Dermatologic emergencies
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Stevens-Johnson syndrome (SJS)
/Toxic Epidermal Necrolysis (TEN)

- Drug induced derm emergencies that exist on a spectrum
- Delayed reaction: 7-14 days after first dose of new med
- Allopurinol, antibiotics (esp. Sulfa), NSAIDs, anticonvulsants

SJS/TEN spectrum

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>EM</th>
<th>SJS</th>
<th>SJS/TEN Overlap</th>
<th>TEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>% BSA involved in detachment</td>
<td>&lt;10%</td>
<td>10%</td>
<td>10%-30%</td>
<td>&gt;30%</td>
</tr>
<tr>
<td>≥1 mucosal membrane affected</td>
<td>Up to 70%</td>
<td>&gt;90%</td>
<td>&gt;90%</td>
<td>&gt;90%</td>
</tr>
<tr>
<td>Typical targets</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Ocular</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Mucosal</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Mortality</td>
<td>Rare</td>
<td>10%</td>
<td>30%</td>
<td>50%</td>
</tr>
<tr>
<td>Common cause</td>
<td>Infection</td>
<td>Medication</td>
<td>Medication</td>
<td>Medication</td>
</tr>
<tr>
<td>Resolution</td>
<td>Yes (20%)</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>sequelae</td>
<td>Rare</td>
<td>Common</td>
<td>Common</td>
<td>Common</td>
</tr>
</tbody>
</table>

* Highly reported medications for both derm emergencies are sulfonamides, monamine oxidase inhibitors, ACE inhibitors, dapsone, quinolones, minocycline.
SJS/TEN pathogenesis

- Thought to involve apoptosis pathway, esp. Fas ligand/receptor interaction (IVIG contains antibodies that block this interaction)
- HLA types predispose
  - HLA-B*1502 in Asians, Indians taking carbamazepine
  - HLA-B*5801 in Han Chinese taking allopurinol
    - FDA recently recommended screening all Asians for this HLA type prior to starting carbamazepine
- HIV/AIDS increases relative risk of TEN by 1000 fold
  - PJP prophylaxis risky
SJS/TEN clinical picture

- Skin peels off in sheets; Nikolsky sign positive
- Mucosal involvement in 90%
  - Erosions and hemorrhagic crusts of eyes, mouth, genitals
  - Can involve larynx, esophagus as well
- Ophtho, ENT, Urology involvement is important
- Biopsy shows full thickness epidermal necrosis

TEN severity - SCORTEN

<table>
<thead>
<tr>
<th>Prognostic factors</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 40</td>
<td>1</td>
</tr>
<tr>
<td>HR &gt; 120</td>
<td>1</td>
</tr>
<tr>
<td>Cancer</td>
<td>1</td>
</tr>
<tr>
<td>BSA &gt; 10% on admission</td>
<td>1</td>
</tr>
<tr>
<td>BUN &gt; 50</td>
<td>1</td>
</tr>
<tr>
<td>Bicarb &lt; 20</td>
<td>1</td>
</tr>
<tr>
<td>Glucose &gt; 250</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SCORTEN score</th>
<th>Mortality rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>5%</td>
</tr>
<tr>
<td>2</td>
<td>12%</td>
</tr>
<tr>
<td>3</td>
<td>36%</td>
</tr>
<tr>
<td>4</td>
<td>58%</td>
</tr>
<tr>
<td>5+</td>
<td>90%</td>
</tr>
</tbody>
</table>

SJS/TEN management

- Stop all nonessential meds
- Transfer patient to burn unit for supportive care
- Supportive care/ Steroids/ cyclosporine/ IVIG /others controversial in terms of best mortality benefit
- Historically steroids favored, currently supportive care favored. Current practice is IVIG if severe/progressing
- IVIG studies showed best results when high-dose (1g/kg/day)
- Society for Derm Hospitalists is pooling data to lead to a more informed, data driven, expert consensus
Symmetric drug-related intertriginous and flexural exanthema

Delayed reaction: 7-14 days after starting a new med
Amoxicillin, cephalosporins
5 criteria
- Systemic medication-induced
- Gluteal cleft involvement with sharp demarcation and/or V-shaped erythema
- Involves at least one other fold (axillae, neck, inframammary)
- Symmetric
- No systemic symptoms/signs

SDRIFE
Mycoplasma mucositis

- SJS in 9-14 year olds caused my Mycoplasma infection

Mycoplasma mucositis

- 9-14 year olds, more common in boys
- Bloodshot eyes, bloody hemorrhagic lips and oral mucosa, penile/urethral involvement common
- Minimal skin rash elsewhere

