Histologic features of this case:

- Atrophic epidermis
- Sclerotic and “layered” appearing dermis
- Areas of histiocytes palisading around paucicellular areas
- Scattered lymphocytes and plasma cells
- Vascular thickening
Our diagnosis

- Necrobiosis lipoidica

Clinical features - NL

- Atrophic annular plaques, most common on shins
- Rarely occur on scalp, face
- More common in women
- 2/3 have frank diabetes
- Virtually 100% with glucose metabolism abnormality

Clinical features - NL

- NL is a disease seen most commonly in patients with relatively advanced diabetes mellitus
- Not usually seen in early cases or in young patients
- Rare that it is presenting sign of disease
Histologic features - NL

- Unremarkable or atrophic epidermis
- Layering appearance in dermis
- Palisaded granulomas
- Sarcoidal granulomas - much less common
- Vascular wall thickening in dermal blood vessels

(continued)

- Pallor to affected dermal collagen - usually mid-to deep reticular dermis
- Minimal mucin present
- Occasional extracellular lipid, multinucleated histiocytes
- Aggregates of lymphocytes, occasional germinal centers
- Plasma cells common
- Fibrosis may extend into subcutaneous fat

Differential diagnosis

- Granuloma annulare
- Actinic granuloma (annular elastolytic granuloma)
- Rheumatoid nodule
- Necrobiotic xanthogranuloma
- Epithelioid sarcoma
Granuloma annulare

- Clinical - more diffuse, smaller lesions
- Disseminated form may also be associated with diabetes (pregnancy, AIDS)
- Smaller foci of granulomatous dermatitis higher in reticular dermis - multiple on one punch biopsy
- Mucinosis degeneration of collagen
- Mixed inflammatory infiltrate

Actinic granuloma

- May represent granuloma annulare occurring on sun-damaged skin
- Usually multiple lesions on sun-exposed body sites
- Small foci of granulomatous degeneration in superficial dermis
- Multinucleated giant cells often containing degenerating elastotic material
- Elastolysis in center of granulomatous foci
**Rheumatoid nodule**

- Peri-articular nodules over smaller joints
- Little to no surface changes to skin
- Single large focus of granulomatous degeneration in dermal collagen
- Present in deep reticular dermis and into subcutaneous fat
- Fibrin covers collagen leading to brick-red color
- Well-circumscribed palisade of histiocytes including multinucleated cells

**Actinic granuloma**

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Necrobiotic xanthogranuloma

Rheumatoid nodule

• More later
• Large foci of degenerating collagen with cholesterol clefts - difficult to distinguish except by characteristic histories and degree of degeneration

Necrobiotic xanthogranuloma

Rheumatoid nodule

Necrobiotic xanthogranuloma
Epithelioid sarcoma

- Single nodule on distal extremity - usually in teens to young adults
- Necrosis of cells present in central area of apparent degeneration
- Cells in palisade demonstrate cytologic atypia
- Mucin not present
- If true concern, immunostains demonstrating cytokeratin positivity are helpful

Necrobiotic xanthogranuloma

Epithelioid sarcoma

Other cutaneous manifestations of diabetes

- Diabetic dermopathy
- Bullosis diabeticorum
- Eruptive xanthomas
Necrobiotic Xanthogranuloma

• HISTOLOGIC FINDINGS
  – Low Power - Normal epithelium and rounded well-circumscribed dermal process
  – Intermediate Power - Dermal palisade of histiocytes including foam cells and numerous giant cells with intervening zones of hyaline necrosis with cholesterol clefts and lymphoid follicles

Necrobiotic Xanthogranuloma

• HISTOLOGIC FINDINGS (cont)
  – High Power - Giant cells of the Touton and foreign-body type often with irregular size, shape and distribution of the nuclei
Necrobiotic Xanthogranuloma

Our diagnosis: Necrobiotic Xanthogranuloma

Necrobiotic Xanthogranuloma - Clinical Features

- Yellow-red indurated nodules and plaques of the face, particularly the infraorbital area
- Rare condition, seen exclusively in adults, equal gender distribution
- Association with paraproteinemia, hyperlipidemia, scleritis and keratitis
Differential Diagnosis of Necrobiotic Xanthogranuloma

