MUCOCUTANEOUS LESIONS

Normal structures in epithelium – cell adhesion to each other and to underlying connective tissue:

Epithelial-Connective tissue junction - Hemidesmosome

1. **LICHEN PLANUS**

- Chronic relapsing and remitting mucocutaneous disorder
- On skin: “Pruritic purple polygonal papules”

**Etiology:**
- A T-cell disease
- Probably MULTIFACTORIAL
- Internal factors play a role in:
  - Graft versus host disease
  - Drug reaction (string of pearls – dotted Immunofluorescence pattern along the basement membrane)
- External factors: Langerhans cells mediate the reaction:
  - External antigen – pattern?
  - Amalgam???
- Stress - controversial

**Clinical features:**
- Middle aged adults; F: M=3:2
- Skin: itchy violaceous flat topped papules, plaques
- Multiple, symmetrical, extremities
- 70% of cases: Oral lesions
- Oral lesions:
  - Reticular
    - Lace-like network of white striae – Wickham striae
    - Bilaterally symmetrical, asymptomatic - usually
    - Posterior buccal mucosa
  - Erosive
    - Atrophic red areas with central ulceration
    - Periphery bordered by fine white striae
    - Symptomatic
    - Desquamative gingivitis
    - Severe erosion → bullous Lichen planus

**Histopathologic features:**
- Ortho- and/or parakeratosis
- Acanthosis, but sometimes atrophy
- Saw-tooth shaped rete ridges
- Hydropic degeneration of the basal layer of the epithelium
- Colloid bodies (Civatte bodies)
- Fibrinogen at basement membrane zone
- Other lesions which mimic LP:
  - Lichenoid drug reaction
  - Lichenoid amalgam reaction
  - Lupus erythematosus
  - Chronic ulcerative stomatitis
  - Oral mucosal cinnamon reaction
Diagnosis:
- Reticular: clinical findings alone
- Erosive: biopsy often necessary

Treatment and Prognosis:
- Reticular: no treatment
- Erosive:
  - Topical corticosteroids
    - Fluocinonide
    - Betamethasone
    - Clobetasol
  - Intralesional injections of corticosteroids
  - Systemic corticosteroids.
- Precancerous?
  - Still controversial

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2. MUCOUS MEMBRANE PEMPHIGOID

= BENIGN MUCOUS MEMBRANE PEMPHIGOID (BMMP), OR CICATRIAL PEMPHIGOID

- Basic lesion: SUB-EPITHELIAL BULLA
- Chronic, antibodies directed against 1 or more basement membrane components
- Oral lesions may:
  - Result in scarring and affect the oral cavity and other mucosal surfaces

Incidence - more common than pemphigus
- F: M = 2:1
- Individuals usually +60 years

Clinical features:
- Oral and pharyngeal blisters which later rupture to form ulcers
- When gingivae affected - DESQUAMATIVE GINGIVITIS
- Healing is slow and may be accompanied by scarring
- In benign mucous membrane pemphigoid there may be:
  - Ocular (leading to blindness),
  - Nasal,
  - Esophageal
  - Laryngeal,
  - Genital,
- Development of new lesions results in chronic oral ulceration

Histopathology
- Sub-epithelial bulla - NO ACANTHOLYSIS
- Mild chronic inflammatory infiltrate
- Immunofluorescence
  - Direct:
    - Linear binding of IgG (or IgM, or IgA, or in combination), C3 to basement membrane
90% of patients

Indirect:
- Circulating auto antibodies may be present but not a consistent or reliable finding in BMMP.

- Similar diseases:
  - Linear IgA disease
  - Angina bullosa hemorrhagica
  - Epidermolysis bullosa acquisita

Treatment:
- Topical steroid therapy
  - hydrocortisone pellets
  - prednisolone mouthwash
- Systemic steroids
  - If topical unsuccessful
- Dapsone (alternative to steroids)
- Tetracycline and nicotinamide
- Symptomatic treatment
  - local anaesthetic lozenges
  - chlorhexidine mouthrinses
- Refer Ophthalmologist for eye lesions

3. **BULLOUS PEMPHIGOID**

- Basic lesion: SUB-EPITHELIAL BULLA
- Antibodies directed against components of basement membrane

