How to Tackle Inflammatory Dermatoses: A Practical Guide

Thomas Brenn
Inflammatory Dermatoses

The Challenge

Vast range of clinical entities
Limited reaction patterns of the skin
Significant morphological overlap
Subtle (if any) distinguishing histological features
Morphologic variability within disease

“The lives of lesions”
Inflammatory Dermatoses
The Challenge

‘New’ emerging entities

Infrequent biopsies of “classic” clinical presentation
Inflammatory Dermatoses
The Challenge

Final diagnosis requires clinico-pathological correlation

- Clinical presentation
- Clinical differential diagnosis

Awareness of

- limitations of histological interpretation and ancillary tests
- impact on treatment
Inflammatory Dermatoses

General

Clinical history:
- Age, gender, site, distribution
- Occupation
- Family history
- Travels, animal contact, drugs
- Systemic disease
- Immunosuppression

Guidance by clinical impression
Lichen Planus
Lichenoid Drug Eruption

Scarring alopecia on hydroxychloroquine
Lichenoid Keratosis
Atypical clinical presentation: clinical challenges are often also histological challenges

Significant number of non-diagnostic biopsies

Pay attention to subtle histological clues

Histological diagnosis only as good as the clinical description and DDx

Histology often only part of a larger puzzle
Inflammatory Dermatoses
Histology
The Algorithmic Approach
Histological Approach to Dermatoses

Normal

- Invisible dermatoses
- Levels
- Special stains

Abnormal

- Matches clinical?

  - no
  - yes

- Locate abnormality
  - Epidermis
  - Dermal-epidermal junction
  - Dermis
  - Subcutis

- Tissue Reaction pattern
- Characterize inflammatory component

Formulate differential diagnosis
<table>
<thead>
<tr>
<th>Major reaction patterns</th>
<th>Inflammatory infiltrate</th>
</tr>
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<tbody>
<tr>
<td>– Spongiotic</td>
<td>– Lymphocytes</td>
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<tr>
<td>– Psoriasiform</td>
<td>– Neutrophils</td>
</tr>
<tr>
<td>– Interface</td>
<td>– Eosinophils</td>
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<tr>
<td>– Vesiculobullous</td>
<td>– Plasma cells</td>
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<tr>
<td>– Superficial and deep dermal</td>
<td>– Histiocytes</td>
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<tr>
<td>– Vasculopathies</td>
<td>– Granulomata</td>
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<tr>
<td>– Panniculitides</td>
<td>– Mast cells</td>
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</tbody>
</table>
Always consider

Drug and Infection
Secondary syphilis

Cervical lymphadenopathy and mild fever
Spongiotic Dermatoses

Acute, subacute, chronic

Inflammatory component
  Lymphocytes
  Eosinophils
  Neutrophils
Spongiotic Dermatoses

Eczematous dermatitides
- Allergic contact dermatitis
- Irritant contact dermatitis
- Atopic dermatitis
- Nummular dermatitis
- Dyshidrotic eczema/pompholyx
- Id reaction
- Seborrhoeic dermatitis
- Pityriasis rosea

Spongiotic drug
- Superficial fungal infection
- Arthropod bite
Psoriasiform
Psoriasiform Dermatoses

Psoriasis
Reiter syndrome
Psoriasiform drug eruption
Chronic eczematous dermatitis
Lichen simplex chronicus
Prurigo nodularis
Pityriasis rubra pilaris
Parapsoriasis
Mycosis fungoides
Interface - vacuolar

Interface - lichenoid
Interface Dermatitis
vacuolar

Lichen planus
Lichen striatus
Lichen nitidus
Lichenoid drug eruption
Lichenoid keratosis
Keratosis Lichenoides Chronica
Interface Dermatitis
vacuolar

Erythema multiforme
SJS/Toxic epidermal necrolysis
Graft-versus-host disease
Lupus erythematosus
Dermatomyositis
Fixed drug eruption
Pityriasis lichenoides
Viral exanthem
Bullous Dermatoses

Level of split
Inflammatory component
Case

46 yo female with blisters and erosions on the trunk for 2 months
Vesiculobullous Disease
intra- and subcorneal

Pemphigus foliaceus
IgA pemphigus
Subcorneal pustular dermatosis
Pustular psoriasis
AGEP
Impetigo
Staphylococcal scalded skin syndrome
Fungal infection
Case

Pemphigus foliaceus
Pemphigus Foliaceus

Rare and less severe than P. vulgaris
Predilections for middle aged adults and elderly but wide age range
Recurrent crops of fragile bullae, erosions and plaques
Face and trunk, no mucosal involvement
Antibodies against DSG1
Case

70 yo female with a 1 week h/o a blistering eruption with superficial pustules. No h/o psoriasis.
Pustular Dermatoses
Differential Diagnosis

Subcorneal Pustular Dermatosis
IgA Pemphigus
Pustular psoriasis
AGEP / Pustular Drug Eruption
Dermatophyte infection
Direct Immunofluorescence

Negative:
- IgG
- IgA
- IgM
- c3
Case

Subcorneal pustular dermatosis / Sneddon Wilkinson disease
Subcorneal Pustular Dermatosis

Rare chronic relapsing
Superficial flaccid pustules
Skin folds
Adults
Female predilection
Case

46 yo female with blisters and erosions on the trunk for 2 months
Vesiculobullous Disease
suprabasilar / acantholytic

