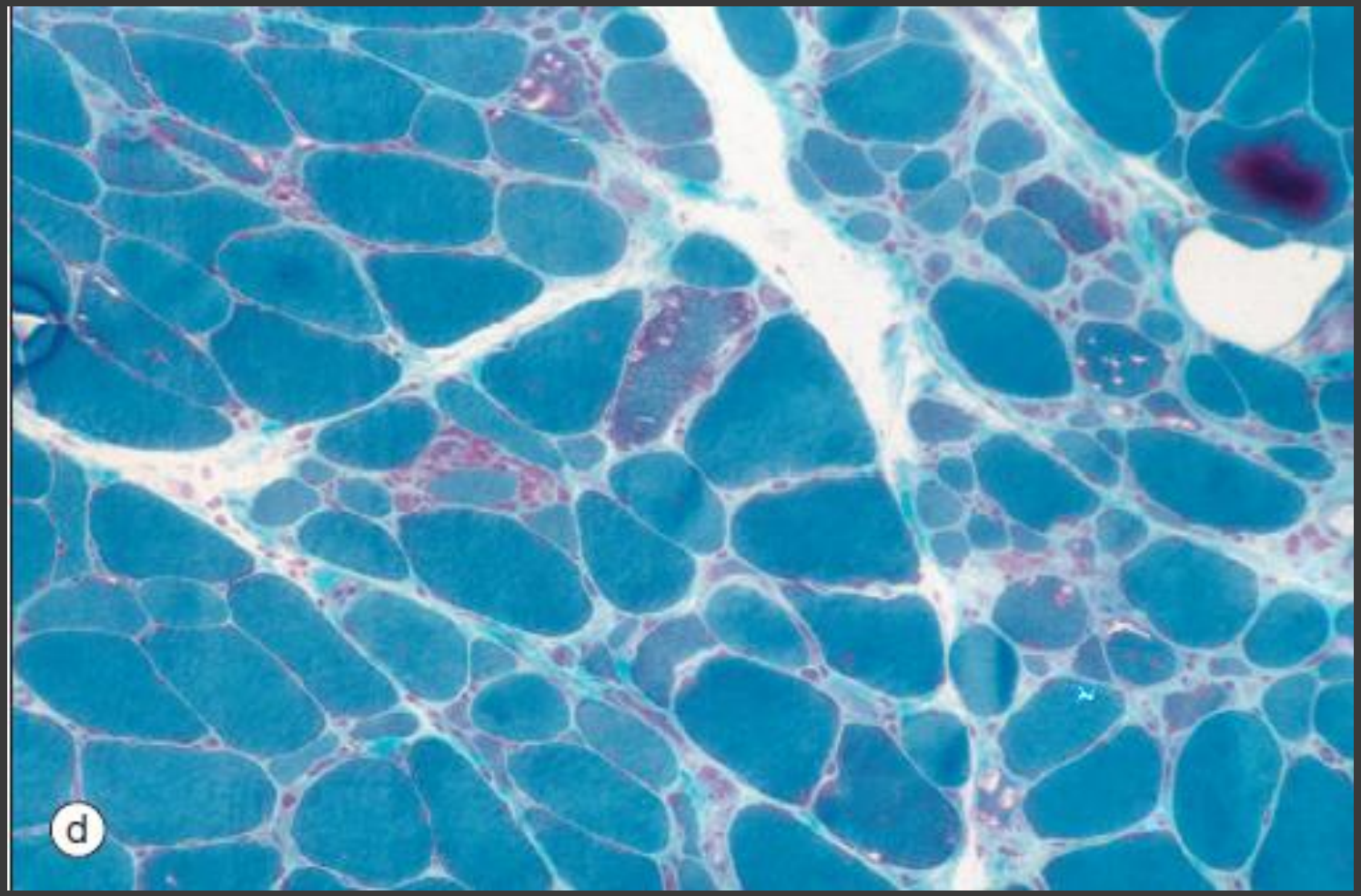


atrophic, small fibers in the periphery of the fascicles (perifascicular atrophy) and the increase in fibrous tissue separating bundles of myofibers