- Granuloma annulare
- Actinic granuloma
- Rheumatoid nodule
- Ruptured epidermal inclusion cyst
- Phaeomycotic ‘cyst’

Clinico-pathologic Features of Ruptured Inclusion Cyst

- Formed following occlusion of the follicle infundibulum
- Common condition particularly in adults in all hair-bearing areas
- Following trauma may rupture inciting host inflammatory response
- See well-circumscribed collection of acute and chronic inflammatory cells, including numerous giant cells, some containing squames
Clinico-pathologic Features of Phaeomycotic ‘Cyst’

- Uncommon condition seen particularly in the southeastern US and tropical areas
- Infection by one or more dermatophyte fungi particularly *Exophiala jeanselmi* and *Wangiella dermatitidis*
- Verrucous or cystic lesions often located on the extremities
- Pathogenesis involves implantation of the organism with penetrating injury (splinter)
Phaeomycotic Cyst

Case #3
Clinical Features of Lupus Erythematosus

- Systemic disease shows macular erythema distributed over malar area, discoid lesions, oral ulcerations, essentially all patients have systemic symptoms (joints, renal, serositis, neurologic, cardiac, pulmonary, and ocular) as well as (+) ANA, dsDNA serologies

Clinical Features of Lupus Erythematosus

- Pathogenesis involves antibodies to various ribonucleoproteins with immune complex formation, minority of patients develop antibodies following exposure to medications (penicillamine, quinidine, procainamide)

Clinical Features of Lupus Erythematosus

- Immune complex formation underlies the utility of the lupus band test (direct immunofluorescence showing granular IgG and C3 deposits along the dermo-epidermal junction

Clinical Features of Lupus Erythematosus

- Common systemic chronic inflammatory disease seen especially in middle-aged women
- Three major clinical variants - discoid (most common), subacute and systemic
- Discoid shows well-demarcated scaly plaques of the face particularly the ear and cheeks with scalp disease associated with scarring alopecia, 20% associated with systemic disease, 70% with (+) ANA, association with C5 deficiency
- Subacute shows annular erythematous macules in sun-exposed areas, 40% have systemic manifestations, 90% have (+) ANA, association with C2 deficiency

Histologic Features

- Low Power - Epidermal atrophy with patchy dermal infiltrates
- Intermediate Power - Follicular plugging, interface dermatitis with peri-eccrine and peri-follicular lymphocytic infiltration
- High Power - Basement membrane thickening and dermal mucin deposits

OUR DIAGNOSIS:

DISCOID LUPUS ERYTHEMATOSUS
Differential Diagnosis of SLE

- Dermatomyositis
- Lichen Sclerosis et Atrophicus

Clinico-pathologic Features of Dermatomyositis

- Rare chronic inflammatory disorder of the skin and skeletal muscles
- Association with visceral malignancy, especially the breast and lung
- See violaceous papules of the first metacarpal joint skin (Gottron’s papules) with violaceous rash of the upper chest and eyelids (heliotrope)
- Serology can be positive for anti-Jo-1
- Histology similar to lupus with lesser degree of dermal inflammation and negative lupus band test
**Dermatomyositis**

- Early lesions show a lichenoid lymphoid infiltrate
- Progressive epidermal atrophy and papillary dermal sclerosis
- Negative lupus band test

**Lichen Sclerosis et Atrophicus**

- Localized inflammatory-induced atrophy of the skin and mucous membranes, more common in women
- Most commonly involves atrophy of the vagina and penis, extragenital disease seen in 20% of patients
- See coalescing white papules with wrinkled “cigarette paper” like epidermal atrophy
- Unlike genital sites there is no risk for malignant degeneration

**Histology**

- Early lesions show a lichenoid lymphoid infiltrate
- Progressive epidermal atrophy and papillary dermal sclerosis
- Negative lupus band test
**Other Cutaneous Variants of Lupus Erythematosus**

