Inflammatory Skins

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Case 1

• 51 M long standing plaque on back
Main Features

• Low power; Not obvious
• Rather square edged biopsy.
• Increased thickness to dermal collagen
• Minimal inflammation
• Collagen of deeper dermis appears swollen lacking normal inter-fibre spaces.
• Eccrine coils; look high up with no surrounding fat
Morphoea

- On histology cannot distinguish from Systemic sclerosis
- Clinical setting all important. Single plaque; morphoea.
- Several variants; Guttate, Linear, Generalised, s/c [profundus].
Differential & distinguishing features

- Systemic Sclerosis; Clinical setting
- GVHD; late stage; Clinical setting and epidermal changes.
- DXT, atypical nuclei. Can get morphoea developing post DXT.
- C.T.Naevus; Different setting, can have ^ elastin
- Scleroedema of Buschke and lichen myxoedematosus. Distinct clinical and increase in mucin as well as collagen.
- Lichen Sclerosus, papillary dermal changes can be identical. Lacks deeper dermal changes and has basement membrane changes.
Case 2

- 40F Papular lesions on hands
Microscopic features

- Multiple nodular lesions in dermis
- Nodules composed of inflammatory cells, mainly histiocytes, with central area of altered collagen. Collagen altered, loss of dermal fibroblasts = Necrobiosis.
- Few neutrophils in centre
- Perivascular lymphocytes
Granuloma Annulare

• Few clinical variants; Localised, Generalised and Deep [pseudorheummatoid nodule esp. in kids]

• Watch out for Epithelioid sarcoma- some mild atypia, more solid proliferation. C.K. pos.
Case 3

- 60F, Lesions on lower legs
Microscopy

• Entire dermis abnormal
• Collagen shows degenerative changes; Necrobiosis
• Collections of giant cells, plasma cells
• Perivascular Lymphocytes
Necrobiosis lipoidica

• Association with diabetes
• Usually lower legs
• Microscopic variant; sarcoidal.
• Differs from GA: Sarcoidal granuloma’s, entire dermis involved, plasma cells.
Case 4

- 40 Male, lump on elbow
Microscopy

• Amorphous material deposits
• Needle like pattern to deposits on higher power.
• Foreign-body reaction
Gouty Tophus

• Typical clinical
• Sodium urate crystals are water soluble, therefore best sent in alcohol and inform lab so processing and sectioning skips aqueous stages.
• If not done, not all lost, can section and use alcohol not water bath to float sections.
Case 5

- 70M, widespread rash with pustules.
Microscopy

• Mild epidermal acanthosis
• Collections of neutrophils [neuts] in corneum and sub-corneal.
• Foci of vacuolar degeneration of superficial epidermis associated with Neutrophils, ‘spongiform pustule of Kogoj’
• Perivascular lymphocytes and neutrophils.
Pustular Psoriasis

• Localised; chronic disease of palms and soles
• Generalised; serious illness. May or may not have history of psoriasis. May have precipitating factor eg illness, drugs. Withdraw of steroids well known.
Differential diagnosis

• Reiter’ Syndrome; Classic triad of Arthritis, urethritis, conjunctivitis.

• Acute generalised exanthematous pustulosis [AGEP]. Type of drug eruption, acute with no parakeratosis, less marked spongiform pustules, has eosinophils, occ. Dyskeratotic cells.
Neut’s in the horn

- Can you name any conditions?
Neut’s in the horn

- Infections
  - Fungi, candida, dermatophytes
  - Bacterial impetigo
- Psoriasis, esp. pustular
- Reiter’s disease
- Sub-corneal pustular dermatosis
- IgA pemphigus
- Syphilis
- Miliaria Crystallina
- Acute generalised Exanthamatous pustulosis
  - Seborrheic dermatitis
Case 6

• 30M Sudden onset of widespread blistering eruption also involving mouth.
Microscopic features

