NOTES
INFLAMMATORY MYOSITIS

GENERALLY, WHAT IS IT?

PATHOLOGY & CAUSES

- Multiple disorders involving autoimmune inflammation, injury of skeletal muscles
- Most commonly include polymyositis, dermatomyositis, inclusion body myositis
  - Dermatomyositis predominantly mediated by humoral immune response; polymyositis, inclusion body myositis by cellular immune response

RISK FACTORS

- Age (more common in older population)
- Dermatomyositis, polymyositis more common in individuals who are biologically female
- Inclusion body myositis more common in individuals who are biologically male
- Chronic viral infections: human T cell lymphotropic virus Type I (HTLV-1), HIV
- Autoimmune diseases
- Malignancies

COMPLICATIONS

- Dysphagia, pulmonary involvement
- Cardiovascular involvement

SIGNS & SYMPTOMS

- Proximal muscle weakness
- Inclusion body myositis
  - Distal muscle weakness
- Dermatomyositis
  - Skin rashes

DIAGNOSIS

LAB RESULTS

- ↑ muscle enzymes, like creatine kinase (CK)
- Muscle biopsy
  - *Dermatomyositis:* perivascular, perimysial inflammation
  - *Polymyositis:* endomysial inflammation
  - *Inclusion body myositis:* endomysial inflammation, intracytoplasmic vacuoles with protein depositions

OTHER DIAGNOSTICS

- Physical examination
  - Muscle weakness

Electromyography (EMG)

- Pathological signals

TREATMENT

MEDICATIONS

- Corticosteroids, immunosuppressive agents

OTHER INTERVENTIONS

- Physical rehabilitation

DERMATOMYOSITIS

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PATHOLOGY & CAUSES

- Autoimmune disorder leading to destruction of small blood vessels in muscles, skin
- Unknown factor activates C3 protein (complement component 3) → formation of membrane attack complex (MAC), accumulation in capillaries → destruction of capillary wall → microinfarctions
- *Juvenile:* around seven years; associated with calcinosis (deposition of calcium in skin)
- *Adult:* > 40; associated with malignancy, treating malignancy may cure myositis

RISK FACTORS

- > 60 years
- Malignancy

COMPLICATIONS

- Respiratory muscle weakness; dysphagia (if esophagus, pharyngeal muscles involved); interstitial pulmonary disease; cardiovascular involvement

SIGNS & SYMPTOMS

- Weakness starts in proximal muscles, slowly progresses (e.g. difficulty getting up)
- Heliotrope rash
  - Purplish eyelids with posible periorbital edema
- Gottron papules
  - Scaling erythema of knuckles, elbow, knees
- V-shaped rash on chest

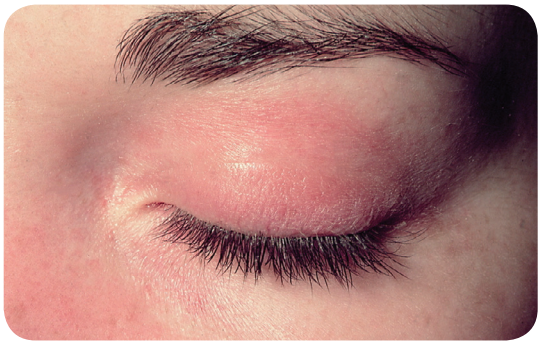

Figure 113.1 A heliotrope rash affecting the eyes of an individual with dermatomyositis.

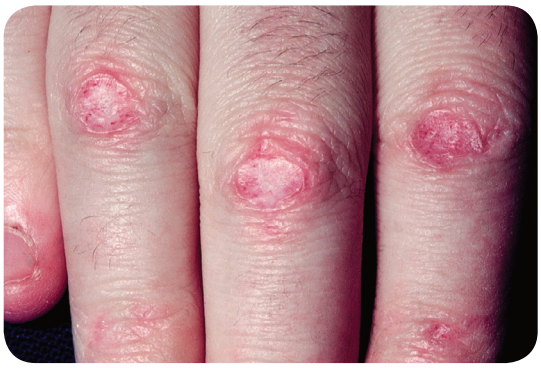

Figure 113.2 Gottron's papules on the extensor surfaces of an individual with dermatomyositis.

