Inflammatory Myopathies

4th year MBBS

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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: periungual 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 association

- 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'
Cuticular overgrowth with periungual erythema and capillary dilatation
V sign
Shawl sign
Involvement of the nasolabial area and forehead distinguishes DM from SLE
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
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
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
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
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
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?