Inclusion body myositis

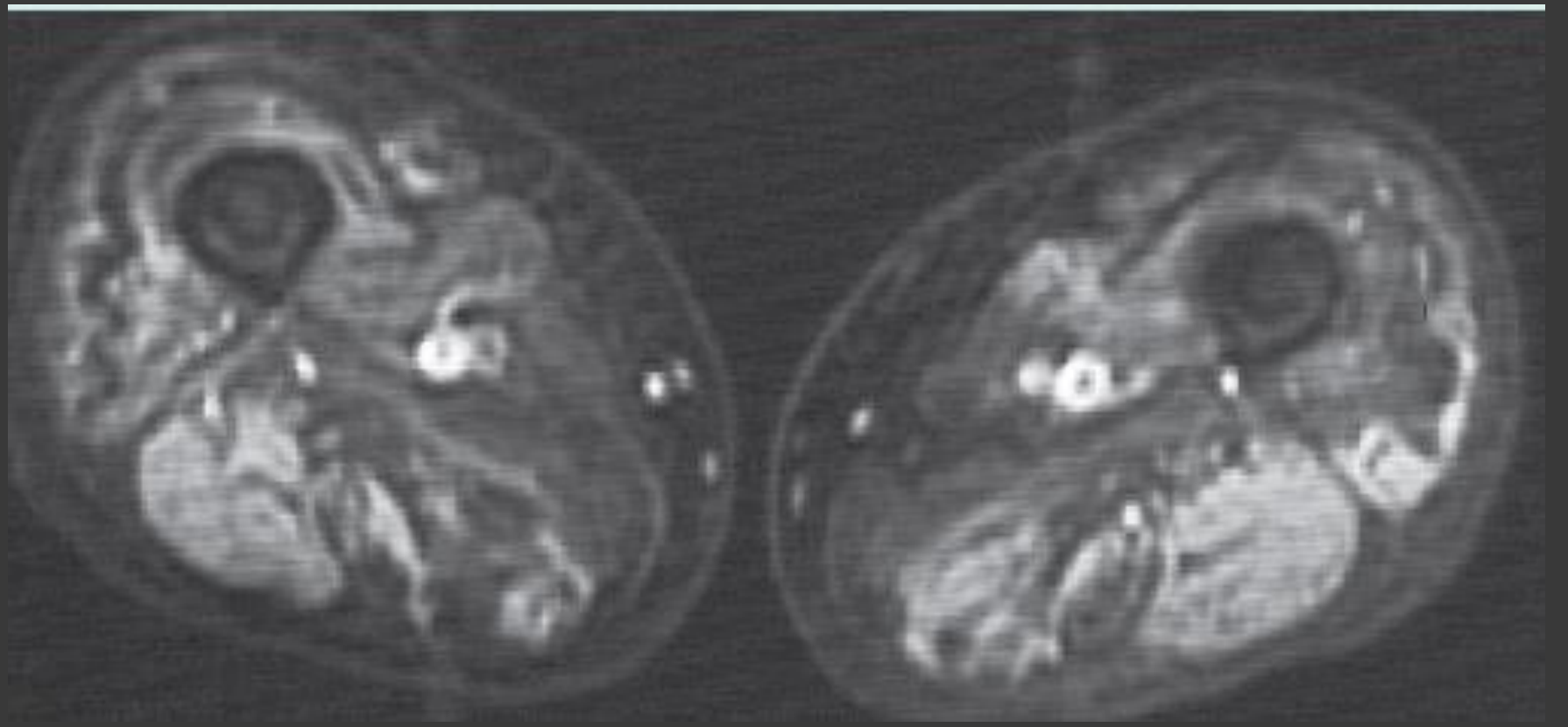
- Begins after age 50
- It is 2-3-fold more common in males.
- onset is insidious
- Distal weakness is common
- Weakness of quadriceps & arm flexors
- Light microscopy: vacuoles rimmed by basophilic material, and small, eosinophilic cytoplasmic, and nuclear inclusions
- Diagnosis is confirmed by electron microscopy or trichrome stain
- Patients do not respond to treatment