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan

- Malignancy suspected

LAB RESULTS

- Blood tests
  - ↑ CK (muscle cells death)
  - ↑ aspartate aminotransferase (AST)

- ↑ lactic dehydrogenase (LDH)
- Antinuclear antibodies (ANA)
- Anti-Mi-2 antibodies (acute phase, better prognosis)

- Biopsy
  - Perivascular, perimysial inflammation
  - Perifascicular atrophy
  - "Ghost fibers" (destroyed fibers, can no longer be stained)

OTHER DIAGNOSTICS

EMG

- Abnormal signals

TREATMENT

MEDICATIONS

- Corticosteroids (e.g. glucocorticoid)
- Immunosuppressive agents (e.g. methotrexate)
- IV immune globulins

OTHER INTERVENTIONS

- Physical therapy (preserve muscle strength)
- Sunscreen, avoid sun exposure (in skin disease)

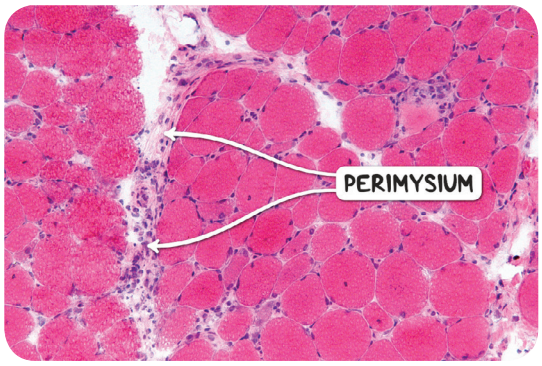

Figure 113.3 The histological appearance of the skeletal muscle of an individual with dermatomyositis. The perimysium and endomysium have been infiltrated by chronic inflammatory cells, with predilection for the perimysium.

INCLUSION BODY MYOSITIS

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PATHOLOGY & CAUSES

- Idiopathic inflammation of muscles leading to weakness, muscle atrophy
- Inflammation, degenerative processes
- Unknown factor causes myofibers to present major histocompatibility complex class I (MHC I) → CD8+ T cells gather, recognize MHC I, bind → express perforin → pores form on myofibers membranes → cell degeneration
- Accumulation of abnormal amyloidogenic proteins (e.g. beta-amyloid), cytotoxic effect
  - *Causes:* misfolding of proteins; damaged/inhibited proteasomes; endoplasmic reticulum stress

RISK FACTORS

- Age > 50
- *Chronic viral infections:* HTLV-1
- *Autoimmune diseases:* Sjögren's syndrome

COMPLICATIONS

- Dysphagia (if esophagus, pharyngeal muscles involved)

SIGNS & SYMPTOMS

- Slowly progressive muscle weakness, sometimes asymmetric
  - Proximal leg muscles (difficulty getting up, frequent falls)
  - Distal arm muscles (weak grip)

- As disease progresses
  - ↑ muscle atrophy
  - ↓ deep tendon reflexes

DIAGNOSIS

LAB RESULTS

- Mild ↑ muscle enzymes (e.g. CK)
- Muscle biopsy
  - CD8+ T lymphocytes, macrophages infiltrating non-necrotic myofibers
  - Vacuoles with amyloides, other protein accumulations (inclusion bodies)
  - ↑ MHC I on immunostaining

OTHER DIAGNOSTICS

- Clinical presentation
  - Muscle weakness

EMG

- Polyphasic motor unit action potentials (MUAPs) with small amplitude, short duration

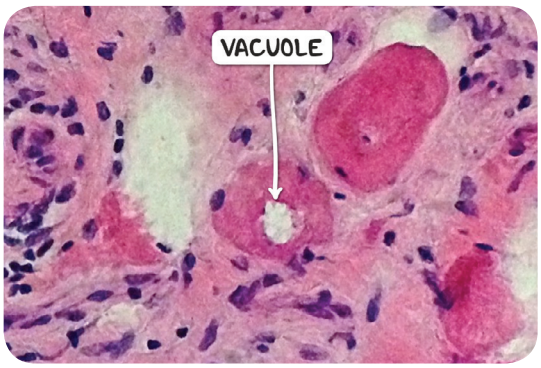

Figure 113.5 A histological section of muscle showing a myofiber vacuole in an individual with inclusion body myositis.

