Skin Signs of Internal Disease

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Advance Dermatology and Cosmetic Surgery
Overview

- Necrobiosis Lipoidica (Diabeticorum)
- Granuloma Annulare
- Pyoderma Gangrenosum
- Acanthosis Nigricans
- Xanthomas
- Neurofibromatosis
- Tuberous Sclerosis
- Dermatomyositis
- Nail Changes
NECROBIOSIS LIPOIDICA
NECROBIOsis LIPOIDICA

- >50% of patients are insulin dependent diabetics
- < 1% of diabetics develop this condition approx. 1 in 300.
- Lesions may appear years before onset of diabetes
- 75% are women in their 3rd or 4th decades.
NECROBIOSIS LIPOIDICA

- Idiopathic collagen degeneration of the skin
- Number or severity of lesions is unrelated to diabetic control
- Unpredictable course, often chronic
- Patients with no history of diabetes should be evaluated
NECROBIOSIS LIPOIDICA

- Starts as slowly expanding violaceous patch
- Central area turns waxy yellow-brown, atrophies, and develops surface telangiectasias
- Ulceration and pain may occur after trauma
NECROBIOsis LIPOIDICA

- **Treatment:**
  - Smoking Cessation
  - Oral aspirin, Dipryridamole, topical steroids, topical Tacrolimus, Pentoxifylline, Thalidomide, Cyclosporine
GRANULOMA ANNULARE
GRANLOMA ANNULARE

- Unknown Etiology
- Benign, self-limiting
- Association with diabetes mellitus ~ 20%.
- **Localized** form is common,
- **Disseminated** form has higher incidence in diabetics.
- Onset can be before diabetes diagnosed, concurrent with diagnosis or in established disease.
GRANULOMA ANNULARE

- Frequently found on distal extremities
- Rarer diffuse form generally seen in adults.
- Initially forms small papules that coalesce into rings. These are flesh colored or violaceous papules/rings.
- Slowly expands with central clearing without significant scaling (no trailing scale as seen in Tinea Corporis).
- KOH is negative (Tinea is KOH positive).
GRANULOMA ANNULARE

- **Treatment:**
- The condition is self-limited and no treatment is absolutely indicated and 50% of lesions generally resolve on their own within two years.
- **Localized:** Topical steroids or dilute intra-lesional steroids or Cryotherapy.
- **Generalized:** Dapsone, Isotretinoin, others.
GRANULOMA ANNULARE
GRANULOMA ANNULARE
Pyoderma Gangrenosum

Chronic ulcerating skin lesion(s) associated with underlying Inflammatory Diseases: the 3 B’s...

› **Bowels**: IBDs (Ulcerative Colitis, Crohn’s Disease)
› **Blood**: Acute Myeloblastic Leukemia, Plasma Cell Dyscrasias, Wegener’s Granulomatosis
› **Bones**: RA, SLE
› 50% no internal disease
Pyoderma Gangrenosum

Lesions may begin spontaneously or at the site of trauma.
Lesions may enlarge with trauma (pathergy) such as injury or biopsy.
Lesional edge is elevated (undermined) and violaceous with small pustules.
Pyoderma Gangrenosum

Differential Diagnosis

- Spider Bite
- Infected ulcer
- Sweet’s syndrome
- Systemic Vasculitis
Pyoderma Gangrenosum

- Most commonly found on the lower legs.
- Location of lesions becomes progressively less common as you move cephalad.
Pyoderma Gangrenosum

- Most commonly seen on lower legs but may be anywhere
- Necrotic ulcer expands peripherally with a red to purple margin
- Diagnosis made clinically; lab tests and biopsy are not diagnostic
- Treatment: IL and/or oral steroids, dapsone, cyclosporin, Enbrel, IVIG, hyperbaric O₂,
Pyoderma Gangrenosum

- In general, patients with this condition have a chronic relapsing course even with adequate treatment.
- Eradication is the goal of therapy but often, treatment regimens are aimed at controlling the condition without chronic systemic corticosteroids.
Acanthosis Nigricans
Acanthosis Nigricans

- Symmetric brown, velvety thickening and hyperpigmentation of the skin.
- Produces symmetric rough, papillomatous, warty appearance. Mainly in axillae and neck areas but may also see in the groin, dorsal digits, umbilicus and popliteal spaces.
- Patients often attempt to scrub this off because it looks unwashed or dirty.
This is Velvet
Acanthosis Nigricans

Skin Disease Diagnosis and Treatment by Thomas Habif
Acanthosis Nigricans:

Types

- **Benign** – most common type, due to obesity
- **Hereditary** – autosomal dominant trait
- **Drug induced** – nicotinic acid, BCP/estrogens, methyltestosterone, Prednisone,
- **Insulin resistant**
Acanthosis Nigricans

