Autoimmune Diseases with Oral Manifestations

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Disclosure Statement

I have no actual or potential conflict of interest in relation to this presentation.
Autoimmune Diseases with major oral M/F manifestations

Lupus Erythematosus
Scleroderma
Dermatomyositis
Rheumatoid Arthritis
Sjogrens Syndrome
Multiple Sclerosis
Pemphigus
Pemphigoid
PEMPHIGUS

- Autoimmune blistering disease mucosa and skin-potentially fatal
- Lesion Intraepithelial
- Highest Incidence - $5^{\text{TH}}$-$6^{\text{TH}}$ decade
- Hereditary Component- Eastern European Jewish Ancestry
PEMPHIGUS VULGARIS

Etiology
IgG autoantibodies directed against:
• Desmosomal adhesion glycoprotein
• Desmoglein 3 - mucosal lesions
• Desmoglein 1 - skin lesions
Pemphigus

- Pemphigus vulgaris - suprabasilar
- Pemphigus vegetans - variant of PV
- Pemphigus foliaceus - granular layer
- Pemphigus erythematous - variant of PF
- Paraneoplastic pemphigus
- Drug related pemphigus
PEMPHIGUS VULGARIS

Most common form-80%
Oral lesions –anti-DSG 3
Skin lesions- anti- DSG 1
Loss of cell to cell adhesion
ACANTHOLYSIS
PEMPHIGUS VULGARIS - ACANTHOLYSIS
PEMPHIGUS VULGARIS

Major Clinical Manifestations

- Skin-thin walled blisters - lesion intraepithelial
- Mucosa - shallow ulcers pealing mucosa
- No inflammation
- Positive Nikolsky sign - manual pressure causes new lesion
Oral Manifestations

- 90% of all patients
- 60% - oral lesions precede skin lesions
- Shallow ulcers
- Irregular borders
- Noninflamed based
- Desquamative gingivitis
Diagnosis
1) Biopsy - routine histology - suprabasilar acantholysis
2) Biopsy - direct immunofluorescence
3) Serum - indirect immunofluorescence
Pemphigus Vulgaris
Direct IF Study

- Take from clinically normal mucosa
- Place in Michel’s medium
- Fluorescein-labeled IgG
- Pemphigus- IgG binds to surface of keratinocytes
Pemphigus Vulgaris - Direct Immunofluorescence
Pemphigus
Indirect IF Study

- Serum placed over mucosa (monkey esophagus)
- Overlay with fluorescein- tagged anti-Ig
- Detect ab intercellular ab with fl microscope.
- Titers used to diagnose PV and monitor disease activity
Pemphigus Diagnosis

ELISA

- Enzyme linked immunosorbent assay
- Assay levels of desmoglein 1 and 3
- More sensitive than IIF
PARANEOPLASTIC PEMPHIGUS

Associated with neoplasm

- Lymphoma
- Chronic lymphocytic leukemia
- Thymoma
PARANEOPLASTIC PEMPHIGUS

Clinical Manifestations
1) Severe blistering, erosions, plus inflammation
2) Severe oral lesions
3) Severe conjunctival lesions
4) Respiratory lesions
Drug-Induced Pemphigus

Major Causes:
- penicillamine- tx heavy metal toxicity,
- rheumatoid arthritis
- captopril- antihypertensive ACE inhibitor

After dx of --r/o drug induced pemphigus
PEMPHIGUS VULGARIS

Treatment

- Corticosteroids-systemic, topical
- Immunosuppressive drugs: azathioprine, mycophenolate, cyclophosphamide
- Rituxumab-Monoclonal ab CD20-depletes B cells
- Intravenous Ig (IVIG)
- Plasmapheresis
MUCOUS
MEMBRANE
PEMPHIGOID
SUBEPITHELIAL BULLOUS DERMATOSES - STOMATITIS

- Mucous membrane pemphigoid
- Bullous pemphigoid
- Linear IgA disease
- Chronic bullous dermatosis of childhood
- Epidermolysis bullosa acquisita
MUCOUS MEMBRANE PEMPHIGOID

PATHOPHYSIOLOGY
- Defect in immune regulation
- Formation of autoantibodies against protein in basement membrane zone: BP-230, BP-180, laminin, type XVII collagen
- Triggers inflammation in BMZ
- Separation of epithelium from connective tissue
MUCOUS MEMBRANE PEMPHIGOID

PATHOPHYSIOLOGY

- Antibody lamina lucida – BP 180
- Antibody lamina densa - epiligren
Relationship to Cancer

- Many reported cases
  - lung cancer
  - GI cancer
  - Gyn cancer
  - lymphoma
- Cancer onset within 15 mos of MMP
MUCOUS MEMBRANE PEMPHIGOID

- Increased in patients over 50
- Increased in women
- Increased cancer risk
  - Anti-epiligrin (Laminin 5) type
Mucous Membrane Pemphigoid

ORAL MANIFESTATIONS

- Oral lesions in 90%
- Desquamative gingivitis
- Ulcers and shallow erosions
- Vesicles and bullae
### MMP

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<th>Location</th>
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<td>Gingiva</td>
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<tr>
<td>Tongue</td>
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<tr>
<td>Nasal mucosa</td>
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<td>(10%)</td>
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<tr>
<td>Esophagus</td>
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<td>(5%)</td>
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LICHEN PLANUS
ORAL LICHENOID LESIONS

LICHEN PLANUS—IDIOPATHIC
LICHENOID CONTACT REACTIONS
LICHENOID DRUG REACTIONS
LICHENOID GRAFT VS. HOST DISEASE (GVHD)
LICHEN PLANUS
CLINICAL TYPES

- RETICULAR-
  Wickham’s straie
- Plaque
- Erythematous
- Erosive(Ulcerative, Bullous)
Reticular
Plaque
LICHEN PLANUS
EROSIVE/ULCERATIVE
LICHEN PLANUS
VS.
LUPUS
LP VS. LUPUS

- Routine histology may be similar
- Use 2nd biopsy-direct I.F.
  - lupus band test-
    (IgG, IgM, C' at dermal-epidermal junction)
ORAL LICHEN PLANUS AND SQUAMOUS CELL CARCINOMA

- 0.2% to 3% of L.P. patients develop oral cancer
- 50X increase in risk
  (Same as smokeless tobacco)