- **Neonatal**, association with anti-Ro antibodies and heart block
- **Bullous**, blisters in patient with established lupus, more common in African-American females
- **Lupus panniculitis (profundus)**, erythematous nodules on face and trunk

**Neonatal Lupus**
Case #4

Lupus Profundus
Our diagnosis:
• Dermatitis herpetiformis

Clinical features - DH
• Intensely pruritic, erythematous papules
• Symmetrical distribution
• Often on extensor surfaces of extremities - elbows and knees
• Sacrum
• Rare to find intact blisters - too pruritic
• Excoriations common
• Most common in young to middle-aged adults

Clinical features (continued) - DH
• Gastrointestinal anomalies seen in all patients - villous atrophy in small intestine
• Usually sub-clinical
• Rare patients with symptoms of celiac sprue
• Autoimmune thyroid disease
• Lupus, rheumatoid arthritis, other autoimmune processes
• Associated with GI lymphomas:
  – MALTomas, some large cell T-cell lymphomas

Histologic features of this case:
• Subepidermal blister
• Predominantly neutrophilic infiltrate
• No epidermal necrosis
• Inflammation largely confined to papillary dermis
• Eosinophils scant
Histologic features - DH (continued)

- Dying keratinocytes not a common feature
- Involvement of deep dermis not expected finding

Dermatitis herpetiformis

Dermatitis herpetiformis

Dermatitis herpetiformis

Histologic features - DH

- Rare intact blisters
- Microabscesses within papillary dermal tips
- Subepidermal blisters often involve only 1-2 rete ridges
- Superficial perivascular lymphocytic infiltrate
- Scattered eosinophils
Dermatitis herpetiformis

Immunologic features - DH
- Granular deposits of IgA within papillary dermal tips
- Must distinguish from linear staining along DEJ seen in linear IgA bullous dermatosis
- Best to biopsy peri-lesional skin
- (Neutrophils may enzymatically degrade immune deposits)

Treatment - DH
- Treat with dapsone and gluten-free diet
- Dapsone alone will cause resolution of the lesions and histologic changes, but IgA deposits will persist
- Long-term gluten-free diet will result in negative direct immunofluorescence
- Also prevents lymphoma risk

Differential diagnosis - DH
- Linear IgA bullous dermatosis
- Bullosis dermatosis of childhood
- Epidermolysis bullosa acquisita
- Bullous lupus erythematosus
- (Cicatricial pemphigoid)
Linear IgA bullous dermatosis

- Larger blisters, may be intact - often associated with drug ingestion in adults (especially vancomycin)
- Larger subepidermal blisters with linear array of neutrophils in papillary dermis
- Linear IgA staining along dermal-epidermal junction

Epidermolysis bullosa acquisita

- Blisters and milia formation often on extremities - at sites of repeated minor trauma
- Most cases non-inflammatory, but can be neutrophil-rich
- Scarring seen in older lesions
- DIF - linear IgG along the floor of the blister (Ab. directed against type VII collagen)
Epidermolysis bullosa acquisita

Bullous lupus erythematosus

- Patients usually with other cutaneous manifestations of LE and focal blisters
- Often superficial and deep perivascular and peri-appendageal lymphocytic infiltrate along with the subepidermal blister and neutrophils
- DIF - granular IgG/IgM/C3 along DEJ (typical of LE)

Bullous LE

Case #5
Histologic features of this case:

- Well-circumscribed proliferation of keratinocytes with clear to pale cytoplasm
- Minimal cytologic atypia
- Entirely intra-epidermal
- Perhaps centered around a hair follicle with overlying parakeratosis

Our diagnosis

- Trichilemmoma
Clinical features - trichilemmoma

- One or multiple small papules or nodules
- Most common on face
- Often have tufts of vellus hairs emanating from surface
- When multiple, must consider Cowden syndrome

Histologic features - trichilemmoma

- Plate-like growth down from epidermis often centered around hair follicle
- Overlying focal parakeratosis
- Keratohyalin clumping in some cases
- Keratinocytes with clear to pale cytoplasm
- Palisade of basal cells with clear cytoplasm at periphery with thickened underlying basement membrane zone (outer root sheath differentiation) - “piano keys”
Cowden syndrome