IBM

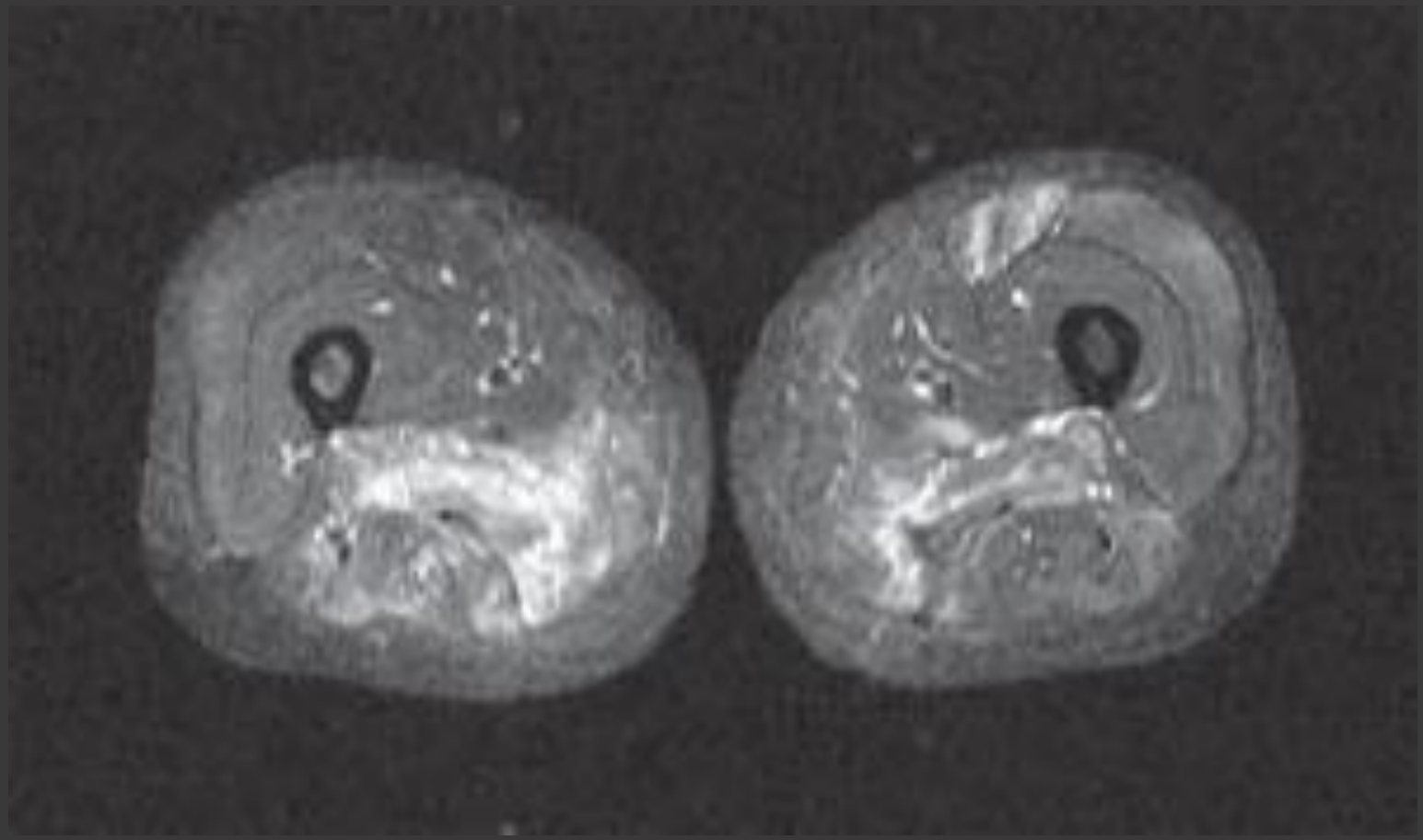


Red-rimmed vacuoles (trichrome stain)

Radiology



MRI (STIR technique):
Inflammation shows up as bright areas



Overlap Syndromes

- Association of inflammatory myopathies with connective tissue diseases
- Eg patients with DM who also have manifestations of systemic sclerosis such as sclerotic thickening of the dermis, contractures, esophageal hypomotility, microangiopathy, and calcium deposits
- Patients with the overlap of DM and systemic sclerosis may have anti-PM/Scl antibody