- **Thyroid or Ovarian dysfunction** - hypothyroidism, polycystic ovary disease

- **Malignant** – common association is gastric adenocarcinoma; in one third of patients skin lesions precede cancer. Skin changes are usually rapid/sudden.
Acanthosis Nigricans

Treatment

- Treat underlying cause if possible
- No treatment is uniformly effective at clearing skin changes
- Condition is asymptomatic and does not require therapy.
- Retinoic acid (Retin-A), lactic acid cream 12% (Amlactin or Lac Hydrin)
Xanthomas

- Systemic Lipid abnormality resulting in:
- Lipid deposits in the skin and tendons.
- Classified according to appearance and location:
  - Xantholasma- facial
  - Plane Xanthoma
  - Eruptive Xanthoma
  - Tendinous Xanthoma
  - Tuberous Xanthoma
Xanthelasma

- Xanthelasma – yellowish plaques on the eyelids, 50% have normal plasma lipids
- Seen in familial hypertriglyceridemia, primary biliary cirrhosis and multiple myeloma
Plane xanthomas – Plaques on palmar creases, face, neck and chest
**Xanthomas**

- Plane xanthoma of the palms start as small papules but become confluent to form linear plaques within the palmar creases.
- Associated with Type III hyperlipoproteinemia with elevations of both tryglycerides and cholesterol.
- Patients have increased incidence of accelerated atherosclerotic vascular disease.
Plane xanthomas
Plane xanthomas
Eruptive xanthomas — Yellowish 1 to 4mm papules appearing in crops, clearing rapidly when serum lipid levels are lowered
Eruptive Xanthoma

- Most common in patients with poorly or uncontrolled diabetes
- Can occur with any hypertriglyceridemias
- Generally occur when triglycerides exceed 1500 mg/dl and may recede when triglycerides are lowered.
- May appear like pustules but no material can be expressed as with a pustle
ERUPTIVE XANTHOMA
Eruptive Xanthoma
Eruptive Xanthoma with “koebnerization”
TENDINOUS XANTHOMA

Smooth deep nodules attached to tendons and ligaments, found mostly on dorsal fingers and Achilles tendons.
Tendinous Xanthoma

- Tend to occur in patients with familial hypercholesterolemia
- They can also occur in Type III hyperlipoproteinemia
- Lipid infiltrates the tendons particularly on the hands, feet, ankles, elbows and Achilles tendons.
- Vascular disease evaluation should be done
Tendinous Xanthoma
Tuberous Xanthomas – Slowly evolving yellowish papules and nodules that occur on knees, elbows, palms and extensor surfaces
Tuberous xanthomas
Tuberous xanthomas
Tuberous xanthomas
Scleroderma

Also known as progressive systemic sclerosis

It has two distinct forms:

1. CREST syndrome: indolent/more benign
   - Calcinosis
   - Raynaud’s phenomenon
   - Esophageal dysmotility
   - Sclerodactyly
   - Telangectasia
Scleroderma

2. Diffuse Systemic Sclerosis
   This form is more progressive with associated internal organ fibrosis and vascular abnormalities especially the heart, GI tract, lungs and kidneys.
   - Female:Male is 3:1
   - 20 cases per million population
   - Prognosis is worse in African Americans and men
Scleroderma

- First presentation may be Raynaud’s phenomenon alone.
- Patient may have intense itching with little skin change.
- Nail fold capillary dilatation is common.
- Pigment changes occur later in the disease.
- Skin becomes “bound down” in appearance especially the fingers and mouth.
Nail Fold Capillary Dilation
TELANGECTASIA
CALCINOSIS CUTIS
TELANGECTASIA
Sclerodactyly / Raynaud’s
SCLERODERMA

Salt and pepper pigmentation
Scleroderma
SCLERODERMA

- Lip telangectasias with radial furrowing
Scleroderma
Telangiectatic mats
Telangiectasias
Scleroderma

Laboratory

- Antinuclear antibody is positive in >90% of patients with the nucleolar pattern being most specific.
- Scl-70 antibodies are associated with truncal scleroderma and pulmonary fibrosis.
- Anti-centromere antibody (speckled pattern ANA) is highly specific for CREST syndrome.
Scleroderma

Complications

 Digital ulcerations and resulting infections
 Esophageal dysfunction
 Gastroparesis
 Interstitial lung disease; pulmonary arterial hypertension; lung involvement is most common cause of death
 Renal involvement occurs in 10-15%
Scleroderma

- Abnormal collagen (connective tissue) metabolism
- Vascular damage resulting in reduced number of capillaries
- Lymphocyte activation resulting in production of IL4 and TGF-β by T-cells
Scleroderma
Scleroderma