- Extracutaneous manifestations:
  - Fibrocystic disease of the breast
  - Thyroid adenomas
  - Ovarian cysts
  - Lipomas
  - Neuromas
  - Gastrointestinal polyps

- Cutaneous findings:
  - Trichilemmoma
  - Gingival fibromas - “cobblestoning”
  - Sclerotic fibroma
  - Acral keratoses
  - Palmar pits
  - Tumor of the follicular infundibulum

- Less common extracutaneous manifestations:
  - Breast and thyroid carcinomas
  - Skeletal abnormalities
  - Acromelanosis
  - Non-Hodgkin’s lymphoma
  - Carcinomas of skin, tongue, cervix

- pTEN mutations on chromosome 10q23
- Tumor suppressor gene
Differential diagnosis - trichilemmoma

- Eccrine poroma
- Verruca vulgaris
- Tumor of the follicular infundibulum
- Inverted follicular keratosis
- Squamous cell carcinoma

Eccrine poroma

- Often acral, may resemble vascular lesion clinically
- Keratinocytes with central hyperchromatic nuclei and clear cytoplasm
- Ductular differentiation present
- Hyalinized type IV collagen helpful when present
- Vascular dilatation present in dermis
Verruca vulgaris

- Often difficult to distinguish from trichilemmoma
- Keratohyalin clumping, parakeratosis, pale-cell changes in keratinocytes similar
- Absence of thickened basement membrane and peripheral palisading of basal keratinocytes may favor verruca vulgaris over trichilemmoma

Tumor of the follicular infundibulum

- Cutaneous tumor with no specific clinical features
- Horizontally-oriented inter-anastamosing cords of more basaloid appearing cells and follicular cysts
- Cysts lined with granular layer - resemble those seen in seborrheic keratosis
- No thickened basement membrane or peripheral palisade
Inverted follicular keratosis

- Similar clinical appearance
- Similar cup-shaped lesion centered around hair follicle and growing down from epidermis
- Squamous eddies, spongiosis and inflammation characteristic
- No thickening of basement membrane or peripheral palisade present

Squamous cell carcinoma

- May have similar appearance to the keratinocytes with cytoplasmic clearing
- More pleomorphism, mitotic activity, cytologic atypia
- No thickening of basement membrane zone or peripheral palisading
- Trichilemmal carcinoma can be difficult to distinguish in some cases

Case #6

Inverted follicular keratosis
OUR DIAGNOSIS:

NECROLYTIC MIGRATORY ERYTHEMA
(GLUCAGONOMA SYNDROME)

Clinical Features of The Glucagonoma Syndrome

- Crops of peripherally expanding annular erythematous patches with surmounted scale and bullae involving the trunk and proximal extremities
- Associated with glucagon secreting pancreatic islet cell tumor (malignant 70% of cases)

CLINICAL FEATURES (continued)

- Other clinical manifestations include glossitis, stomatitis, weight loss and venous thrombosis
- Laboratory findings include hyperglycemia, normochromic, normocytic anemia and decreased serum amino acids associated with spectacular elevations in the serum glucagon level

Histologic Features of Glucagonoma Syndrome

- **Low Power** - Slightly thickened epidermis with normal dermis
- **Intermediate Power** - Broadly pale epithelium with confluent parakeratosis
- **High Power** - Abrupt transition to parakeratotic zone without an interposed granular layer
  - Pallor follows cytoplasmic vacuolar change with ballooning necrosis and intercellular cleft formation
**Pellagra/Hartnup Disease**
- Niacin deficiency with classic triad of dermatitis, diarrhea and dementia
- Dermatitis involves a scaly annular hyperpigmented rash of the sun-exposed V-of-neck area, face and upper extremities
- Hartnup disease is a rare autosomal recessive disorder of intestinal tryptophan absorption in gut and renal tubules
- Also niacin deficiency with malabsorption syndromes, medications that interfere with tryptophan metabolism such as isoniazid, 5-fluorouracil and chloramphenicol, and carcinoid syndrome

