Gastrointestinal Disease and Dermatopathology

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Key Points

- Subtle dermatologic signs may suggest significant gastrointestinal and systemic disease
- Check family history
- Several dermatologic disorders may be present
24 y.o. Male
Perioral spotting
Peutz-Jegher Disease
Cutaneous Changes

- Excessive freckling or spots on the skin
- Sites
  - Inner lining of the mouth, gums, the lips, around the mouth
  - Around the eyes
  - Fingers or toes
  - Genitalia
Cutaneous Changes

- Oral lesions remain through adulthood
- Bluish black to dark brown to blue
- > 95% of pts.
- No correlation with GI symptoms
GI Disease

- Numerous hamartomatous polyps in stomach and intestines
- Variant of FAP a genetic defect on the APC gene (5q21)
- 500-2500 colonic adenomas with a minimum of 100 needed for diagnosis
<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Characteristics</th>
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<tbody>
<tr>
<td>FAP</td>
<td>Genetic defect on the APC gene (5q21) 500-2500 colonic adenomas with a minimum of 100 needed for diagnosis</td>
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<tr>
<td>Gardner Syndrome</td>
<td>Variant of FAP Colonic adenomas, osteomas of the bone, epidermal cysts, thyroid cancer, and fibromatosis</td>
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<tr>
<td>Turcot Syndrome</td>
<td>Adenomatous colon polyps and tumors of the central nervous system (usually gliomas) Polyps arise from 10-20 yrs, cancer follows after 10-15 yrs</td>
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</tbody>
</table>
44 y.o. F
Diabetes mellitus x15 yrs
Complaining of dirty neck and armpits
Acanthosis Nigricans
Clinical Appearance

- Symmetrical, hyperpigmented, velvety plaques
- Intertriginous areas (axilla, groin, posterior neck)
- Posterior neck common in children
Clinical Appearance

- Vulva in obese hyperandrogenic females
- Acrochordons (skin tags) in affected area
- Nail changes rare
Clinical Variants

Obesity associated
Syndromic
Acral
Unilateral
Familial
Drug induced
Malignant
HAIR-AN SYNDROME

Hyperandrogenemia

Insulin resistance

Acanthosis nigricans syndrome
HAIR-AN Syndrome-Type A

- Familial, affecting primarily young women
- Polycystic ovaries
- Signs of virilization (e.g., hirsutism, clitoral hypertrophy)
- High plasma testosterone levels
- Infancy with progression
HAIR-AN Syndrome-Type B

Uncontrolled diabetes mellitus
Ovarian hyperandrogenism
Autoimmune disease-Ab to insulin
Circulating antibodies to the insulin receptor
Varying symptomatology
<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Gastric</td>
<td>69-90%</td>
</tr>
<tr>
<td>Oral (tongue, lips)</td>
<td>25-50%</td>
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</tbody>
</table>
Histopathology

- Slight papillomatosis
- Minimal basal melanin pigment
- Hyperkeratosis
- Horn pseudo-cysts
- DDX: SK, lentigo
35 y.o. F
Watery stools
Weight loss for 3 months
Rash on trunk and extremities
Dermatitis Herpetiformis with Celiac Sprue
Malabsorption and Skin Disease

- Ichthyosis and pruritis
- Hair and nail changes
- Hyperpigmentation
- Skin texture and elasticity
- Eczematous and psoriatic rashes
Malabsorption and Skin Disease

- Zinc
- Essential fatty acids
- Vitamins
Malabsorption and Skin Disease

- Collagen vascular disease
- DH and celiac disease
Laboratory Evaluation

- IgA Tissue Transglutaminase Antibodies
- IgA Anti-Endomysium Antibodies
- Anti-Gliadin Antibodies
Histopathology

- Subepithelial collections of neutrophils with vesicle
- Tips of papillary dermal papillae
- Minimal eosinophilis
- DDX: Linear IgA disease
DIF

- Subepidermal granular collection of IgA
- DDX: Linear IgA disease
57 y.o F
S/P Roux-en-Y for PUD
Bowel Bypass Associated Arthritis and Dermatosis
Quick Facts

- Blind loop
- Pts. with bowel bypass surgery, inflammatory bowel disease, and ulcer surgery
- Resolves with correction of the bowel anatomy
- Tetracycline or metronidazole
Histopathology

- Neutrophilic dermatosis
- DDX: Sweet’s, LCV
37 y.o. F
Persistent diarrhea, occ. bloody
Ulcerative lesion on ankle
Pyoderma Gangrenosum arising in patient with Ulcerative Colitis
Skin Lesions in IBD