Incidence
- Most common of the autoimmune blistering diseases
- 10/million/year
Clinical features:
- Older people 60 – 80 years
- No gender or race predilection
- Pruritis, multiple tense bullae
- Rupture, crust, healing without scarring
- Oral lesions rare
- Orally, clinical course limited (BMMP protracted)

Histopathology
- Sub-epithelial separation
- Modest acute on chronic inflammatory cells
- Eosinophils in bulla
- Immunofluorescence
  Direct:
  - Linear binding of IgG, C3 to basement membrane
  - May bind to hemidesmosome proteins:
    - BP 180 and BP 230
    - BP 180 in lamina lucida
  Indirect:
  - 40 – 70% of patients; titre does not correspond with disease activity, unlike pemphigus

Treatment:
- Systemic corticosteroids
  - Prednisone - alternate day
- Azathiaprine (steroid sparing)
- Alternative: Dapsone
- Tetracycline and niacinamide
- Severe resistant cases:
  - Prednisone and cyclophosphamide
- Prognosis good: spontaneous remission after 2 - 3 years
4. PEMPHIGUS

- Basic lesion - Intra-epithelial bullae which rupture and show no tendency to heal.
- 4 types:
  < Pemphigus vulgaris
  < Pemphigus vegetans
  < Pemphigus erythematosus
  < Pemphigus foliaceous
- Rare – pemphigus vulgaris affects the mouth oral lesions “1st to show, last to go”. Up to 50% cases begin in the mouth

Incidence: 1/million
- Both sexes equally affected
- Rare under 30 years (average about 50)

Etiology unclear; pathogenesis autoimmune

Pathogenesis
- Antibody binds to epidermal cell surface glycoproteins, desmoglein 3, and desmoglein 1. These proteins are components of desmosomes
- Separation of epithelial cells occurs - acantholysis
- Blister forms within epithelium
- Other pemphigus-like conditions:
  < Medication, e.g. penicillamine-induced
  < Paraneoplastic pemphigus

Clinical features:
- Oral:
  < Sudden onset of oral blisters which rupture early to form superficial spreading erosions.
  < Chronic oral erosions and ulcers
  < Little tendency to healing with continued formation of new ulcers
  < Any oral mucosal location
- Skin:
  < Flaccid vesicles, bullae
  < Nikolsky sign – mechanical pressure which induces blister formation.
Histopathology
- Loss of attachment between prickle cells (acantholysis)
- Intra-epithelial bulla with loose acantholytic, rounded cells - TZANCK CELLS
- Basal layer resembles “row of tombstones”
- Bulla ruptures
- Ulceration
- Moderate chronic inflammatory cell infiltrate

Immunofluorescence
Has to be on perilesional fresh tissue
- Direct:
  < Highly specific
  < Binding of IgG or IgM, and C3 between epithelial cells: directed at Desmoglein 3 in the desmosome.
- Indirect:
  < 80-90% patients have circulating auto antibodies
  < Titre usually parallels severity of disease

Treatment:
- High doses of systemic steroids (prednisolone) initially
- Taper dose to minimum necessary to control ulceration
- Azathioprine may be given (steroid sparing)

DESQUAMATIVE GINGIVITIS

Clinical term, used to described loss of the superficial epithelium of the gingiva, leaving redness
Associated with:
- Lichen planus
- Pemphigus
- BMMP
- BP
THE EPULIDES

• Localised Hyperplasias of fibrous tissue (Epulides):
  • Focal fibrous hyperplasia (Irritation fibroma)
  • Peripheral ossifying fibroma
  • Peripheral giant cell granuloma
  • Pyogenic granuloma

Other which may present as epulides:

• Peripheral odontogenic tumors/cysts
• Soft tissue tumors (eg neurilemmoma, neurofibroma, angioleiomyoma)
• Granulomatous inflammation.

Epulis: A clinical term: localized, subepithelial gingival mass.

The BIG FOUR:

• Focal fibrous hyperplasia (Irritation fibroma)
• Peripheral ossifying fibroma
• Peripheral giant cell granuloma
• Pyogenic granuloma

1. FIBROMA

(Focal fibrous hyperplasia; Irritation fibroma; Traumatic fibroma; Fibroepithelial polyp):

• Probably not a true neoplasm and is a reactive lesion.