Treatment

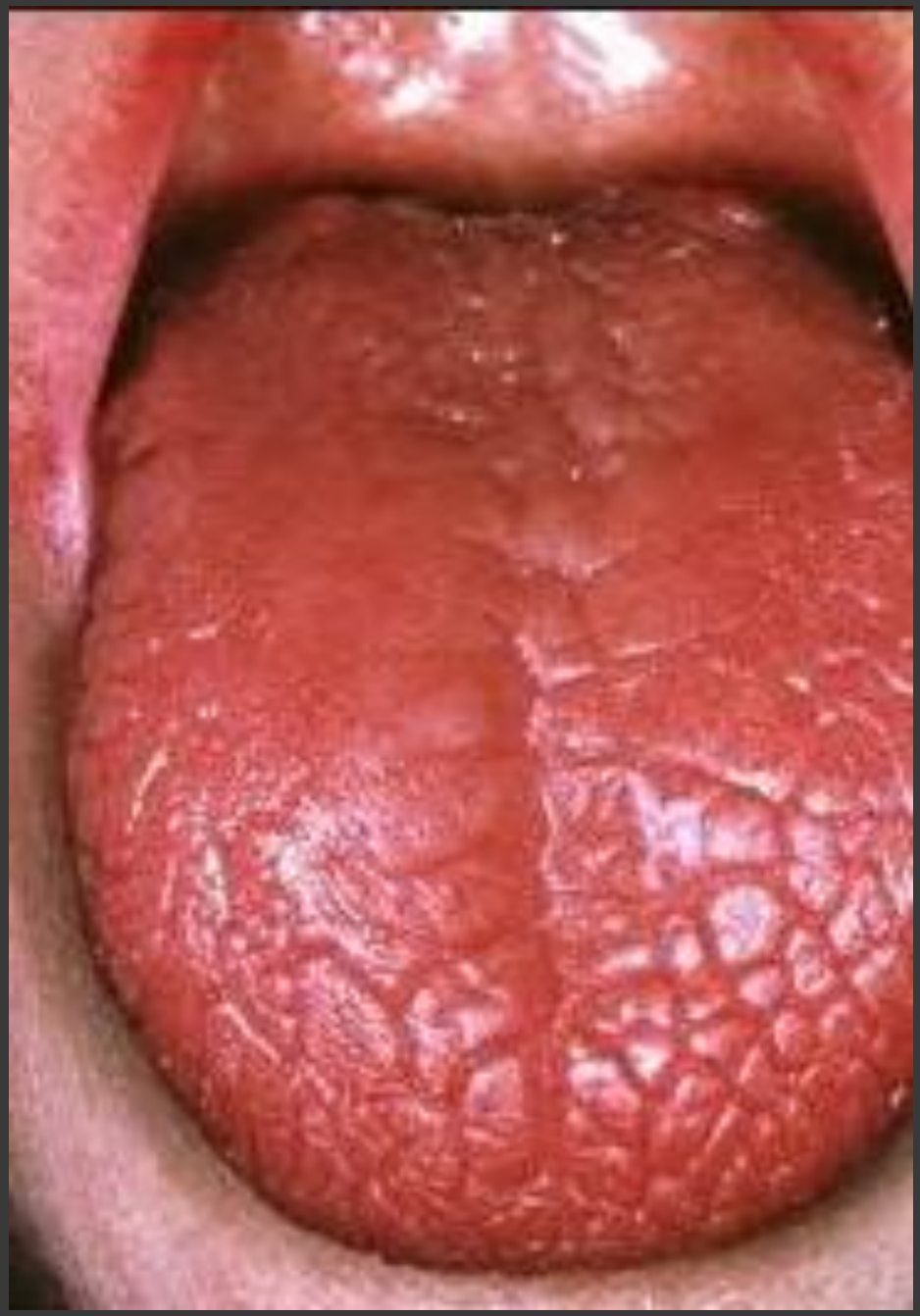
- Corticosteroids
- **Indications for immunosuppressive agents:**
  - (i) failure to respond to high-dose steroids
  - (ii) persistent disease activity after prolonged therapy despite initial improvement
  - (iii) inability to taper the steroids without recurrence
  - (iv) severe steroid side-effects.
- MTX and azathioprine are the immunosuppressives used most in myositis.
- Duration of therapy is 18-24 months