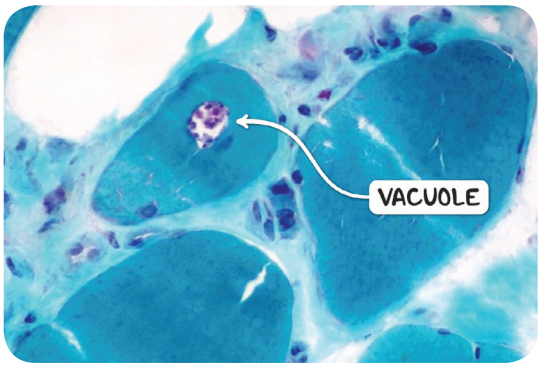

Figure 113.4 Gomori staining highlights the rimmed vacuoles in inclusion body myositis.

TREATMENT

MEDICATIONS

- Immunosuppressive therapy
  - Administered when another systemic autoimmune disease present

OTHER INTERVENTIONS

- Physical therapy
  - Muscle strengthening
- Speech therapy
  - If dysphagia present
- Occupational therapy

POLYMYOSITIS

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PATHOLOGY & CAUSES

- Inflammatory destruction of muscles leading to muscle weakness
- Unknown factor induces CD8+ T cells, macrophages to recognize nuclear, cytoplasmic antigens of muscle cells → immune cells surround nonnecrotic muscle cells → muscle cell destruction

RISK FACTORS

- Autoimmune disease
- Chronic viral infection (HIV, HTLV-1)

COMPLICATIONS

- Aspiration pneumonia
- Interstitial lung disease
- Dysphagia → malnutrition, anorexia

SIGNS & SYMPTOMS

- Symmetrical weakness of proximal leg, arm muscles (e.g. difficulty climbing stairs)
- Neck flexor weakness
- Mild myalgia, tenderness
- Dysphagia (if esophagus, pharyngeal muscles involved)

DIAGNOSIS

DIAGNOSTIC IMAGING

Chest X-ray, CT scan

- Pulmonary involvement

LAB RESULTS

- Blood tests
  - ↑ CK, aldolase; ANA; antisynthetase antibodies (anti-Jo-1)
- Muscle biopsy
  - Endomysial inflammation; intact blood vessels; myofibers surrounded by CD8+ T lymphocytes, macrophages

OTHER DIAGNOSTICS

- Physical examination
  - Muscle weakness, tenderness

EMG

- Low amplitude, short duration potential; repetitive discharges

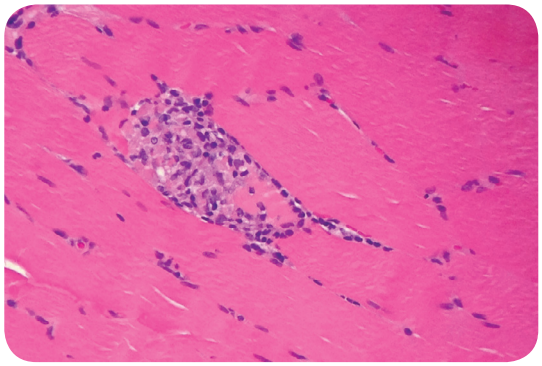

Figure 113.6 A muscle biopsy from an individual with polymyositis. The lymphocytes penetrate individual myofibers. In this example, the inflammation has progressed to phagocytic destruction by macrophages.

TREATMENT

MEDICATIONS

- Corticosteroids
- Immunosuppressive agents (if nonresponsive to corticosteroids)
- IV immune globulins (if severe, life-threatening)

OTHER INTERVENTIONS

- Physical therapy (preserve muscle strength)

INFLAMMATORY MYOSITIS SUMMARY

	DERMATOMYOSITIS	INCLUSION BODY MYOSITIS	POLYMYOSITIS
MAIN IMMUNE RESPONSE	Humoral	Cellular	Cellular
HISTOLOGIC FINDINGS	Perimysial, perivascular inflammation	Endomysial inflammation, inclusion bodies	Endomysial inflammation
SEX PREDISPOSITION	Individuals who are biologically female	Individuals who are biologically male	Individuals who are biologically female
MANIFESTATION	Proximal muscle weakness, skin rash	Proximal, distal muscle weakness	Proximal muscle weakness
MUSCLE ENZYMES	↑ CK	Slightly ↑ / normal CK	↑ CK
TREATMENT	Corticosteroids, immunosuppressive agents	Nonresponsive	Corticosteroids, immunosuppressive agents