Skin Block

- Introduction To Diseases Of The Skin
- Acneiform, Alopecias, and Pigmentary Disorders
- Eczemas, Papulosquamous, and Vesiculobullous Skin Disease
- Skin Neoplasms
- Drug Eruptions
- Skin Signs of Systemic Disease
Skin Signs of Systemic Disease

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Learning Objectives

At the end of the session the students will be able to:

• Recognize the cutaneous clinical presentation and describe the epidemiology and pathogenesis and internal organ involvement in connective tissue disease of the skin, including lupus erythematosus, dermatomyositis, and systemic sclerosis

• Recognize the cutaneous clinical presentation of small vessel vasculitis and describe the internal organ involvement that may be involved

• Recognize the cutaneous clinical presentation of neutrophilic disorders such as Sweet’s syndrome and Pyoderma Gangrenosum and describe the systemic diseases that may be associated.

• Recognize the cutaneous clinical presentation of skin conditions such as acanthosis nigricans and erythema nodosum, which may be presenting signs of internal disease

• Recognize the cutaneous clinical presentation of the most common paraneoplastic skin diseases, including necrolytic migratory erythema, paraneoplastic pemphigus, and list their associated malignancies
Overview

• Cutaneous manifestations of systemic disease are frequently encountered in the practice of medicine
• Skin disease may be the initial sign of an internal disease
Diabetes Mellitus

- Diabetic dermopathy
- Bullous diabetcorum
- Necrobiosis lipoidica
Liver Disease

- Spider angiomas
- Telangiectasias
- palmar erythema
Liver Disease: Terry’s nails
Renal disease:
Lindsay nails (half and half nails)
Autoimmune connective tissue disease

- Lupus erythematosus
- Dermatomyositis
- Systemic sclerosis
Systemic lupus erythematosus (SLE)
Systemic lupus erythematosus (SLE)

- Chronic autoimmune disease that can affect multiple organ systems (skin, joints, pulmonary, renal, hematologic, nervous system, ...)
- Relapsing/remitting course
- 90% female, ages 14-45
- Wide range in manifestations and severity
- Pathogenesis: autoantibody response to cytoplasmic and nuclear antigens
  - Anti-nuclear antibody (ANA) (highly sensitive, not specific). 99% of SLE patients
  - Anti-dsDNA (highly specific). 55-65% SLE patients. Poorer prognosis
  - Anti-Smith (highly specific). 25-30% of SLE patients
  - Anti RNP (highly specific). 5% of SLE patients
  - Anti-histones (highly specific) for drug induced SLE
Systemic lupus erythematosus (SLE)

American Rheumatologic Association (ARA) SLE criteria for diagnosis (need 4 of 11)—specific cutaneous criteria in red

- **Malar rash**—"butterfly" rash of erythema and scaling over nose and cheeks, sparing nasolabial fold
- **Discoid rash**—hypo or hyperpigmented, scarring papules and plaques
- **Photosensitivity**—photo-distributed erythema on V of neck, face, dorsal hands, arms
- **Oral ulceration**
- **Arthritis**
- **Serositis** (pleuritis, pericarditis)
- **Renal disorder** *(nephritis – diffuse proliferative glomerulonephritis or membranous glomerulonephritis -- common cause of death)*
- **Neurologic disorder**
- **Hematologic disorder**
- **Immune disorder** (anti-dsDNA, anti-Smith, anti-phospholipid)
- Presence of **anti-nuclear antibody (ANA)**
Systemic lupus erythematosus (SLE): Malar Rash
Systemic lupus erythematosus (SLE): Discoid Lesion
Systemic lupus erythematosus (SLE): Photosensitivity
Systemic lupus erythematosus (SLE): Oral Ulceration
Subacute Cutaneous Lupus Erythematosus (SCLE)

- photosensitive eruption (UVB>UVA)
- annular scaly plaques with central clearing on sun-exposed skin
- 10-15% go on to develop systemic internal disease
- Laboratory
  - anti-(SSA)Ro+ in 70%
- 35% of cases are drug induced: HCTZ, terbinafine, CCBs, ACE inhibitors, NSAIDs
Discoid Lupus Erythematosus (DLE) (Chronic Cutaneous Lupus Erythematosus)

- Photosensitive eruption
- discrete, red, scaly atrophic scar-like plaques that result in dyspigmentation, follicular plugging, disfiguring scarring with atrophy, **scarring** alopecia
- Scalp, Face (bridge of nose, lips, ears) over solar induced areas
- One of the 11 diagnostic criteria for SLE (20% of patients with SLE have these lesions)
- 5-10% of patients progress to SLE (need work up to exclude SLE)
Neonatal Lupus Erythematosus

- Autoimmune disease of the newborn (2/3 present at birth; 1/3 appear by age 5 months)
- Scaly, annular erythematous plaques on face, especially periorbital and forehead. May worsen with sun exposure (photosensitive)
- Mothers have +anti-Ro (SS-A), La (SS-B), or U1RNP antibodies
- Histology similar to SCLE
- Almost 100% babies with neonatal LE have +Ro antibodies (maternal autoantibodies) that clear in approximately 6-8 months
Neonatal Lupus Erythematosus: Systemic Concerns