**Differential Diagnosis of Glucagonoma Syndrome**
- Acrodermatitis enteropathica
- Pellagra/Hartnup Disease

**Acrodermatitis Enteropathica**
- Autosomal recessive disorder of zinc metabolism
- Triad of alopecia, diarrhea, scaly periorificial and acral rash seen in infants/children following weaning
- Other features include photophobia, nail dystrophy, short stature, and stomatitis
- Zinc deficiency also seen in adults with Crohn’s disease, patients receiving total parenteral nutrition, following intestinal bypass surgery, AIDS, cystic fibrosis, and anorexia nervosa
- Pathogenesis thought to involve qualitative defect in zinc transporter or zinc deficiency

**Case #7**

**Differential Diagnosis of Glucagonoma Syndrome**
- Acrodermatitis enteropathica
- Pellagra/Hartnup Disease
Our Diagnosis: Paraneoplastic Pemphigus

Clinical Features of Paraneoplastic Pemphigus

- Disseminated polymorphous erythematous papules and plaques with mucosal ulcers
- Usually associated with internal malignancies particularly non-Hodgkin lymphoma
- Circulating antibodies to desmoplakin I, an intercellular adhesion molecule
- Intercellular and basement membrane staining with IgG and C3 on direct immunofluorescence

Histologic Features of Paraneoplastic Pemphigus

- **Low Power** - Ragged appearing epidermis with band-like inflammatory infiltrate along the dermo-epidermal junction
- **Intermediate Power** - Dense infiltrate of lymphocytes with basal layer dyskeratosis and vacuolar alteration
- Histology may show variable features including pemphigus-like acantholysis with intraepidermal blister formation or bullous pemphigoid-like subepidermal blister formation
Paraneoplastic Pemphigus

Paraneoplastic Pemphigus

Paraneoplastic Pemphigus

Paraneoplastic Pemphigus

Paraneoplastic Pemphigus

Paraneoplastic Pemphigus
Differential Diagnosis of Paraneoplastic Pemphigus

- Lichen planus
- Erythema multiforme
- Pemphigus vulgaris
- Bullous pemphigoid

Clinico-Pathologic Features of Lichen Planus

- 5 P’s of Pruritic, Purple, Polygonal, Papules and Plaques
- No association with visceral malignancy, although weak association with diabetes mellitus
- Histologic features include epidermal hypergranulosis with a dense band-like infiltrate with basal layer dyskeratosis and vacuolar change
- Subepidermal vesiculation, and acantholysis exceptional
- Direct immunofluorescence shows non-specific positivity with IgM and C3 within dyskeratotic cells

Clinico-Pathologic Features of Erythema Multiforme

- Disseminated annular and targetoid erythematous papules especially involving the palmar surfaces
- Hypersensitivity reaction to occult or concurrent infections including HSV, mycoplasma, streptococci, and histoplasmosis as well as an association with autoimmune disorders (RA, SLE) and inflammatory bowel disease

Clinico-Pathologic Features of Erythema Multiforme

- Histology yields interface lymphocytic dermatitis with basilar vacuolar change
- DIF shows non-specific binding with IgM within dyskeratotic cells

Clinico-pathologic Features of Lichen Planus

- Disseminated annular and targetoid erythematous papules especially involving the palmar surfaces
- Hypersensitivity reaction to occult or concurrent infections including HSV, mycoplasma, streptococci, and histoplasmosis as well as an association with autoimmune disorders (RA, SLE) and inflammatory bowel disease

Erythema Multiforme

Lichen Planus
Erythema Multiforme

Clinico-Pathologic Features of Pemphigus Vulgaris

- Uncommon disseminated vesiculobullous disorder with widespread fragile blisters, crusts and oral ulceration
- 15% mortality in association with secondary cutaneous infection
- Rare association with visceral malignancy (lung, breast)
- Prominent intraepidermal acantholysis with intraepidermal blister formation
- Circulating antibodies to desmoglein 3 and DIF with intraepidermal intercellular IgG and C3 staining
Bullous Pemphigoid