- Pyoderma gangrenosum
- Granulomas
- Erythema nodosum
- Aphthous ulcers
- Malnutrition
- Erythemas, lichen planus, and vascular thrombosis
- Rashes at ileostomy and colostomy sites
GI Bleeding and Skin Disease

- Hereditary hemorrhagic telangiectasia
- Ehlers-Danlos syndrome
- Pseudoxanthoma elasticum
- Kaposi’s sarcoma
- Vasculitis
- Polyposis
- IBD
- Tumors
Pyoderma Gangrenosum

- Systemic diseases in 50%
- Diagnosis of exclusion
- Pathergy
Clinical Variants

- Two primary variants of PG exist
  - Classic ulceration on legs
  - Superficial (Atypical PG) on hands
- Prognosis good
- Recurrences may occur, and residual scarring is common
Clinical Variant

- Extracutaneous changes
  - Culture-negative pulmonary infiltrates
- Overall-NSAIDS, corticosteroids, immunosuppressive agents
Histopathology

- Neutrophilic dermatosis
- Diagnosis of exclusion
54 F
BRBPR
BE with tumor at SC
Dermatomyositis
### Dermatomyositis and Malignancy

<table>
<thead>
<tr>
<th>Study</th>
<th>Pts</th>
<th>Malignancy</th>
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</thead>
<tbody>
<tr>
<td>Sparsa A etal.</td>
<td>33</td>
<td>39% (13/33)</td>
</tr>
<tr>
<td>Stockton D et al.</td>
<td>705 with DM or PM</td>
<td>7% (50 DM and 40 PM)</td>
</tr>
<tr>
<td>Buchbinder R et al.</td>
<td>537 with biopsy proven myositis</td>
<td>116 malignancies in 104 pts</td>
</tr>
<tr>
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<td>Highest risk in DM pts</td>
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</tbody>
</table>
Histopathology

- Cell poor lichenoid interface dermatitis
- Orthokeratosis
- Dermal mucinosis
- DIF for C5b-9 at DEJ and endothelial cells
C5b binds C6 and C7

C5b, 6, 7, complexes bind to membrane via C7

C6 binds to the complex and inserts into the cell membrane

C9 molecules bind to the complex and polymerize

10-16 molecules of C9 bind to form a pore in the membrane
41 y.o. M
S/P Colectomy for Dukes B2 cancer
Sebaceous Carcinoma occurring with Muir-Torre Syndrome
Quick Facts

- Keratoacanthomas, sebaceous neoplasms including sebaceous carcinoma
- Internal visceral malignancies particularly of the gynecological and gastrointestinal tract
- Autosomal dominant
Pathogenesis

- LOH in the chromosomal regions containing hMSH2 and hMLH1 Mismatch repair genes
- hMSH2 > hMLH1
Hereditary nonpolyposis colorectal cancer syndrome (HNPCC)

- Two HNPCC-related cancers
  - Synchronous and metachronous colorectal cancers or associated extracolonic cancers (endometrial, ovarian, gastric, hepatobiliary, or small bowel cancer or transitional cell carcinoma of the renal pelvis or ureter)

- Colorectal cancer and a first degree relative with colorectal cancer or HNPCC-related extracolonic cancer or colorectal adenoma
  - One diagnosed <45 years and adenoma diagnosed <45 years
HNPCC-Criteria cont.

- Colorectal cancer or endometrial cancer <45 years
- Right-sided colorectal cancer with an undifferentiated pattern (solid/cribriform) on histopathology age <45 years
- Signet-ring-cell-type colorectal cancer diagnosed <45 years (>50% signet ring cells)
- Colorectal adenomas diagnosed at age <40 years
### Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Results</th>
</tr>
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<tr>
<td>Mathiak M, et al.</td>
<td>28 skin lesions from 17 MT pts</td>
<td>15/18 tumors with known MSH2 mutations in pt.</td>
</tr>
<tr>
<td>Machin P, et al.</td>
<td>10 skin lesions and 11 visceral tumors from 6 MT pts</td>
<td>All cases with MI 5 pts. Neg for MSH2 1 pt neg. MHL1, pos. for MSH2</td>
</tr>
</tbody>
</table>
Histopathology

- Sebaceous cells in varying stages of maturation
- Lack peripheral palisading
- ORO positive
- EMA+, CD15+?
Key Points

- Subtle dermatologic signs may suggest significant gastrointestinal and systemic disease
- Check family history
- Several dermatologic disorders may be present