Skin signs of endocrine disorders

Anna Haemel MD
Assistant Professor
UCSF Dermatology

Skin and systemic disease:
A framework

Crohn’s disease
- Directly related (cutaneous Crohn’s)
- Reactive condition (neutrophilic dermatosis)
- Associated condition (alopecia areata)
- Treatment side effect (TNFi induced psoriasis)

DM1
- Directly related (scleredema adultorum)
- Reactive condition (N/A)
- Associated condition (dermatitis herpetiformis)
- Treatment side effect (insulin injection reaction)
Overview

• Skin manifestations of nonmalignant endocrine d/o incl:
  – Thyroid
    • Hyper
    • Hypo
  – Pancreas
    • Diabetes
  – Androgen excess
    • PCOS

• Skin manifestations of neoplastic endocrine conditions incl:
  – Genetic
    • MEN syndromes
  – Metabolic
    • Glucagonoma
  – Paraneoplastic
    • Dermatomyositis

Case 1: Textural changes to legs
Case 1

• 1 year hx of textural changes to shins> upper extremities
• Consult question: Does this patient have scleromyxedema?
• Skin bx forearm – dermal mucinosis
• Labs – SPEP/IFE/free light chains neg
Case 1

- Prior hx Graves’, incl Graves’ ophthalmopathy
  - Significant proptosis
  - Significant ocular surface exposure OD>OS
  - No signs of optic nerve compromise
  - Intermittent diplopia that is not bothersome to the patient

Graves’ disease
Cutaneous Features

- Ophthalmopathy (30%)
- Pretibial myxedema (4%)
- Acropachy (1%)

- Stimulation of thyrotropin receptor results in mesenchymal tissue expansion
- Correction of thyroid level has no effect on skin lesions

Thyroid Dermopathy
Pretibial Myxedema

- Accumulation of glycosaminoglycans
- Bilateral, localized
- Nonpitting infiltration
- Nodules and plaques
- Elephantiasis-like

- Usually have ophthalmopathy
- Acropachy is variable


Case 1

- Treatment approach
  - Ophtho consult for thyroid associated orbitopathy: Currently inactive
    - Encouraged current attempts to quit smoking
  - Skin directed therapy:
    - Topical/intrallesional triamcinolone
    - Compression garments orders (sleeves, gloves, stockings)
Case 1

Thyroid Acropachy

- Clubbing
- Soft tissue swelling of hands and feet
- Periosteal reaction of extremity bones
- Thyroid acropachy is associated with severe Graves’ orbitopathy and need for orbital decompression

Thyroid. 2003 Dec;13(12):1141-4.
thyroid acropathy: periosteal bone formation at the metacarpophalanges and proximal phalanges

soft tissue swelling

onycholysis

Hypothyroidism
Myxedema = systemic mucinosis

- Skin is cold, xerotic, pale
- Coarse hair
- Loss of outer third of eyebrow = madarosis
- Puffy face
- Broad nose
- Thick lips and large tongue (macroglossia)
- Drooping eyelids and periorbital swelling
  - MPS deposition
- Cutis verticis gyrata
- Carotenemia → yellow palms and soles

Hyperthyroidism

- Skin is warm, moist, and smooth
- Palmar erythema
- Facial flushing
- Hair is thinned, downy
- Hyperpigmentation
- Hyperhidrosis
- Nail changes
  - Plummer nails: concave with distal onycholysis

Hyperthyroidism
Other Cutaneous Features

• Vitiligo
  – 7% of patients with Graves’ disease
  – Increased in patients with Hashimoto's thyroiditis

• Urticaria
  – Check thyroid antibodies in chronic urticaria

Case 2: Referral for “morphea”
Case 2

- Skin bx: thickening of the reticular dermis with a slight increase in the amount of interstitial mucin in the deep dermis
- Dx: Scleredema adulterorum
  - Sclerodermiform mucinosis
  - Glycosylation of proteins
# Scleredema adultorum

- Painless non pitting swelling/induration starting on upper back/neck and can spread to upper torso
- 2.5-14% of pts with DM; more common in men
- Increased deposition of collagen due to irreversible nonenzymatic glycosylation of collagen/resistance to degradation
- Very challenging to treat – PUVA, MTX, IVIG, other…


---

## Skin Signs of diabetes

<table>
<thead>
<tr>
<th>Directly related</th>
<th>Associated conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scleredema</td>
<td>Candidiasis</td>
</tr>
<tr>
<td>Diabetic cheiroarthropathy</td>
<td>Fungal infections</td>
</tr>
<tr>
<td>Diabetic dermopathy</td>
<td></td>
</tr>
<tr>
<td>Bullous diabeticorum</td>
<td>Necrobiosis lipidica</td>
</tr>
<tr>
<td>Acanthosis nigricans</td>
<td>Granuloma annulare?</td>
</tr>
<tr>
<td></td>
<td>Psoriasis</td>
</tr>
</tbody>
</table>