Clinical features:

• Most common (60%), F>M, all ages (wide peak 20-40yrs).
• Occurs: Buccal mucosa along biting line; labial mucosa, tongue, gingiva.
• Pink/firm, Sessile or pedunculated.
• Some represent fibrous maturation of a pyogenic granuloma.

Histological features:

• Non encapsulated nodular mass of dense, poorly cellular fibrous tissue.
• Covered by stratified squamous epithelium.

Treatment:

• Conservative surgical excision.
• Recurrence is rare

2. GIANT CELL FIBROMA:

Is considered a variant of focal fibrous hyperplasia.
It contains binucleate, trinucleate and stellate fibroblasts which lie close to the epithelium.
3. **PERIPHERAL OSSIFYING FIBROMA:**

Relatively common tumor like growth considered to be reactive rather than neoplastic, of uncertain pathogenesis.

Possibly derived from long-standing pyogenic granuloma.

Clinical features:
- 20%, F:M=2:1, all ages (wide peak 10-30).
- Slightly more common in maxillary arch.
- Occurs exclusively on the gingiva: incisor, canine region.
- Nodular, sessile or pedunculated, pink/red firm mass.
- Surface often ulcerated.

Histological features:
- Cellular fibrous tissue with bone, cementum-like material or dystrophic calcification.

Treatment
- Surgical excision - recurrence 20%.

4. **PYOGENIC GRANULOMA**

Common tumor-like growth which is reactive in nature. Not a true granuloma.

Etiology:
- Gingival irritation due plaque and calculus.

Clinical features:
- 10%, F>M, all ages (peak 15-35yrs).
- Pedunculated, surface ulcerated, red, bleeds easily.
- Size varies from few mm to cm.
- 75% occur on the gingiva, anterior and maxillary more common.
- Association with vascular effects of female hormones during pregnancy - pregnancy tumor.

Histological features:
- Vascular proliferation that resembles granulation tissue; looks like a bag of capillaries/venules.
- Sometimes the vessels are arranged in lobules (lobular capillary hemangioma).
- Has a mixed acute on chronic inflammatory cell infiltrate.
- Surface epithelium is usually ulcerated and replaced by a pyogenic membrane (fibrinopurulent membrane).

Treatment:
- Excise – recurrence 15%.
- Important for plaque and calculus to be removed.
- Pregnancy tumor: wait till after pregnancy → fibroma, excise.
5. PERIPHERAL GIANT CELL GRANULOMA:
• No agreement - true nature of lesion, origin - periodontal ligament or mucoperiosteum.
• Unusual proliferative response to injury.
• giant cells!! 5%,

Clinical features:
• ± 30 years, but also in children
• Mandible, females 60%
• Gingiva, anterior to molars
• Often in edentulous area - swelling on crest of ridge
• Red, haemorrhagic in appearance

Histological features:
• Non-encapsulated.
• Delicate connective tissue stroma, spindle-shaped cells.
• Large numbers of multinucleate giant cells.
• Osteoclasts, endothelial cells.
• Numerous capillaries, giant cells often within.
• Hemosiderin, inflammatory cells.

Radiological features:
• Soft tissue lesion but can cause “cuffing of bone”, superficial erosion.

Treatment:
• Excise – recurrence 10%.

•Others which may present as epulides:
• Peripheral odontogenic tumors/cysts
• Soft tissue tumors (eg neurilemmoma, neurofibroma, angioleiomyoma)
• Granulomatous inflammation.

COMMON MUCOSAL INJURIES:

1. FOREIGN BODY GINGIVITIS
Patchy, red, sore areas of the gingiva occur at the gingival margin and interdentally. Older lesions may be white or lichenoid. Microscopically there are fine particles distributed through the connective tissue, usually polishing agents or abrasives, which shine under polarized microscopy.

2. TUGSE (traumatic ulcerative granuloma with stromal eosinophilia)
• Deep ulcer usually involving skeletal muscle, typically on the lateral border of the tongue caused by biting.
• Painful at first. Does not heal for 6 to 8 weeks.
• Clinically mimics squamous cell carcinoma
• Microscopically shows ulceration with chronic inflammation and eosinophils; and granulation tissue.
• Infants: anterior tongue, Riga-Fede disease.