Course and Prognosis

- Variable and unpredictable course
- Survival can be roughly predicted by the extent of skin involvement within 1 year of diagnosis
- Truncal involvement heralds the worst prognosis with only 21% 10 year survival
Scleroderma

Treatment

- No reliable and effective treatment
- ACE inhibitors can be helpful in scleroderma renal crisis
- Raynaud’s can be treated with cold avoidance, Ca+ channel blockers or amlodipine.
- No smoking, this is critical esp. in Raynaud’s
- Patient education: www.scleroderma.org
MORPHEA

- Morphea is a limited form of Scleroderma
- It has no systemic effects
- Idiopathic dermal plaques with violaceous boarders and central hypopigmentation
- Localized (1 or 2 plaques) or generalized (>3)
- Female:Male is 6:1
- Slow or rapid onset
MORPHEA
MORPHEA
Linear type
Morphea
en coup de sabre
Morphea

Treatment

• As with scleroderma there is no reliable treatment protocol
• Topical mid to super potent steroids
• Intraleisonal kenalog
• Calcipotriene ointment
• Oral corticosteroids for rapidly changing disease
Morphea

Treatment

• Hydroxychloroquine daily by mouth
• Immunosuppressants such as methotrexate or cyclosporine
• Narrow Band UVB treatments
• Lesions tend to darken in the sun so sunblock should be used to prevent hyperpigmentation
NEUROFIBROMATOSIS

- An inherited disorder of the skin and central nervous system
- At least 7 clinical sub-types or variants
- Neurofibromatosis type 1 is the most common
- This type is also known as: Von Recklinghausen’s disease
- Inheritance is autosomal dominant but 50% of cases arise from a new mutation
NEUROFIBROMATOSIS

- An inherited disorder of the skin and central nervous system
- At least 7 clinical sub-types or variants
- Neurofibromatosis type I is the most common
- This type is also known as: von Recklinghausen’s disease
- Inheritance is autosomal dominant but 50% of cases arise from a new mutation
NEUROFIBROMATOSIS

- Male:Female is 1:1
- Neurofibromas are flesh or pink colored soft, pedunculated papules on the skin that vary from a few to hundreds or thousands.
- These generally become noticeable around puberty and increase in number with age and pregnancy.
- Plexiform neurofibromas occur along the course of peripheral nerves. 20% have these.
Neurofibromatosis
Plexiform neurofibroma
NEUROFIBROMATOSIS

- Crowe’s sign...axillary or inquinal freckling is specific for the neurofibromatosis
- Café-au-lait macules (CALMs) are randomly distributed tan to brown patches which increase in number and size until about 5 years of age. Having >6 CALMs greater than 5mm in diameter in prepuberty is suggestive of neurofibromatosis type I. Post-puberty the 6 CALMs should be >15mm
Crowe’s Sign

The axillary and inguinal areas do not normally have freckles since these areas of the body are generally protected from sun and UV light exposure which is required for freckle development, “Crowe’s sign”.
Crowe’s Sign
NEUROFIBROMATOSIS

- Café-au-lait macules
- Size & number increase with age
- Significant for NF if:
  - Child: Six or more > 5mm
  - Adult: Six or more > 15mm
Multiple neurofibromas

• First begin to appear in puberty
• May have a few to hundreds
Lisch Nodule

Asymptomatic small brown papules on the iris, developing during teens and increasing in number with age

Present in 90% of patients with NF
Neurofibromatosis

- Lisch nodules are asymptomatic iris hamartomas that occur in >90% of patients over age 6. If seen in a patient >6 years of age it is considered diagnostic of the condition. This is best done by slit lamp examination.
- Genetic counseling for patients and patient’s family is recommended
- No definitive treatment
- www.nf.org
Neurofibromatosis
TUBEROUS SCLEROSIS

- Autosomal dominant disease (25%) 75% of cases are new mutations
- Incidence of 1 per 10,000 births
- Cutaneous signs:
  - Angiofibroma
  - Shagreen patch
  - Ash leaf macules (hypopigmented spots)
  - Periungual fibromas
- Systemic signs:
  - Seizures
  - Mental retardation
TUBEROUS SCLEROSIS

Ash Leaf Macule
Shagreen patch

- Soft, flesh-colored to yellow, 1-10cm plaque with an irregular surface, most commonly in the lumbosacral region
- A type of dermal connective tissue nevus, in ~80% of pts.
TUBEROUS SCLEROSIS

Angiofibroma
Shagreen:

1. The rough hide of a shark or ray, covered with numerous bony denticles and used as an abrasive and as leather.

2. An un-tanned leather with a granular surface that is often dyed green.
Ash leaf macules

- Hypopigmented macules on the arms, legs and trunk
- Earliest sign of tuberous sclerosis
- Present at birth and increase in size and number throughout life, 1 to 32 in number
- Wood’s light can accentuate the white macules
TUBEROUS SCLEROSIS
TUBEROUS SCLEROSIS
TUBEROUS SCLEROSIS