- Epidermal death. Areas full thickness. Other areas scattered apoptotic cells through epidermis.
- Minimal Inflammatory cell inflammatory cell infiltrate.
- Blister due to epidermal death.
- Corneal layer normal.
Differential diagnosis?
Toxic epidermal Necrolysis

- Serious condition. Treat like a burn.
- Serious form of Erythema Multiforme.
- Associations; Infections, Drugs, Malignancy, Connective tissue diseases.
Differential Diagnosis

- GVHD, acute
- L.E.- Sub-acute
- Drugs eruption- Fixed, lichenoid
- Pityriasis Lichenoides
- Eruption of lymphocyte recovery
Case 7

• 40 M, Previous BM transplant. Now widespread rash
Microscopy

• Upper dermal infiltrate, perivascular and interface.
• Vacuolar change to basal keratinocytes.
• Satellite cell necrosis
• No eosinophils
Differential diagnosis

• See under TEN
• Main problem is with drugs. No eosinophils. Usually not possible to distinguish between them.
Case 8

- 70 M, itchy rash with on legs
Main features

- Sub-epidermal blister
- Inflammatory with eosinophils ++
Differential diagnosis

• Bullous Pemphigoid [BP]
• Herpes gestationis
• Insect bites
Bullous pemphigoid

• Immunofluorescence very helpful.
Case 9

- 75 F, urticarial rash
Case 9, main features

- Epidermal spongiosis
- Intra-epidermal vesicle
- ? Small sub-epidermal split
- Infiltrate with many eosinophils
Differential diagnosis

• Eosinophilic spongiosis
  – Pemphigus
  – BP
  – Allergic contact dermatitis
  – Insect bite
  – Incontinentia pigmenti [infants]
Bullous pemphigoid

• IMF again useful
BP, Immunofluorescence
IgG Basement membrane
Case 10

• 40 Male, pigmented papular rash
Case 10

- Low power, very little to see.
- Closer examination, marked dermal melanin pigmentation.
- Even closer examination, small pink deposit in Papillary dermis.
Differential Diagnosis

• Post inflammatory hyper pigmentation.
• Papular/macular amyloid
Macular Amyloid

- Easy to miss the small amyloid deposits. Almost invisible on standard H+E.
- There is marked dermal melanin pigmentation.
- Small globular eosinophilic deposits in the papillary dermis. If rack down condenser, easier to see, cracked deposits.
- Stain with Congo red, Thioflavin T and broad spectrum cytokeratins.
Macular Amyloid

- Clinically; very itchy eruption.
- Innumerable small papules, often on the trunk.
- Pigmentation, which can have a ripple appearance.
- Derived from epidermal keratin. Pruritis plays a role. Amyloid K
BIOPSIES WITH VERY LITTLE TO SEE

• DO NOT DISPAIR

• REMEMBER INVISIBLE DERMATOSES
Invisible dermatoses

• Subtle changes to epidermis
  – Ichthyosis
  – Granular parakeratosis
  – Mild change in melanin pigment, e.g. Vitiligo

• Subtle Dermal changes
  – Interstitial GA, anetoderma, PXE, atrophoderma

• Infections – Fungi [Tinea incognito, erythrasma]
Invisible dermatoses

• Deposition disease
  – Amyloid
  – Iron
  – Argyria
  – Mucin

• Mast cell disease.
  – Urticaria pigmentosa, Telangiectasia macularis perstans [TMEP].
Case 11

• 70M Post-op. ?drug rash.
Microcopy

- Papule
- Acantholysis.
- Occasional dyskeratotic cell
- Minimal inflammation
- Small amount of scale.
Supra basal blister with acantholysis

- Pemphigus Vulgaris
- Hailey-hailey disease
- Dariers Disease
- Grovers Disease
- Solar keratoses
Diagnosis; Grovers Disease

- Clinical picture; multiple itchy papules on trunk.
- Negative immunofluorescence [IMF].
- Often mixed picture on histology; spongiotic, acantholysis, dykeratotic.
Case 12

- 73M, Nodular lesions on lower legs.
Microscopy

- Squamo-proliferative lesion
- Inflammation, mainly lymphocytes but a few eosinophils.
- Scattered colloid bodies
- At edge, pointed rete ridges.
Hypertrophic Lichen Planus

