

# DRESS SYNDROME:

Common Medications and Dangerous Reactions

Sara Sussman, MD

LSU-New Orleans

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Red River Potpourri



# Disclosures

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- ▣ I have no relevant financial or nonfinancial relationships to disclose.

# Case Presentation

- 16 year old African American male with history of Ulcerative Colitis
- Being treated for ulcerative colitis with mesalamine
- An insurance-based medication change required a switch from mesalamine → sulfasalazine



# Initial Presentation

- 3 weeks later the patient presents to the hospital with fever, abdominal pain
- Diagnosed with “presumed viral illness” and discharged home
- Subsequently treated by pediatrician with a course of amoxicillin due to possible strept throat infection



# Final Presentation

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- One week later, patient presents to hospital with:
  - Diffuse erythematous rash
    - Rash started on arms, spread to neck and chest then to legs and feet bilaterally
  - Continued daily fever (Tmax 104°)
  - Lymphadenopathy
    - Cervical, submandibular and supraclavicular (R>L)
  - Eosinophilia
    - AEC: 800 cells/ $\mu$ L
  - Elevated transaminases
    - AST 174, ALT 295
  - Hyponatremia
    - Na<sup>2+</sup> 124

- Other labs:
  - ▣ Normal WBC, normal platelets, “slight” atypical lymphocytes
  - ▣ Maximum AEC was 1700cells/ $\mu$ L
  - ▣ Remainder of CMP WNL
- Exam: no HSM, heart and lungs WNL
- Patient diagnosed with DRESS Syndrome due to the temporal relationship to an inciting medication, his characteristic rash, eosinophilia and liver injury



# DRESS SYNDROME

# Overview

- Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a rare, potentially life threatening adverse drug reaction
- An immunologic adverse reaction to medications which may result in multi-system organ failure
- Occurs in both adults and children
- Has cutaneous manifestations as well as internal organ involvement
- Characterized by a later onset and longer duration than other drug reactions
  - ▣ Typically has a latent period of **2-6 weeks** after drug introduction



# Presentation



# Rash

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- Begins 2-6 weeks after initiation of the offending medication
- Morbilliform rash
  - ▣ diffuse, pruritic, macular exanthem
- Usually face → upper trunk and upper extremities  
→ lower extremities
- Becomes infiltrative and indurated with associated edema
- Can evolve in appearance to an exfoliative dermatitis with diffuse scaling in 20-30% of patients



## Morbilliform eruption

Patient with DRESS syndrome secondary to piperacillin-tazobactam



## Diffuse scaling of the legs

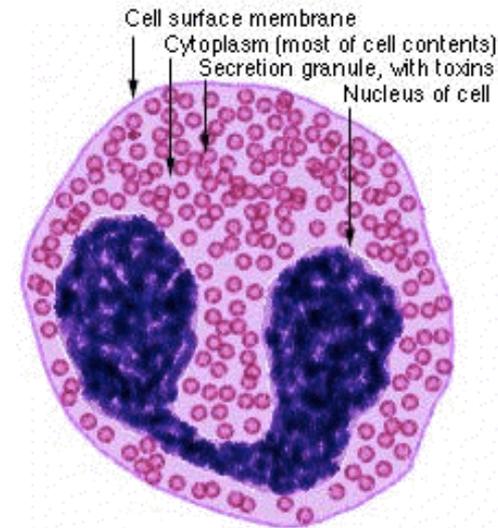
Patient with phenytoin induced DRESS

# Lymphadenopathy

- Present in 75% of cases
- Can be limited or more generalized lymphadenopathy
- Typically have localized tenderness
- Most likely to affect cervical, axillary and inguinal lymph nodes

# Hematologic Abnormalities

- Prior to initial presentation there is often leukopenia
- Eosinophilia is present in 50-90% of cases
  - ▣ Can be delayed for 1 to 2 weeks
- Marked leukocytosis
  - ▣ Atypical lymphocytes are present
- Hemophagocytic syndrome is rare





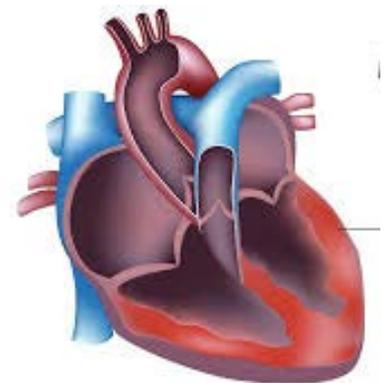
# Liver Dysfunction

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- Most common meds: phenytoin, minocycline and dapsone
- Can present with hepatosplenomegaly
- Often accompanied by hepatitis
  - ▣ Elevated AST, ALT, alkaline phosphatase and creatinine
- Found in approximately 70% of patients
- Can last several days to months for complete resolution after withdrawal of offending medication
- Hepatic necrosis: can lead to fulminant liver failure, coagulopathy and sepsis
  - ▣ Primary cause of mortality in DRESS

# Other organ system involvement

- Renal: 10-30% of patients exhibit renal disease
  - ▣ Manifests as acute interstitial nephritis
  - ▣ Most commonly associated with allopurinol
- Pulmonary:
  - ▣ Cough fever, and dyspnea
  - ▣ Most associated with minocycline
- Cardiac:
  - ▣ Associated with ampicillin and minocycline
  - ▣ Most commonly presents as myocarditis





# ETIOLOGY and PATHOGENESIS



# Etiology-Typical Drugs:

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- Many drugs have been reported, but a few prominent ones are most common
- Aromatic anticonvulsants
  - ▣ Phenytoin, carbamazepine and phenobarbital
- Sulfonamides
  - ▣ Sulfasalazine
- Other meds
  - ▣ Dapsone, minocycline
  
- Immunosuppression



# Proposed Mechanisms of Pathogenesis

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## □ Deficient drug metabolism

- Accumulation of drug reactive metabolites
- Triggering autoimmune responses against skin or liver cells
- Particularly seen in cytochrome P450 pathway
- Documented in :
  - Anticonvulsants
  - sulfonamide-induced DRESS



# DIAGNOSTIC CRITERIA



# RegiSCAR

RegiSCAR <sup>72</sup>
Acute rash <sup>†</sup>
Reaction suspected to be drug-related <sup>†</sup>
Hospitalization <sup>†</sup>
Fever >38°C <sup>‡</sup>
Enlarged lymph nodes involving ≥2 sites <sup>‡</sup>
Involvement of ≥1 internal organ <sup>‡</sup>
Blood count abnormalities <sup>‡</sup>
Lymphocytes above or below normal limits
Eosinophils over laboratory limits
Platelets under laboratory limits

<sup>†</sup> Necessary criteria for diagnosis according to RegiSCAR.

<sup>‡</sup> Three of these 4 criteria required for diagnosis according to RegiSCAR.



# TREATMENT





# Withdrawal of drug and supportive care

- Immediate withdrawal of offending drug
- Supportive care:
  - Antipyretics
  - Topical steroids
  - Avoid extraneous medications
  - Treat as serious burn
- Systemic Corticosteroids



# Follow Up

- Patients must strictly avoid the offending agent in the future
- Since this is an immunologic phenomenon, these patients are not candidates for desensitization
- Future reactions are unpredictable and can be life-threatening



# Hospital Course

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- Started on IV solumedrol
- Solumedrol was then transitioned to PO steroids
- Topical steroids were provided for pruritic rash
- LFTs continued to be trended and were improved upon discharge
- Patient was discharged on a four week wean of oral steroids and referral to Allergy/Immunology

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