Ash Leaf Macules
TUBEROUS SCLEROSIS

Koenen’s tumors
Can cause nail deformities even without visible tumors
TUBEROUS SCLEROSIS
# TUBEROUS SCLEROSIS

## Diagnostic Criteria for Tuberous Sclerosis Complex

### Major Features
- Facial angiofibromas or forehead plaque
- Non-traumatic ungual or periungual fibromas
- Hypomelanotic macules (three or more)
- Shagreen patch
- Multiple retinal nodular hamartomas
- Cortical tubers
  - Subependymal nodules
  - Subependymal giant cell astrocytoma
- Cardiac rhabdomyoma, single or multiple
- Lymphangioleiomyomatosis
- Renal angiomyolipoma

### Minor Features
- Multiple, randomly distributed pits in dental enamel
- Hamartomatous rectal polyps
- Bone cysts
- Cerebral white matter radial migration lines
- Gingival fibromas
- Non-renal hamartoma
- Retinal achromatic patch
- Confetti skin lesions
- Multiple renal cysts

### Definite Tuberous Sclerosis
- Either two major features or one major feature plus two minor features

### Probable Tuberous Sclerosis
- One major plus one minor feature

### Possible Tuberous Sclerosis
- Either one major feature or two or more minor features
Candidiasis can be seen in immunocompromised pts. It is also seen in obese, poorly controlled diabetics.

- Diagnosed by KOH
- Consider FBS and other lab based on H&P.
DERMATOMYOSITIS

- Acquired idiopathic connective tissue disease
- Proximal muscle weakness, violaceous skin rash on eyelids, scalp, knuckles and bony prominences
- Seen with underlying malignancy
- Can be seen without muscle involvement (sine myositis)
DERMATOMYOSITIS

- Female:Male is 2:1
- Muscle involvement manifests as difficulty combing the hair or getting up from a chair
- Skin changes precede muscle involvement and ~10% have no associated muscle involvement
- Heliotrope rash describes facial/periorbital appearance
- Gottron’s papules describe changes on hands/knuckles
DERMATOMYOSITIS

Heliotrope Rash
DERMATOMYOSITIS

- Periungual changes show ragged cuticles, erythema and teleangectasia
- Adult and juvenile forms. Only the adult form is associated with possible underlying malignancy
- Ovarian, breast, lung, gastric are the most commonly found underlying malignancies
DERMATOMYOSITIS

Gottron’s Papules
DERMATOMYOSITIS
DERMATOMYOSITIS

- Treatment is to find the underlying cause...
- Evaluation for malignancy based on H&P
- If none is found then treatment is with immunosuppressives
  - Oral corticosteroids
  - Methotrexate
  - Cyclosporine
  - IVIG
NAILS
NAILS

• **Fingernails** grow approx. 0.1mm/day - $365 \times 0.1 = 3.5\text{cm/year}$

• **Toenails** grow approx. 0.05mm/day - $365 \times 0.05 = 1.8\text{ cm/year}$
BEAU’S LINES

- Horizontal, grooved indentations that run from side to side of the nail.
- Not to be confused with vertical/longitudinal ridges that run the length of the nail and are associated with normal aging changes of the nails.
- Due to temporary interruption of matrix cell division.
BEAU’S LINES

Causes:
Chemotherapy
Acute Coronary Occlusion
Malnutrition
Trauma
Hypothyroidism, Diabetes
Psoriasis
TERRY’S NAILS
TERRY’S NAILS

CAUSES:

Liver Failure/Cirrhosis
Renal Failure
Diabetes
Congestive Heart Failure
Hypothyroidism
Malnutrition
Idiopathic
PSORIASIS

Nail Pitting  Nail Dystrophy
KOILONYCHIA
(Spoon Nails)

CAUSES:

Iron Deficiency
Anemia

Chemotherapy

Malnutrition

Coronary Occlusion

Trauma
ONYCHOMADESIS

- Onychomadesis is an idiopathic shedding of the nails beginning at its proximal end, possibly caused by the temporary arrest of the function of the nail matrix.
- One cause in children is hand foot and mouth disease. This generally resolves without complication.
ONYCHOMADESIS

CAUSES:

Idiopathic
Acrodermatitis Enteropathica
Bullous Diseases (Epidermolysis Bullosa)
Stevens-Johnson Syndrome
Malnutrition
Dermatology Texts

- Habif:
- Great Text for Primary Care Specialists
Dermatology Texts

General Dermatology
Andrews Clinical Derm.

Dermatology Treatments
Treatment of Skin Disease