- Clinical setting important; both lower legs. Often known LP.
- No cytological atypia
- Lichenoid infiltrate not as marked. Can be limited to lower rete. Eosins can be present.
- Increased risk of SCC’s. Cytological atypia, deep infiltration.
Case 13

- 23F, widespread papular rash.
Microscopy

- Focal process
- Lichenoid infiltrate
- Mixture of lymphocytes and histiocytes. Occasional multinucleate cell.
Lichen Nitidus

• Distinct clinical; pinpoint papules in young Afro-Caribbean, trunk and limbs.
**Lichenoid;** Dense band like infiltrate of lymphocytes in papillary dermis which obscures D-E junction.

- LP
- Lichen Nitidus
- Lichen Striatus
- Lichenoid Drug
- Lichenoid reaction to tumours; AK, halo naevus

- Pityriasis Lichenoides
- Lichen Aureus
- MF
- GVHD
Case 14

- 45F, nodule on leg
Microscopy

- Nodular infiltrate in dermis
- Composed of an admixture of large cells with copious eosinophilic cytoplasm, scattered eosinophils, neutrophils and lymphocytes.
Reticulohistiocytoma

• One form of non-langerhan’s cell histiocytosis.
• Has distinct appearance to histiocytes ‘ground glass’ cytoplasm.
• If multiple, can involve joints and cause arthritis, usually fingers.
Non-Langerhans Histiocytoses

- Xanthogranuloma’s; Juvenile Xanthogranuloma archetypal lesion
- Can be xanthomatous, spindle cell, ground glass histiocytes.
Case 15

- 50M, persistent boil on leg.
Microscopy

- Dense diffuse dermal infiltrate.
- Infiltrate composed by histiocytes with abundant pale cytoplasm.
- Background of mixed inflammatory cells.
- Within histiocytes; small dots.
Leishmaniasis

- Various forms. Classical persistent sore; Baghdad boil.
- Protozoal infection transmitted by sandfly.
- Main differential; Histoplasmosis. Rare in skin. PAS or Grocott will help.
Case 16

• 25F ? SCC on foot.
Microscopy

• Squamous proliferation.
• Dense infiltrate in dermis.
• Collections of Neutrophils. Surrounding histiocytes.
Differential diagnosis

• Suppurative granulomas;
  – Fungal
  – Atypical mycobacteria
  – Pyoderma gangrenosum, superficial granulomatous variant.
?SCC, Grocott
Pseudoepitheliomatosus hyperplasia

- Infections, esp Fungus
- Chronic friction
- Lymphomas, esp. CD30 related diseases
- Tumours, granular cell tumour
- Connective tissue diseases, Lupus
- Hypertrophic lichen planus
Case 16

- Fungal infection with pseudoepitheliomatous hyperplasia.
Types of Granuloma

• Sarcoidal
• Tuberculoid
• Necrobiotic
• Foreign body
• Suppurative
• Xanthogranuloma
• Vasculitis associated
Case 17

- 60 m, crusted lesion on forehead.
Microscopy

- Intra-epidermal vesicle.
- Necrosis of keratinocytes
- Ballooning degeneration, multinucleate cells.
- Intranuclear inclusions
Herpes infection

• Herpes varicella-zoster, and simplex 1&2 all produce similar changes.
• Can involve hair follicles
• Can be widespread if immunosuppressed.
Case 18

- 40M, recurrent oval lesion on arm.
Microscopic features

- Scattered epidermal cell death
- Corneal layer normal
- Mild perivascular lymphocytic infiltrate.
- Exocytosis of lymphocytes with satellite cell necrosis.
Fixed drug eruption

• Inflammatory patch which recurs at same site each time drug taken.
• Differential; see under TEN.
Case 19

- 45 Male with orange plaque on leg
Case 19

- Superficial perivascular inflammation.
- Lymphocytes and occasional eosinophil.
- Epidermis shows mild acanthosis and hyperkeratosis.
- Scattered macrophages in interstitium shows iron deposition.
Pigmented purpuric dermatosis

• Several variants; usually middle aged men, producing purpuric to orange/brown lesions on lower legs.