• **Congenital heart block** (almost always irreversible)
  – Check EKG and echocardiogram
  – Pediatric cardiology consultation

• **Thrombocytopenia, anemia, neutropenia, liver abnormalities** (resolve once maternal antibodies clear)
  – check CBC with differential
  – check LFTs
Autoimmune connective tissue disease

- Lupus erythematosus
- Dermatomyositis
- Systemic sclerosis
Dermatomyositis

- Autoimmune connective tissue disease that affects multiple organ systemic with inflammatory myopathy (can be amyopathic) and characteristic cutaneous findings

- Bimodal incidence
  - Adult form: 45-60 years old
  - Juvenile form: 10-15 years old
Dermatomyositis: systemic manifestations

• Fatigue
• Malaise
• Myalgias/myositis
  – Proximal extensor muscle group inflammation (triceps, quadriceps) → muscle pain and weakness
  – Perimysial inflammation and atrophy with CD4+ T cells
  – Seen on MRI
  – elevated CK, aldolase, LDH, LFTs
• Gastrointestinal (dysphagia)
• Pulmonary (interstitial fibrosis)
• Cardiac (arrhythmias)
• Malignancy
  – up to 40% of adults (not juvenile) with occult malignancy
  – commonly: colon, ovarian, breast, pancreas, lung, gastric, lymphoma
Dermatomyositis: skin manifestations

- **Heliotrope rash**: erythematous to violaceous edematous patches on periorbital area
- **Pruritus**
- **Gottron’s sign** (80% of patients): red/purple scaly flat topped papules on dorsal knuckles
- **Poikiloderma**: Hyperpigmentation, Hypopigmentation, Telangiectasias, Epidermal atrophy
- **Cuticular (nail-fold) changes**: Inflamed, thick/rough, hyperkeratotic cuticles with ragged edges; Nail-fold telangiectasias/dilated capillary loops
- **Calcinosi cutis**
- **Mechanic’s hands**: hyperkeratosis, scaling, fissuring, hyperpigmentation on ulnar thumb, radial fingers
- "shawl" sign
- "holster” sign
- **Scalp involvement**: erythematous, atrophic, scaly plaques
Dermatomyositis: Heliotrope Rash
Dermatomyositis: Gottron’s sign
Dermatomyositis: Gottron’s sign
Dermatomyositis: Poikiloderma
Hyperpigmentation, Hypopigmentation, Telangiectasias, Epidermal atrophy
Dermatomyositis: Shawl Sign
Dermatomyositis: Holster Sign
Dermatomyositis: Mechanic’s Hands
Dermatomyositis: Cuticular Changes
Dermatomyositis: Calcinosis Cutis
Autoimmune connective tissue disease

• Lupus erythematosus
• Dermatomyositis
• Systemic sclerosis
Systemic Sclerosis (SSc)

• Fibrotic/sclerotic changes and thickening of skin and internal organs

• Two subtypes (depending on degree of cutaneous involvement; both confer internal organ involvement)
  – Limited Systemic Sclerosis
  – Diffuse Systemic Sclerosis

• **ANA** (90%) limited or diffuse. Discrete speckled or nucleolar pattern; **Anti Scl-70 antibody** (increased pulmonary risk); **Anti-centromere antibody** (limited SSc); **Anti-RNP antibody** (diffuse SSc)
Systemic Scleroderma: Systemic manifestations

- **Pulmonary disease** leading cause of mortality
  - Pulmonary hypertension
  - Interstitial lung disease
- Esophageal fibrosis/dysmotility
- Arthralgias
- Raynaud’s phenomenon
- Renal hypertensive crisis
- Cardiomyopathy
Limited Systemic Sclerosis (SSc)

- Skin involvement usually distal extremities, face, neck
- CREST syndrome (calcinosis, Raynaud’s phenomenon, esophageal dysmotility, sclerodactyly, telangiectasias)
- SSc sine scleroderma (limited scleroderma with internal organ involvement and positive serologies, but no cutaneous disease)
- Anti-centromere antibody

Diffuse Systemic Sclerosis (SSc)

- Skin involvement usually trunk, proximal extremities
- Rapid, early visceral involvement
- Anti Scl-70 antibody (anti-DNA topoisomerase I antibody)
Systemic Sclerosis: Cutaneous manifestations

- Symmetric sclerosis of skin proximal to MCP and MTP joints. Morphology: indurated, taut, shiny skin
- Sclerodactyly, loss of skin creases
- Digital pitting scars
- Substance loss of finger pad
- Diffuse hyperpigmentation and depigmentation with sparing of perifollicular skin (salt-pepper appearance) on back and legs
- Telangiectasias on lips, palms, proximal nail folds (flat/mat)
- Calcinosis cutis
- Raynaud’s with digital ulcers
- Face with beak like appearance, no wrinkles
Systemic Sclerosis:
Symmetric *sclerosis* of skin proximal to MCP and MTP joints leading to indurated, taut, shiny skin.
Systemic Sclerosis:
Diffuse hyperpigmentation and depigmentation with sparing of perifollicular skin (salt-pepper appearance) on back and legs
Systemic Sclerosis: Telangiectasias
Systemic Sclerosis:

Face with beak like appearance, no wrinkles
Systemic Sclerosis: Raynaud’s Phenomenon
Systemic Sclerosis: Digital Ulcers
Systemic Sclerosis: Calcinosis Cutis
Cutaneous Leukocytoclastic Vasculitis

- small vessel vasculitis (inflammation/necrosis of small blood vessels—post-capillary venules)
- Clinically manifests as "palpable purpura"
- Distribution: Lower legs and ankles/dependent areas and pressure points (buttocks)
Leukocytoclastic Vasculitis

Pathogenesis Related to:

- Infection (hepatitis, HIV, streptococci)
- Medication (NSAIDs, PCN, sulfa, cephalosporins, PTU, biologics—7-21 days after initiation of drug)
- Malignancy
- Autoimmune connective tissue disease
- Foods
- Idiopathic

Signs suggestive of systemic vasculitis

- Fever, myalgias, arthralgias, abdominal pain, melanoma, diarrhea, hematuria, lower extremity edema, paresthesias
Henoch Schonlein Purpura

- Usually children <10 years old, 1-2 weeks after URI
- IgA deposition in vessel walls
- Fever, arthralgias, renal (hematuria), GI involvement (abdominal pain)
Dermatitis Herpetiformis

- Pruritic papules and vesicles and bullae on elbows, lower mid back
- Immunofluorescence: IgA at dermal papillae tips
- Associated with celiac disease
Erythema Nodosum

- Inflammation of subcutaneous fat
- Tender erythematous nodules, usually on anterior shins.
- Associated with Crohn’s disease, TB, coccidioidomycosis, histoplasmosis, streptococcal infections, drugs
Pyoderma Gangrenosum

- Small red papule or pustule that evolves into larger ulceration
- Systemic illness in 5-%
  - IBD: Ulcerative Colitis, Crohn's disease
  - Also hematologic diseases such as leukemia
Paraneoplastic Skin Disease
Acanthosis Nigricans

• Symmetric, hyperpigmented, velvety plaques, most commonly axillae, groin, posterior neck

• Pathogenesis: unknown. Possible stimulation of growth factors in keratinocytes leading to epidermal hyperplasia
Acanthosis Nigricans

Associated systemic illnesses

• Benign form is related to hyperinsulinemia/insulin resistance/diabetes

• Atypical distributions (palmar/tripe palms, mucosal) may be associated with internal malignancy (Most commonly GI adenocarcinoma)
Sign of Leser Trelat
Acute Febrile Neutrophilic Dermatosis (Sweet’s syndrome)

- Abrupt tender, red-purple edematous well-demarcated, sometimes vesiculating papules and plaques,
- Distribution: face, neck, upper extremities most common
- +pathergy (lesions may tend to occur in sites of skin trauma such as IV insertion sites)
Acute Febrile Neutrophilic Dermatosis (Sweet’s syndrome)

• Reactive inflammatory disorder associated with infections, medications (G-CSF), hematologic malignancies (AML most commonly) in 20%

• Fever, headaches, myalgias, arthralgias

• May have extra-cutaneous symptoms: Pulmonary (most common), GI tract, CNS, kidney, heart
Paraneoplastic pemphigus

• Severe and painful cutaneous and mucosal blistering disease

• Autoantibodies to multiple antigens (desmoplakin, envoplakin, periplakin, bullous pemphigoid antigen 1)

• Associated malignancies
  – Chronic lymphocytic leukemia (CLL)
  – Castleman’s disease (angiofollicular lymph node hyperplasia)
  – Thymoma

• Systemic
  – Pulmonary bronchiolitis obliterans → dyspnea
Take Home Points

• Systemic Lupus erythematosus is a chronic autoimmune disease that can affect multiple organ systems. The anti-nuclear antibody (ANA) is highly sensitive and positive in 99% of patients with SLE. The four SLE-specific cutaneous eruptions are malar rash, photosensitivity, mucositis, and discoid lesions.

• Dermatomyositis is an autoimmune connective tissue disease that affects multiple organ systemic, and classically presents with a heliotrope rash, Gottron’s papules, and myositis leading to elevated CK. In adults, dermatomyositis may be a presenting sign of occult malignancy.

• Limited Systemic Sclerosis may present with features of Calcinosis, Raynaud’s phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasias (CREST syndrome). Anti-centromere antibody is typically positive. Pulmonary disease is the leading cause of mortality.

• Acanthosis nigricans presents as symmetric hyperpigmented velvety plaques, most often in the axilla and neck and may be a sign of underlying insulin resistance. When acanthosis nigricans develops over atypical areas such as the upper lip, or palms, this may be a sign of internal malignancy.
Thank you!

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