Clinico-Pathologic Features of Bullous Pemphigoid

- Systemic subepidermal vesiculobullous disorder characterized by widespread tense blisters without oral ulceration
- Association with medications particularly penicillins, sulfas, NSAIDS and diuretics also with autoimmune disorders (SLE, RA, PBC, DM, and UC)
- Circulating antibodies to bullous pemphigoid antigens 1 and 2 - hemidesmosome components
- DIF positive for IgG and C3 along the dermoepidermal junction
Histologic features of this case:

- Well-circumscribed, lobular proliferation of sebocytes
- Sebocytes not fully mature, but minimal cytologic atypia
- Occasional mitoses (none atypical)

Our diagnosis:

- **Sebaceous adenoma**

Histologic features - sebaceous adenoma

- Well-circumscribed islands of keratinocytes within the dermis
- Peripheral cells are basaloid with progressive orderly maturation to sebocytes towards center of aggregates
- Basaloid cells usually comprise less than 50% of cells in tumor
- Mitoses seen on occasion, but no atypical forms
- Necrosis not a feature
- Tumors associated with Muir-Torre often with unusual histologic features

Clinical features - sebaceous adenoma

- Non-descript cutaneous tumor with slightly yellowish hue in some cases
- NOT the same as *adenoma sebaceum* (angiofibroma) associated with tuberous sclerosis
Muir Torre syndrome

- Autosomal dominant
- Cutaneous manifestations
  - Multiple sebaceous neoplasms (not sebaceous hyperplasia)
  - Keratoacanthomas
  - Epidermal cysts
- May precede or follow GI tumors

Sebaceous adenoma

Muir Torre syndrome

Keratoacanthoma

Sebaceous adenoma
**Muir Torre syndrome**

- Extracutaneous manifestations
  - Gastrointestinal carcinomas
    - Tend to be indolent with low metastasis rate
  - Colonic polyps
  - Laryngeal carcinomas
  - GU tumors in men
  - Ovarian and uterine neoplasms
  - Rarely lymphoma

**Sebaceous hyperplasia**

- Often multiple yellow papules on sun-exposed skin
- Frequently confused with BCC clinically
- Full maturation with only a peripheral layer of basaloid cells
- Crucial distinction - not associated with Muir-Torre syndrome

**Differential diagnosis - sebaceous adenoma**

- Sebaceous hyperplasia
- Sebaceous epithelioma
- Sebaceous carcinoma
- Nodular (clear cell) hidradenoma
- Balloon cell nevus
- Metastatic renal cell carcinoma
Sebaceous epithelioma

- No distinguishing clinical characteristics
- More than 50% basaloid cells - may be BCC with sebaceous differentiation
- No capacity for metastasis
- Not an important distinction - also associated with Muir-Torre syndrome

Sebaceous carcinoma

- Majority around eyelids, but can be at other body sites
- In general, high rate of metastasis, but not so in patients with Muir-Torre syndrome
- Nuclear atypia, pleomorphism, mitotic activity, necrosis, lack of circumscription, Pagetoid spread all favor carcinoma over adenoma

Nodular (clear cell) hidradenoma

- No scalloped nuclei
- Cytoplasmic vacuole larger, no microvesiculation
- No palisade of basaloid cells around periphery of tumor lobules
- Ductular formation
- Reduplication of type VI collagen (hyalinized)

Nodular hidradenoma

Sebaceous epithelioma
Nodular hidradenoma

Balloon cell nevus

- Nesting pattern
- Usually areas with more typical melanocytes or pigment
- Intraepidermal melanocytes in many cases
- Maturation present
- S100 positive

Nodular hidradenoma
Balloon cell nevus

Metastatic renal cell carcinoma
- Cytologic atypia and mitoses
- Increased vascularity
- No peripheral palisade of basaloid cells
- Nuclei without scalloping
- S100 positive (unlike sebaceous tumor)
Metastatic renal cell carcinoma

Case #9
Clinical features - multicentric reticulohistiocytosis

- Multiple nodules, often ulcerated on dorsum of hands, overlying joints
- Mutilating arthritis frequently present
- Onset in middle age, rare in childhood
- More common in women
- Resolves spontaneously in 5 -1 years