- Complications include:
  - inability to eat/failure to thrive
  - severe long term sequelae to the eyes
  - urethral strictures

Mycoplasma mucositis

- Diagnosis can be confirmed with Mycoplasma serologies

- Treatment plan
  - Supportive care only
  - NG tube almost always needs to be placed to ensure nutrition
  - Ophtho and Urology consults
  - Ophtho frequently places an amniotic membrane graft over the eyes to encourage healing and stimulate re-epithelialization
DRESS

- Drug Rash with Eosinophilia and Systemic Symptoms
- VERY delayed reaction (eruption begins 2 weeks – 8 weeks after first dose)
- Anticonvulsants, sulfa, allopurinol, NSAIDs, dapsone, abacavir
- Morbilliform drug eruption PLUS
  - Facial edema
  - Fever
  - Lymphadenopathy
  - Atypical lymphocytes
  - Eosinophilia
  - Organ involvement (Liver > Kidneys > Thyroid > Heart/lung)

DRESS pathogenesis

- HHV-6 reactivation thought to play a role
- HLA subtypes may predict risk
  - HLA-A *301 predicts carbamazepine risk in Northern Europeans
DRESS – RegiSCAR scoring

<table>
<thead>
<tr>
<th>Symptom</th>
<th>No</th>
<th>Ye</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever &gt; 38.5℃</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Atypical lymphocytes on peripheral smear</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Hypereosinophilia (&lt;700 to &lt;1500)</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Hypereosinophilia (≥1500)</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Rash with BSA &gt; 50%</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Rash clinically fits with DRESS</td>
<td>-1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Biopsy fits with DRESS</td>
<td>-1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Internal organs involved</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Thyroid</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Persist at least 2 weeks</td>
<td>-1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>3 or more negative: ANA, BLU, Hep A/B/C, Chlamydia/Mycoplasma</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

DRESS treatment approach

- Traditionally, high dose prednisone for months (rebound is common)
- Some literature suggests that topicals are adequate for mild disease.
  - Funck-Brentano et al JAAD 2015 showed in a case series that use of topicals rather than systemics in mild and moderate DRESS associated with both lower sepsis rate, lower DRESS relapse rate
- Per Bolognia: *Systemic corticosteroids are recommended for life-threatening involvement of the lung and heart because the inflammation is responsive to corticosteroids. They are not particularly useful for reversing kidney and/or liver disease.*

DRESS follow up

- Thyroid, and rarely brain or GI involvement can occur as a delayed reaction
- Recommended to check TSH 2-3 months after initial DRESS presentation
Case scenario

- Young man with lifelong history of atopic dermatitis on body and ears, frequent Staph superinfections
- Comes in today with spreading of rash to entire face

Eczema herpeticum

- Opportunistic viral infection on impaired skin barrier
- Frequently occurs in individuals with atopic dermatitis
- Can spread quickly and be a source for ocular involvement
Eczema herpeticum

- **Diagnosis**
  - Clinically, orange crusted papules on inflamed skin
  - Viral swab can be sent for HSV PCR

- **Treatment**
  - Empiric treatment with (val)acyclovir x 7 days
  - Ophtho consult if anywhere near the eye
Case 2
- Scenario: Pt presents to derm clinic
- Exam findings:
  - Erythroderma (red rash covering at least 90% of the body)
  - Extremely warm
  - Pt visibly shivering
  - Pt toxic appearing

Case 2
- History:
  - Psoriasis for 25 years
  - Treated over the decades with topical steroids, UVA phototherapy, methotrexate, acitretin with no real relief
  - “Worst its ever been” with no identifiable trigger
  - Feels and looks toxic

Erythroderma
- Is a finding, not a diagnosis
- Most commonly from pre-existing skin condition
  - Psoriasis
  - Atopic dermatitis
  - Drug eruption
- Skin biopsy is completely nonspecific and not helpful
- Complications include thermoregulatory and electrolyte abnormalities
- Treatment aimed at correcting underlying disorder rapidly
Case 2 (continued)

- Admitted for close observation
- Known history of severe psoriasis
- Rapid acting treatments include infliximab, cyclosporine
  - Must get baseline Cr for cyclosporine
    - CsA contraindicated in this patient due to history of chronic PUVA treatments ➔ greatly increased risk of skin cancer
  - Must get quantiferon for infliximab use
- Full body clobetasol ointment twice daily
- Occlusion with sauna suit
  - Increasing humidity enhances topical steroid penetration
Case 2 (continued)

