22- SJS/TEN

Background:

- **Rare** but potentially **fatal drug rashes** that lead to **keratinocyte death**, **full-thickness necrosis** of the **epidermis** and **severe desquamation** of the **skin** and **mucosal** surfaces
- SJS/TEN exist on a spectrum (BSA: body surface area)
    - **SJS < 10% BSA**
    - **TEN > 30% BSA**
    - SJS/TEN overlap syndrome: 10-30% BSA

Pathogenesis:

- Pt w/ **predisposition exposed** to **drug/metabolites** → **activation** of **FAS death receptor** on **keratinocytes** → **secretion** of **granulysin**, **granzyme B**, and **perforin** from **immune cells** → causing **apoptosis** of **keratinocytes** → **necrosis** and **sloughing** of **skin** and **mucous membranes**
- Onset**:** typically **1-2 weeks** after drug exposure
    - **Exceptions**:
        - Few days if pt has already taken medication (e.g. Bactrim)
        - Many weeks in the case of anti-convulsants
    - **Predispositions**: slow acetylators of meds, certain HLA subtypes
        - HLA- B-1502: Asians & East Indians exposed to carbamazepine;
        - HLA-B-5801: Han Chinese exposed to allopurinol)
        - HIV/AIDS patients
    - **Medications**: >100 medication associations
        - Sulfamethoxazole-Trimethoprim
        - Allopurinol
        - Phenytoin, Carbamazepine, Lamotrigine
        - Penicillins, Cephalosporins, Carbapenems, Monobactams
        - NSAIDs
        - Abacavir, Nevirapine

Clinical Presentation:

- **Prodrome** of **fever** & **flu-like sx 1-2 weeks after initial medication**
- **1-3 days** later **mucocutaneous** changes noted. Look for erythema or erosions on mucous membranes. **Skin findings** typical start on **trunk** as **erythematous macules** and **targetoid** w/ a **dusky** or **purpuric center**.
- Lesions will be **tender** to touch and **quickly coalesce** in hours to days
- May **progress** to **flaccid blisters** and sheets of skin that start to **desquamate**.

PEARL: Nearly all pt w/ SJS/TEN will have mucosal involvement. ALWAYS look in the pt's eyes, nose, mouth and genital mucosa if you are suspecting SJS/TEN!

PEARL: How to distinguish SJS from EM? 1) Think about the distribution of lesions. EM tends to involve the distal extremities, whereas SJS/TEN is much less likely to involve these regions. 2) SJS has atypical macular targets and are not raised or palpable as in EM.

PEARL: What's on your differential for desquamating rashes?

SJS, TEN, EM Major, SSSS, toxic-shock syndrome, *Mycoplasma pneumonia*-induced rash and mucositis (MIRM), DRESS (DIHS), purpura fulminans, acute graft-versus-host dz, and pemphigus vulgaris

Diagnosis:

- **Hx + Physical Exam**
- **Biopsy**

Histology:

- **Scattered apoptotic keratinocytes**
- Unimpressive **perivascular lymphohistiocytic infiltrate** w/ **eosinophils**
- As lesions progress, there will be **full thickness epidermal necrosis** & development of **subepidermal blisters**

Prognosis:

- Calculate **SCORTEN** (On arrival + 48 hrs later)
- Think "**TAMEBUG**"
    - **T**achycardia >120 BPM
    - **A**ge >40
    - **H**x of malignancy
    - **E**pidermal loss >10%
    - **B**icarb level >20 mEq/dL
    - **U**rea (BUN) >27 mg/dL
    - **G**lucose >250 mg/dL

Points	% Mortality
0-1	3
2	12
3	35
4	58
5+	90

PEARL: What are some complications of SJS/TEN that we try to prevent? (Most common: ocular changes: chronic dry eyes, symblepharon, blindness)

Short Term: Fluid loss leading to electrolyte abnormalities, hypovolemic shock, multiple organ dysfunction syndrome, bacterial infections → septic shock, pneumonia, ARDS

Long Term: Poor skin healing, dyspigmentation, scarring → hair loss & disfiguration (symblepharon, vaginal adhesions)

Treatment

- **Step 1: Stop** the offending **drug**!
- **Step 2: Supportive care** and **Systemic tx**

Supportive Care:

- Wound Care
    - Areas of sloughed skin can be covered in petrolatum-impregnated gauze or nanocrystalline gauze until affected area re-epithelialize
- Infection prevention
    - Antibiotic ointments or petrolatum are applied around mouth and nose
- Monitoring fluids and electrolytes
    - Foley catheter
- Nutrition
- **Consult ophthalmology**
    - Often recommend ophthalmic antibiotic ointments for eyelids and antibiotic or steroid eyedrops to reduce infection and scarring
- **Consult OB/GYN**
    - Study of female TEN pts: 70% had vulvovaginal lesions → 30% of which had long-term issues
        - Prophylactic vaginal dilation and topical corticosteroids

Systemic Tx:

- Systemic Corticosteroids
    - Use advocated early on in dz course, however they also increase risk of infection in these predisposed patients.
- IVIG
    - 0.75 mg/kg/day x 4 days
    - Check coagulation panel and an IgA level (rule out IgA deficiency)
- Cyclosporine
- TNF-alpha inhibitors (e.g. infliximab and etanercept)