• Diabetic dermopathy
  – Most common cutaneous marker of DM
  – 70% of adults w DM


• Bullous diabeticorum
  – Rare but specific (0.05% of pts)
  – Large noninflammatory monolocular bullae on dorsal foot/ankle

Image courtesy of Lindy Fox MD

Acanthosis nigricans associated with insulin resistance

- AN is a sign of peripheral insulin resistance
- Increased in groups with DM commonly (NA, Hispanics, AA’s) and in obesity
- Elevated insulin levels bind to Insulin Growth Factor receptors on keratinocytes causing AN

Skin Signs of diabetes

Directly related
- Scleredema
- Diabetic cheiroarthropathy
- Diabetic dermopathy
- Bullous diabeticorum
- Acanthosis nigricans

Associated conditions
- Candidiasis
- Dermatophytosis
- Necrobiosis lipoidica
- Granuloma annulare?
- Psoriasis
Necrobiosis lipoidica diabeticorum
- 0.3% to 1.6% of pts w DM
- BUT 75% of cases of NLD occur in pts who have or will develop DM

Case 3: Severe adult female acne

- 28 YOF
- Acne in teens, now recurrent again in late 20s
- Irregular menses, excess hair growth, thinning scalp hair
- A1c = 5.8%
PCOS and skin

- 72-82% of pts w PCOS have cutaneous signs of hyperandrogenism
- Acne - 61% of pts w PCOS – not a reliable marker
- Hirsutism – 53% of pts w PCOS – excellent marker
- Acanthosis nigricans – 37% of pts w PCOS – excellent marker
- Hirsutism and AN are both assoc w elevated free testosterone level and increased insulin resistance

Hirsutism - a specific sign in PCOS

Photo courtesy of Kanade Shinkai MD, PhD

Photo courtesy of Kanade Shinkai MD, PhD
Acanthosis nigricans is specific sign in PCOS

Photo courtesy of Kanade Shinkai MD, PhD

Androgenetic alopecia - not a reliable marker of PCOS

Treatment

• Weight loss
• Dietary changes
• OCPs
• Metformin as needed for hyperglycemia
• Spironolactone for hirsutism, acne

Dermatology & disorders of androgen excess

• PCOS (most common)
• CAH
• Ovarian tumors
• Adrenal tumors
Case 4
Necrolytic migratory erythema (assoc w glucagonoma)

- Glucagonoma syndrome: NME skin findings, incr glucagon levels, diabetes/glucose intolerance
- NME: Migratory plaques w superficial epidermal necrosis, central flaccid bullae, and crusted erosions
  - Favors flexural areas
  - Skin may respond to somatostatin analog (octreotide)

Skin manifestations of neoplastic endocrine disorders

- **Metabolic/neuroendocrine**
  - Glucagonoma

- Paraneoplastic
  - Dermatomyositis

- Genetic
  - MEN syndromes

Necrolytic migratory erythema (assoc w glucagonoma)

- Pathogenesis: metabolic etiology involving excess glucagon, amino acid deficiency, zinc deficiency, and free fatty acid deficiency
  - Skin may impove w IV amino acid supplementation or zinc
  - Clinically appears similar to eruption of acrodermatitis enteropathica

Skin manifestations of neoplastic endocrine disorders

– Metabolic/neuroendocrine
  • Glucagonoma

– Paraneoplastic
  • Dermatomyositis

– Genetic
  • MEN syndromes
Malignancy in dermatomyositis

- Most studies have found an increased risk of cancer with DM in up to **30% of patients**
- **Ovarian cancer over-represented**
- Risk is **highest in first 2 years**, but remains elevated out to 5 years
- **Disease may improve with cancer treatment**

Palmar fasciitis - polyarthritis: Assoc w ovarian cancer

Skin manifestations of neoplastic endocrine disorders

– Metabolic/neuroendocrine
  • Glucagonoma
– Paraneoplastic
  • Dermatomyositis
– Genetic
  • MEN syndromes

MEN Type I: Wermer

- Endocrine: Parathyroid hyperplasia, islet cell tumors, pituitary adenomas
- Skin: Facial angiofibromas, collagenomas, (sometimes) lipomas


MEN IIA: Sipple

- Endocrine: Parathyroid hyperplasia, medullary thyroid carcinoma, pheochromocytoma
- Skin: Macular and lichen amyloid, notalgia paresthetica

MEN IIA and lichen amyloid

MEN IIB: Multiple mucosal neuromas syndrome

- Endocrine: Medullary thyroid cancer, pheochromocytoma
- Skin: Multiple mucosal neuromas, marfanoid habitus, joint laxity
Questions?