• ‘Capilleritis’ but no true leukocytoclastic vasculitis seen.
Differential diagnosis

- Non-specific inflammation.
- MF
Invisible Dermatoses

• If stuck, remember above list and do some basic histochemical stains eg Congo red, Toludine blue, perls, elastic stain, Mucin stain, Fungal stain.
Case 20

- 50F, ? cellulitis
Microscopy

- Superficial and deep inflammation
- Many eosinophils.
- Flame figures
Well’s syndrome [eosinophilic cellulitis]

• Clinically resembles cellulitis, but no infection found.

• Differential;
  – Insect bite
  – Parasite infection
  – BP
  – Allergic eczema
  – Drug eruption
  – Churg- Strauss Disease
CASE 21

- 20 F, numerous small macules with scale.
Microscopy

- Lymphocytic vasculitis; perivascular lymphocytes and red cell extravasation. No fibrin or nuclear debris.
- Vacuolar interface with exocytosis of lymphocytes and RBC’s.
- Epidermal degenerative changes with vacuolar change and cytoid bodies.
- Overlying scale crust
Pityriasis Lichenoides

• Acute and chronic forms.
• Differential diagnosis:
  – Lymphomatoid papulosis, similar clinical and pathology but has clusters of atypical CD30 positive T-cells.
• 50F large patches on trunk.
Microscopy

• Band-like infiltrate in upper dermis
• Exocytosis. Cells in small clusters and pairs.
• Cells in epidermis of moderate size, irregular nuclear margin.
• Mild epidermal acanthosis, minimal spongiosis
• Papillary dermal fibrosis
Differential diagnosis

- Lichenoid drug eruption
- Chronic superficial dermatitis
- Mycosis Fungoides
Diagnosis; MF

• Need correct clinical setting. Large plaques on trunk with slight scale [cigarette paper-like appearance].

• Immuno; CD4/CD8 ratio; reactive usually predominantly CD8, MF CD4:CD8 2:1.

• Antigen aberrance; CD2, CD4, CD5, CD7.

• Clonality; T cell gene rearrangement.
Case 23

- 65F, Renal failure, ulceration on leg
Microscopy

- Superficial ulceration. Epidermis shows thinning and necrosis.
- Dermal inflammation with many neutrophils.
- Superficial vessels contain thrombi.
- S/c vessels show Ca deposition in small vessel walls. Lumen occluded.
Diagnosis

• Calciphylaxis; very serious disease. Often causes death. Usually history of chronic renal disease.
Case 24

- 60F, Nodule on nose.
Microscopy

- Dense dermal inflammation. Grenz zone. Adnexal structures spared.
- Polymorphous infiltrate; Neutrophils, eosinophils, histiocytes.
- Neutrophils centred upon small vessels. Focal nuclear dust and small amount of fibrin.
- Small amount of fibrosis.
Granuloma Faciale

- One type of chronic vasculitis.
- Erythema Elivatum Diutinum, similar, occurs on limbs over bony prominances.
Neuts in the dermis

- Infections, Cellulitis
- Vasculitis, and variant's
- Sweets syndrome
- Behcet’s
- Blistering disorders; DH,
- AML, but abnormal primitive forms.
Case 25

- 60F with skin rash and muscle weakness
Microscopy

• Epidermis, thin with basal vacuolar change
• Dermis contains a perivascular lymphocytic infiltrate.
• Dermis, appears pale, collagen fibres widely separated. Due to mucin, [useful for diagnosis].
Dermatomyositis.

