Diagnosis and treatment of pemphigus

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Conflicts of Interest
• Co-founder, Cabaletta Bio • Inventor on licensed patents, Cabaletta Bio, Novartis • Past consultant, Syntimmune • Past grants, Sanofi • Will be discussing off-label use of drugs (not FDA-approved for pemphigus)
What causes pemphigus?

- An autoimmune disease caused when antibodies mistakenly attack the skin and mucous membranes, rather than foreign viruses or bacteria.

B cells = "soldiers"

T cells = "generals"

Antibodies = "weapons"

Viruses and bacteria

# Pemphigus (and Pemphigoid) 101

<table>
<thead>
<tr>
<th>Disease</th>
<th>Structure</th>
<th>Protein targeted by antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pemphigus foliaceus</td>
<td>Desmosome</td>
<td>Desmoglein 1</td>
</tr>
<tr>
<td>Pemphigus vulgaris</td>
<td>Desmosome</td>
<td>Desmoglein 3 +/- 1</td>
</tr>
<tr>
<td>Bullous pemphigoid</td>
<td>Hemidesmosome</td>
<td>BP180 and/or BP230</td>
</tr>
</tbody>
</table>

- **stratum corneum** ("dead" layer of skin)
- **basement membrane zone** ("velcro")

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**Figures:**
- Diagram of skin layers and structures.
- Illustration of protein targeting by antibodies in different diseases.
Who gets pemphigus?

- Average age of onset: 45-65
- Roughly equal male:female
- About 2000 new cases per year in the US
- Approximately 17,000 total cases nationwide

Does stress or diet cause pemphigus?

- No, but stress makes pemphigus (and most autoimmune diseases) worse

- Lunch presentation: nutrition, Monique Dowd, MA, RD, LDN, CDE, CSG

- Sunday workshops:
  - Workshop #2: Stress management, Mei Ling Moore
  - Workshop #3: Caregiving, Janet Segall
  - Workshop #3: Mental health and chronic illness, Lynne Mitchell, MES, Med, RSW
Superficial blisters
Occasionally itchy, burning
Affects only skin, not mucous membranes

“cornflake crust”
Pemphigus vulgaris: mucosal +/- skin blisters

Mucosal blisters
- Mouth
- Throat
- Nose
- Inner eyelids
- Genitals
- Rectum

*Check out “Below the Belt”, Razzaque Ahmed, MD, Sunday Workshop #2
Why is pemphigus hard to diagnose?

• ~1/3 of medical schools do not have a dermatology program

• Even in medical schools that have dermatology, most students don’t learn about it

• Other common diagnoses can look like pemphigus

Pemphigus vulgaris  Herpes gingivitis
Diagnosis of pemphigus

• Skin or oral biopsy to see the location of the blister

• At least one positive immunology test to prove it’s autoimmune
  - Direct immunofluorescence (skin or oral biopsy)
  - Indirect immunofluorescence (blood)
  - Enzyme-linked immunosorbent assay (ELISA – blood)

* Check out “Oral biopsies”, Takako Tanaka, DDS, Sunday Workshop #3
Diagnosing pemphigus: skin biopsy

Pemphigus foliaceus: Superficial blisters

Pemphigus vulgaris: “row of tombstones”
Diagnosing pemphigus: immunofluorescence

Fluorescent detection of antibodies

Patient skin
(Has antibodies bound to skin cells)

Cell surface staining of antibodies
“fishnet” pattern
Diagnosing pemphigus: ELISA

- **Pemphigus vulgaris**
  - Desmoglein 3
  - Sensitivity: 100%
  - Specificity: 98%

- **Pemphigus foliaceus**
  - Desmoglein 1
  - Sensitivity: 96%
  - Specificity: 98-100%

Desmoglein antibody levels fall to normal levels in patients in remission.

Goals of pemphigus therapy

- **Suppress antibody production**
  
  - Steroids
  - Mycophenolate, azathioprine, methotrexate
  - Rituximab

- **Reduce inflammation**
  
  - Doxycycline, dapsone, IVIg

- **Dilute out bad antibodies or remove antibodies**
  
  - IVIg, plasmapheresis

- **Goal = complete remission (complete healing of blisters)**
  
  *Rituximab for pemphigus, Grant Anhalt, MD, coming up next*
  
  *IVIg in pemphigus, Animesh Sinha, MD, right after Dr. Anhalt*

*Wound healing, David Margolis, MD, Sunday workshop #1*
Therapeutic ladder for pemphigus

*Self-advocacy in medicine, Annette Czernik, MD and Becky Strong

• Topical steroids (eg, dexamethasone elixir, clobetasol)
  *Eric Stoopler, DMD, Sunday Workshop #2

• Anti-inflammatories (doxycycline)

• Oral steroids (prednisone), because they work fast
  *Rob Micheletti, MD, afternoon session

• Rituximab or other immune-suppressing agents
  (mycophenolate, azathioprine, methotrexate)

• IVIg (only therapy that’s not immunosuppressive)
Prognosis

• 0% survival for pemphigus vulgaris before corticosteroids
• 40-50% for pemphigus foliaceus

• >95% now, but patients suffer from complications of chronic therapy (infection, steroid-induced fractures and other side effects)

*Drug Development and Clinical trials in pemphigus, afternoon session*
Thank you

Pemphigus and Pemphigoid patients

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