Pemphigus vulgaris
Paraneoplastic pemphigus
Darier disease
Hailey-Hailey disease
Grover disease
Case

Negative DIF

Circulating antibodies to DSG3 and BP180

Subsequent work-up revealed dedifferentiated retroperitoneal liposarcoma
Case

Paraneoplastic Pemphigus
Paraneoplastic Pemphigus

Elderly patients, M>F

Painful oral mucosal erosions

Polymorphous skin lesions

Most commonly associated with underlying lymphoproliferative disorder

Ab to plakins, BP230, DSG1 and 3

McKee’s Pathology of the Skin, 5th ed
Case

72 yo male with recent onset of superficial blistering. Rash on trunk and upper limbs with superficial erosions. Severe oral involvement with blisters and ulcers.
<table>
<thead>
<tr>
<th>Vesiculobullous Disease</th>
<th>Subepidermal</th>
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<tbody>
<tr>
<td>Epidermolysis bullosa</td>
<td>Dermatitis herpetiformis</td>
</tr>
<tr>
<td>Porphyria/pseudoporphyria</td>
<td>Linear IgA dermatosis</td>
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<tr>
<td>Burns</td>
<td>Cicatricial pemphigoid</td>
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<tr>
<td>Bullous pemphigoid</td>
<td>Bulous lupus erythematosus</td>
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<td>Epidermolysis bullosa acquisita</td>
<td>Erythema multiforme</td>
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<td>Herpes gestationes</td>
<td>Fixed drug eruption</td>
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<td>Lichen planus</td>
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DIF

Linear deposition at BMZ of

IgG

IgA

c3
Case

Linear IgA disease
Linear IgA Disease

Clinical

- Adulthood onset; wide age range
- Bullae on trunk and limbs
- ‘cluster of jewels’ sign
- Mucosal involvement
- Genetic predisposition

Heterogeneous disorder, Ab to various BMZ Ag
Vesiculobullous Disease
intraepidermal

Spongiotic dermatitides
Herpes simplex/zoster virus
Friction blister
Bullous drug
Vasculopathies

Vasculitis
Vascular damage + inflammation

Thrombotic vasculopathies
Vascular occlusion
Classification of vasculitis

From: Robbins Textbook, 6th ed
Case

45 yo female with a palpable purpura affecting both legs
Neutrophilic Vasculitis
Differential Diagnosis

Leukocytoclastic vasculitis
Henoch-Schoenlein purpura
Urticarial vasculitis
Mixed cryoglobulinaemia
Microscopic polyangiitis
Wegener granulomatosis
Polyarteritis Nodosa
Case

Wegener granulomatosis
Remember

Small vessel neutrophilic vasculitis seen in a number of clinical settings

- LCV, HSP, urticarial vasculitis
- Microscopic polyangiitis
- Wegener’s granulomatosis
- Churg Strauss disease
Histological classification of vasculitis

- Fibrinoid necrosis of vessel walls + inflammation
- Size and location of affected vessels
- Character of inflammatory cell infiltrated
- Dependent on adequacy of biopsy
- Consider systemic disease
Classification of vasculitis

CLA, HSP

ANCA+, Cryo, CTD

PAN, GCA, Nod Vas

(C) Bernard Ng

From: JA Carlson Histopathology 2010: 56:3-23.
Eosinophilic Vasculitis

- Churg-Strauss syndrome
- Leukocytoclastic vasculitis
- Urticarial vasculitis
- Erythema elevatum diutinum
- Granuloma faciale
Granulomatous Vasculitis

- Churg-Strauss syndrome
- Wegener’s granulomatosis
- Drug eruptions
- Sarcoidosis
- Infection
- Polyarteritis nodosa
- Giant Cell Arteritis
- Takayasu’s Arteritis
- Buerger’s disease
Lymphocytic Vasculitis

Connective tissue disease
Pernio
Polymorphous light eruption
Pigmented purpuric dermatoses
Degos’ disease
Drug eruptions
Gyrate erythemas
Pityriasis lichenoides
Infection (Rickettsial + viral)
Insect bite
Superfical and Deep Dermal Cellular Infiltrates
Case

54 yo male with a well-demarcated 5 cm erythematous plaque on the left buttock.

?Extramammary Pate disease, allergic contact dermatitis
Superficial and Deep lymphocytic
Erythema annulare centrifugum
Erythema gyratum repens
Jessner’s lymphocytic infiltrate
Reticular erythematous mucinosis
Polymorphous light eruption
Perniosis
Tumid lupus erythematosus
Case

Patient died 4 months after initial biopsy
Case

NK/T cell lymphoma, nasal type
Superficial and Deep neutrophils

Pyoderma gangrenosum
Sweet’s disease
Rheumatoid neutrophilic dermatitis
Behcet’s disease
Urticaria
Superficial and Deep eosinophils

Urticaria
Hypereosinophilic syndrome
Pruritic urticarial papules and plaques of pregnancy
Arthropod bite reaction
Drug eruption
Panniculitides
Panniculitides

Erythema nodosum
Lupus profundus
Infection
Vasculitis
Trauma
Scleroderma
Alpha-1-antitrypsin deficiency
Pancreatic panniculitis
Cold panniculitis
Inflammatory Dermatoses

Conclusion

Subtle “invisible” dermatosis

Levels and special stains as appropriate

Tissue reaction + cell type = DDx

Correlate with clinical impression

Call the dermatologist

Be aware of the implications

Accurate diagnosis is not always possible