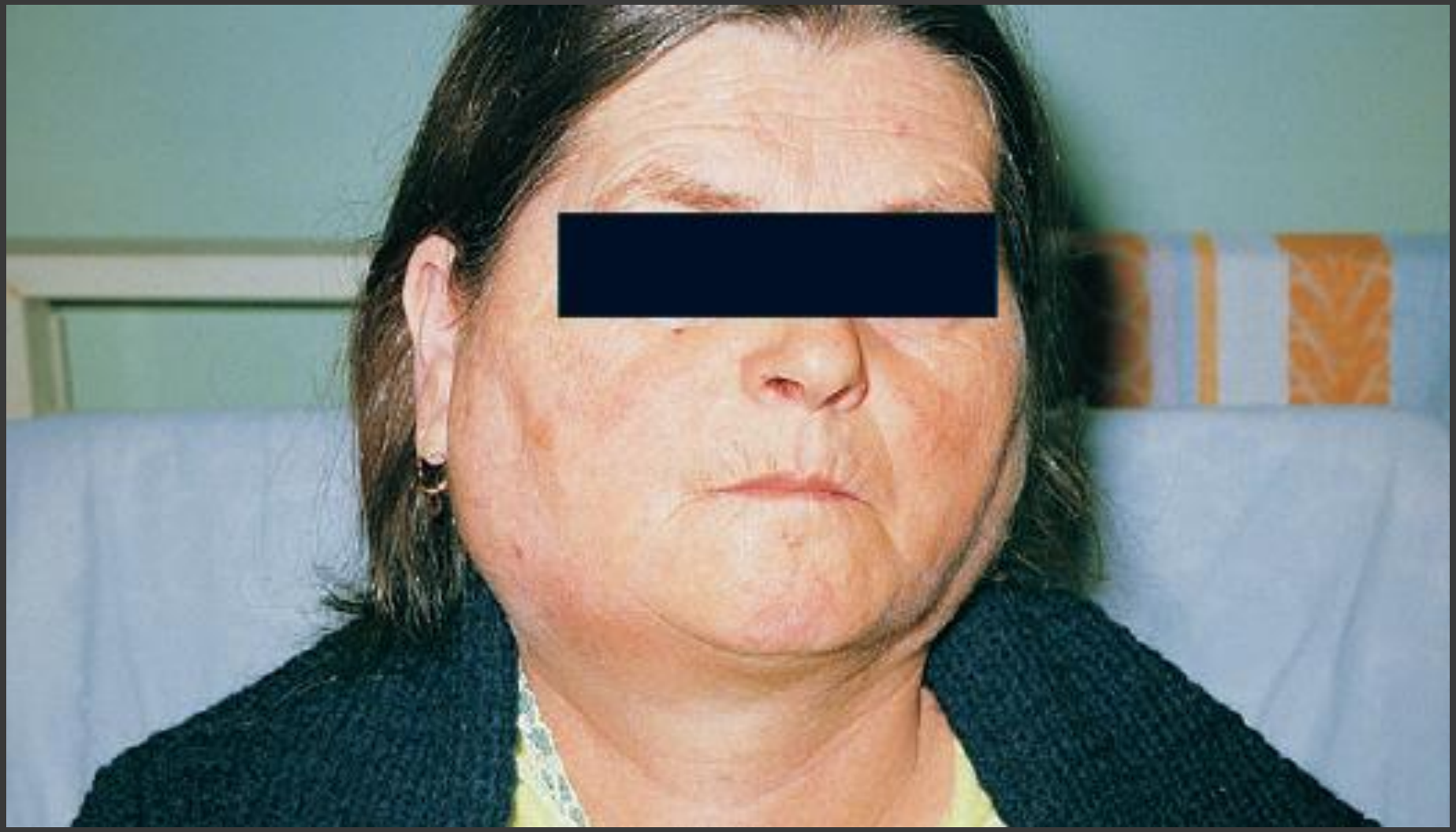
Cancer screening

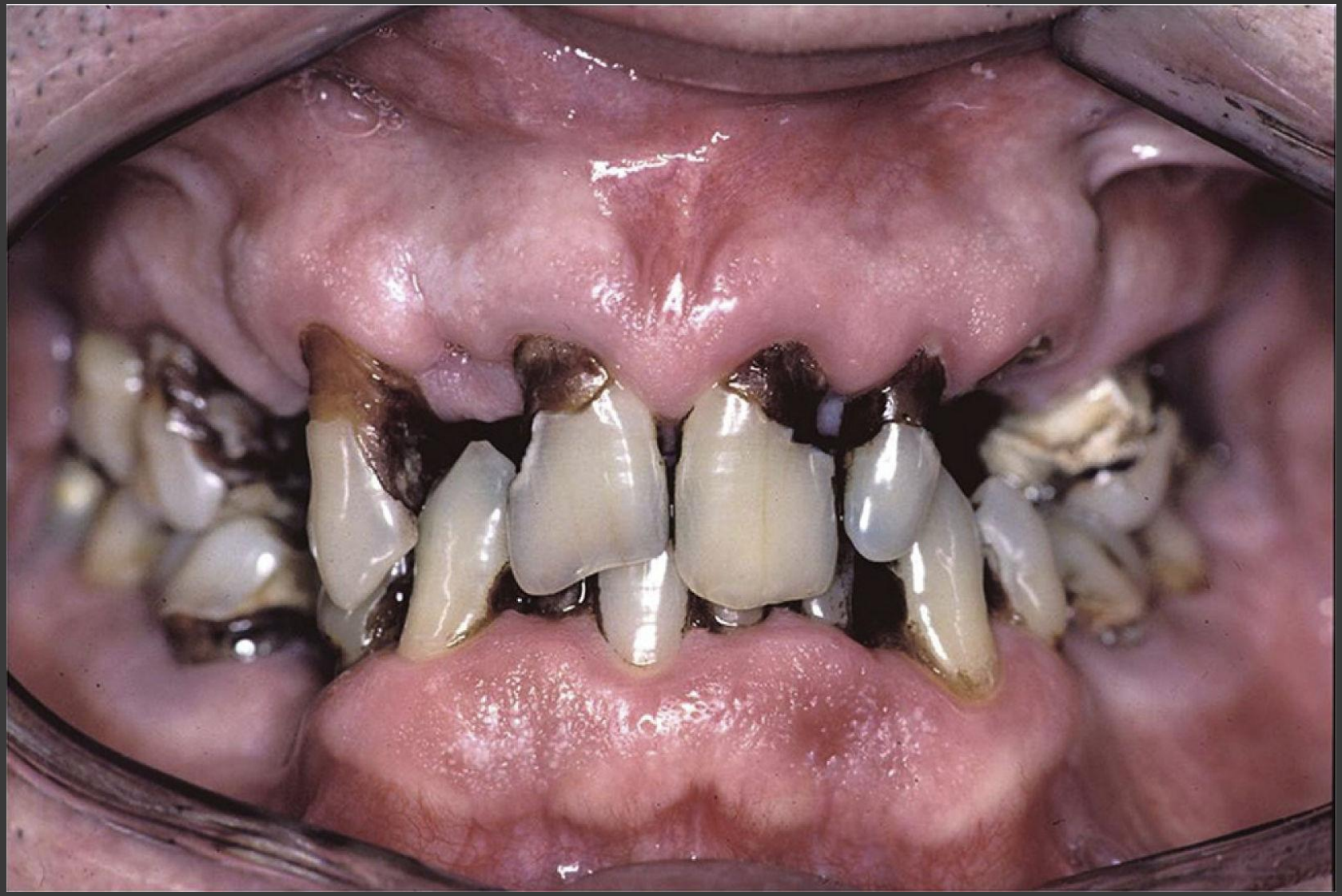
- **All patients >50 years of age should have:**
  - CXR
  - Chest/abdomen/pelvis CT scans
  - Mammography and gynaecological examination (F)
  - Testicular examination in males (M)
  - Faecal occult blood
  - Gastroscopy/colonoscopy