• Peri-ocular oedema and erythema
• Erythema in photosensitive distribution.
• Myositis; proximal muscle weakness. Can check for creatinine kinase.
• Gottron’s papules on acral skin.
• In adults 25% associated with underlying visceral cancer.
Dermatomyositis

• Not possible to exclude L.E. on histology.
• Clinically distinct.
• IMF; negative.
Case 26

- LH08-15290 15F Linear lesion on arm.
Cornoid Lamella

- Columns of parakeratotic scales, loss of granular layer, vacuolated or dyskeratotic cells in spinous layer
- ? Clonal abnormality
- Seen in
- Porokeratosis: Mibelli, DSAP, D.S. (Non-A)P, linear, punctate (palmar/plantar)
- Other - Seb K, A.K, SCC
CASE 26

• Linear Porokeratosis
Blaschko's lines

• An unexplained phenomenon of human anatomy first presented in 1901 by German dermatologist Alfred Blaschko. Many inherited and acquired diseases of the skin or mucosa manifest themselves according to these patterns, creating the visual appearance of stripes.

• The cause of the stripes is thought to result from mosaicism; they do not correspond to nervous, muscular, or lymphatic systems. It is theorized that the lines define the natural areas of growth between the original cells of the embryo and the later (copied) cells of mature adults.
Blaschko's lines

- Genetic disorders
  - Epidermal Naevi [ILVEN]
  - Incontinentia pigmenti
- Acquired skin disorders
  - Lichen Striatus
  - Linear LP
  - Linear LE
  - Linear Porokeratosis
Case 27

- 60F Diffuse swelling
Microscopy

- Not much to see
- Collagen fibres widely spaced
Differential Diagnosis

- Dermal mucinosis
- Lymphoedema
Pre-tibial myxoedema

• Occurs in hyperthyroisism [Graves disease].
• Use AB with Van Gieson or Hale’e colloidal iron to demonstrate.
• Diagnosis needs clinico-pathological correlation.
Dermal Mucinoses

• Increase Mucin only
  – Pre-tibial myxoedema
  – Focal mucinosis
  – Generalised myxoedema [subtle]

• Increased fibroblasts
  – Papular mucinosis, Scleromyxedema

• Increased collagen
  – Scleredema

• Inflammation
  – REM, SLE, Dermatomyositis
Case 28

- 68M, Intense deep inflammation lower legs.
Microscopy

• Deep inflammatory process centred upon s/c fat, panniculitis
• Whole lobule affected. ‘lobular pattern’.
• ‘Ghost cells’ of fat cells
• Dense acute and chronic inflammatory cell infiltrate.
• No vasculitis
Pancreatic Panniculitis

• Fat necrosis due to release of enzymes from pancreas. Can do serum amylase.
• Legs most affected.
• Associated with pancreatic disease; benign and malignant.
• This case had pancreatic carcinoma
Case29

• 3 year old male with multiple brown macules on trunk.
Microscopy

- Superficial perivascular infiltrate,
- Epidermis not inflamed.
- Prominent basal pigmentation.
Urticarial Pigmentosa

- Number of mast cell very variable.
- Mast cell can look like lymphocytes so easily missed.
- Often a few eosinophils present.
- Can be associated with systemic disease, especially in adults.
- CD117 and Toludine blue can identify.
Mast cell disease

- Range from benign end, urticaria pigmentosa, mastocytoma to borderline systemic mastocytosis to malignant; Malignant mastocytosis, Mast cell leukemia.

- At lower end; can look just like a lymphocytes. Often a few eosinophils around.
Mast cell disease

- Range from benign end, urticaria pigmentosa, mastocytoma TMEP to borderline systemic mastocytosis to malignant; Malignant mastocytosis, Mast cell leukemia.

- At lower end; can look just like a lymphocytes. Often a few eosinophils around.
Case 30

- 21F; numerous papules
Microscopy

• Follicles dilated.
• Increased amount of mucin within follicle.
• Minimal inflammatory infiltrate. No atypia.
Case 30

• Follicular mucinosis
• 2 main types;
  – 1] Inflammatory/benign,
  – 2] Lymphoma associated.
• Range from limited group papules, often scalp [Alopecia mucinosa] to widespread papules.
• Careful follow up required as may transform from benign to malignant.
THE END