Our diagnosis:

- Multicentric reticulohistiocytosis

Clinical features - multicentric reticulohistiocytosis (continued)

- Associated with internal malignancy, especially hematopoietic in up to 30% of cases
- Normolipemic
- Frequent xanthelasmas
- Rarely involves lungs, bone marrow, lymph nodes
- May involve mucosa of oral cavity, nose, pharynx

Histologic features of this case:

- Atrophic epidermis
- Aggregation of large histiocytes with abundant eosinophilic (oncocytic) cytoplasm
- Occasional multinucleated giant cells
- Minimal cytologic atypia, scattered mitoses

Histologic features - multicentric reticulohistiocytosis

- Flattened epidermis
- Grenz zone
- Dermal aggregation of mononuclear and multinucleated histiocytes with “ground glass” or oncocytic cytoplasm
- Rare foamy cells
- Lymphocytic infiltrate common
- Mitoses unusual
- Cells express CD68, but not CD1a or MAC387

Our diagnosis:

- Multicentric reticulohistiocytosis
Differential diagnosis - multicentric reticulohistiocytosis

- Solitary reticulohistiocytoma
- Xanthogranuloma
- Xanthoma disseminatum

Solitary reticulohistiocytoma

- Histologically indistinguishable
- Only one lesion clinically
- Essential differential diagnosis as solitary form not associated with systemic illness

Xanthogranuloma
Juvenile xanthogranuloma

- Most common in children
- No predilection for extremities
- No underlying joint changes
- Similar histology but without oncocytic changes in cytoplasm (subtle), and more Touton giant cells (in well-developed lesions)
- Normolipemic

Xanthogranuloma (juvenile)

Juvenile xanthogranuloma

Xanthoma disseminatum

- Diffuse orange-yellow papules
- Diabetes insipidus in many cases
- Histology indistinguishable from xanthogranuloma but markedly different clinical presentation
- Normolipemic

Xanthoma disseminatum

- Diabetes insipidus in many cases
- Histology indistinguishable from xanthogranuloma but markedly different clinical presentation
- Normolipemic
HISTOLOGIC FEATURES

- Low Power - Normal appearing epidermis with slight blurring of the dermo-epidermal junction
- Intermediate Power - Lymphocytes aligned along the dermo-epidermal junction with capillaritis, purpura and interstitial eosinophils

OUR DIAGNOSIS:
DRUG ERUPTION
CLINICAL FEATURES OF DRUG ERUPTION

- ‘Great Masquerader’ capable of presenting in a variety of guises simulating numerous inflammatory conditions
- Most common presentation is of a rapid-onset disseminated non-blanching erythematosus papules within 10 days of starting a new medication

CLINICAL FEATURES OF DRUG ERUPTION

- Among the more common medications known to produce eruption are antibiotics particularly penicillins, diuretics and anti-hypertensives
- Some medications have classic associations such as gold - lichenoid papules, ACE-inhibitor - photo-distributed, vancomycin - Red Man Syndrome
- Often confirmed by cessation of an offending medication or with provocation (re-challenge)
- Ongoing experiments with serum MIF (macrophage inhibition factor) assay which characteristically increases when the patient is challenged with a medication

Pathogenesis and Types (cont)

- Toxic Epidermal Necrolysis - Disseminated blisters with oral involvement, Anti-convulsants and sulfonamides
  - Histologically see trans-epidermal necrolysis without inflammatory cells
- Halogenoderma- Verrucous papules/plaques with exposure to iodine (soft drinks) or bromine (Sominex) containing compounds
  - Histologically see pseudoepitheliomatous epidermal hyperplasia

Drug Eruption

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  - Histologically see pseudoepitheliomatous epidermal hyperplasia

Pathogenesis and Types

- Pathogenesis involves all four of the Gell and Coombs reactions
- Specialized forms of cutaneous drug reactions include:
  - Fixed Drug - Recurring hyper-pigmented patches with exposure to an offending medication- phenolphthalein and Septra most common, histologically see interface dermatitis with melanoderma

Drug Eruption