- 2 days later patient discharged comfortably with the aid of topical steroids alone
- Later started on TNF-alpha inhibitor (Humira) with essentially complete clearance
- Pt so happy he wrote me a thank you letter and donated money to OHSU
- He still likes to wear his sauna suit once a week

Case 2 - other thoughts

- Systemic steroids great for rapid relief of eczema and many other conditions but can trigger severe flares of psoriasis
- Clobetasol comes in 50-gram tubes. In a grown adult one full body application requires 2 tubes
- Triamcinolone comes in a 1-lb jar
- We prefer ointments over creams
  - More potent
  - Fewer inactive ingredients, less risk for contact allergy

Case 3

- G3P2 patient at 37 weeks gestation
- New onset itchy rash on arms and legs not responding to permethrin or hydrocortisone ointment
Case 3 continued
- On exam, no “primary lesions” present. Essentially covered in scratch marks without any actual rash
- Itching described as worst at night
- Likely to be “prurigo of pregnancy” (now called atopic eruption of pregnancy)
- Differential also included intrahepatic cholestasis of pregnancy
- Screening LFTs taken

Case 3
- LFTs normal, with exception of Alk Phos – 300
- Serum bile acids ordered and elevated as well
Case 3

- Diagnosis: Intrahepatic cholestasis of pregnancy
- Potential complications:
  - Premature labor
  - Clotting/bleeding abnormalities
  - Fetal distress
  - Stillbirth (risk correlates with level of bile acids)
- Recommended treatment
  - Start Ursodiol immediately
  - Encourage early delivery, between 35-38 wks depending on level of bile acids

Case 4

- 53yo healthy obese woman with headache, cough, myalgias became suddenly and profoundly ill, transferred to OHSU for ICU level care requiring pressors and ventilator
- Found to have CK level of 14,000
- Markedly swollen arms and legs – found by Ortho to have 4-limb compartment syndrome
Case 4
- Skin lesions here can be described as stellate or retiform purpuric patches
- Sharply defined, purple, non-blanching, network pattern
- Indicative of clotting off blood vessels/coagulopathy and necessitate a hypercoagulable workup

Case 4
- Skin biopsy performed – showed small vessel platelet plugging as expected
- Labs revealed severe reduction in Protein C activity, consistent with?

Case 4
- Diagnosis: Purpura fulminans
  - Severe infection causes a transient loss of Protein C and the patient becomes hypercoagulable, clotting off skin vessels and developing widespread bizarrely shaped bruises that then develop into bullae
  - Classic scenario is bacteremia from Pseudomonas
- Source of infection in this case:
  - Pt found to be Influenza B positive, which explained her myositis and subsequent renal failure
  - Influenza B also described in literature to cause 4 limb compartment syndrome
Case 5

- 39yo woman frail and appearing much older with a history of systemic lupus, systemic scleroderma, and hereditary angioedema
- Homeless, poor medical follow up, presents to ER monthly for pain medications
- This month, said the pain in her abdomen was “different”
- Also found to have acute kidney injury
- Skin rash noted acrally

Case 5

- Problem list continues to grow
  - Abdominal pain
  - Renal failure
  - Anemia, thrombocytopenia
  - Schistocytes on peripheral smear

- At this point, main differential would include TTP
Case 5

- Skin thought to be vasculitis, probably related to underlying autoimmune
- Skin biopsy performed, and to our surprise showed platelet plugging indicating a hypercoagulable state
- Antiphospholipid antibody was positive

Case 5

- Diagnosis:
  - Catastrophic antiphospholipid antibody syndrome (CAPS)
  - Definition includes rapid involvement of 3 or more organs
    - She was found to have splenic, renal, and bowel infarcts on imaging that week
    - Lupus anticoagulant usually positive
    - Consumptive anemia and thrombocytopenia common
    - More common in women
    - Lupus is a risk factor, but infection a common trigger as well
    - Skin exam: Purpura of hands and feet

Case 5

- Catastrophic antiphospholipid antibody syndrome (CAPS)
  - Can involve any organ
  - Has a 50% mortality and is rapidly fatal
  - Despite treatment, our patient rapidly deteriorated and died a week after admission
  - Treatment includes:
    - Heparin (first-line)
    - Prednisone
    - Plasma exchange
    - IVIG