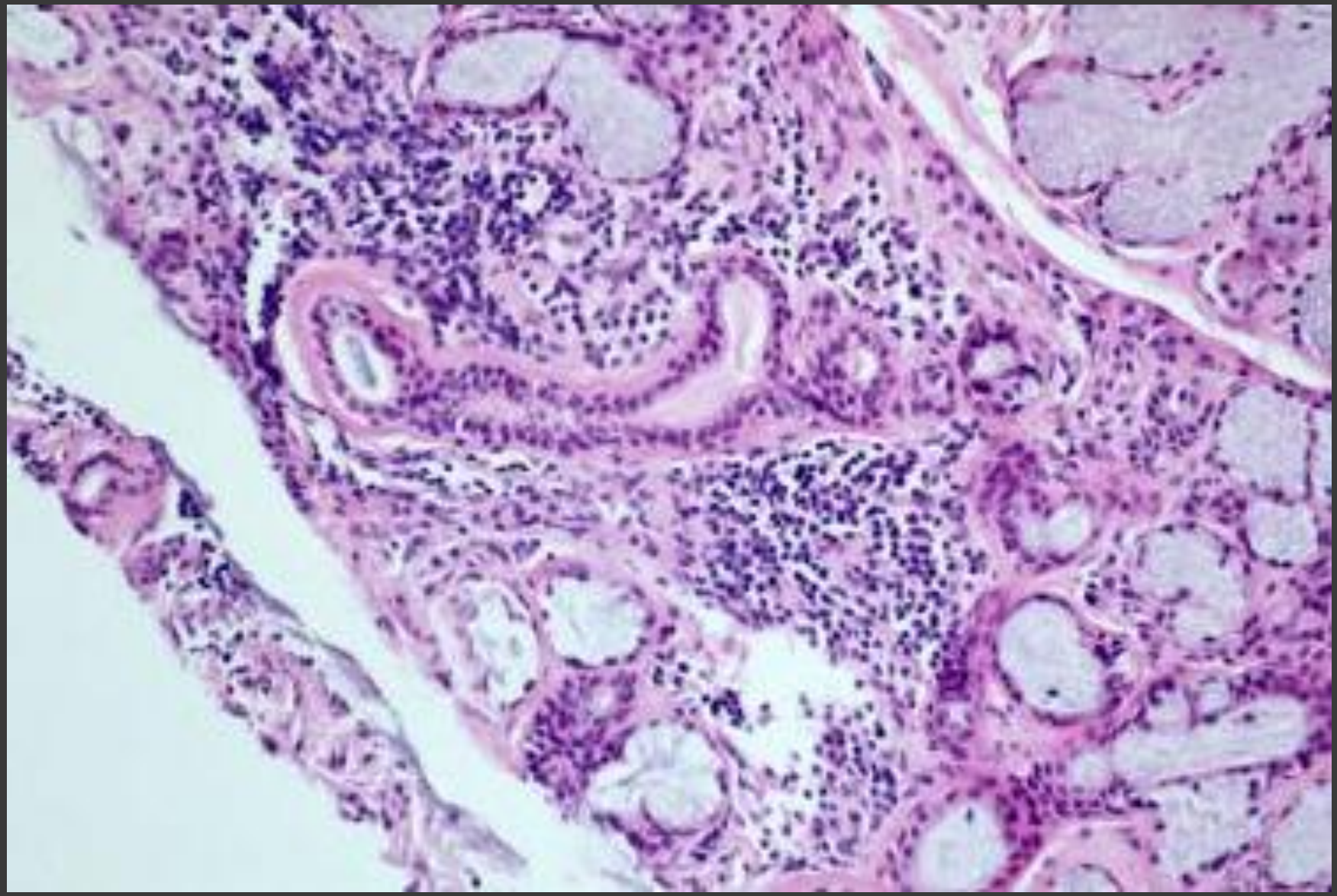
Sjögren syndrome

- Inflammatory autoimmune disease affecting primarily the exocrine glands.
- Lymphocytic infiltrates replace functional epithelium, leading to decreased exocrine secretions.
- Mucosal dryness is manifested as xerophthalmia (keratoconjunctivitis sicca) and xerostomia
- There is salivary gland enlargement.









- Characteristic autoantibodies (anti-Ro/SS-A and anti-La/SS-B)
- There is non-erosive polyarthritis & Raynaud's phenomenon
- **Extra-glandular manifestations:**
  - vasculitis
  - peripheral neuropathy
  - glomerulonephritis

- There is increased risk for lymphoma.
- Associated with other autoimmune diseases such as RA, SLE, SSc & PM

Treatment

- Stimulation of salivary flow by sugar-free flavored lozenges
- dry food, smoking, and drugs with anticholinergic side effects, which further decrease salivary flow, should be avoided
- Adequate oral hygiene after meals to prevent dental disease
- Pilocarpine to increase salivary secretion
- Artificial tears
- Hydroxychloroquine for joint pain

Questions?