

DRESS SYNDROME:

Common Medications and Dangerous Reactions

Sara Sussman, MD

LSU-New Orleans

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Red River Potpourri



Disclosures

- ▣ 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

- 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/ μ L
 - Elevated transaminases
 - AST 174, ALT 295
 - Hyponatremia
 - Na²⁺ 124

- Other labs:
 - ▣ Normal WBC, normal platelets, “slight” atypical lymphocytes
 - ▣ Maximum AEC was 1700cells/ μ 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

- 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

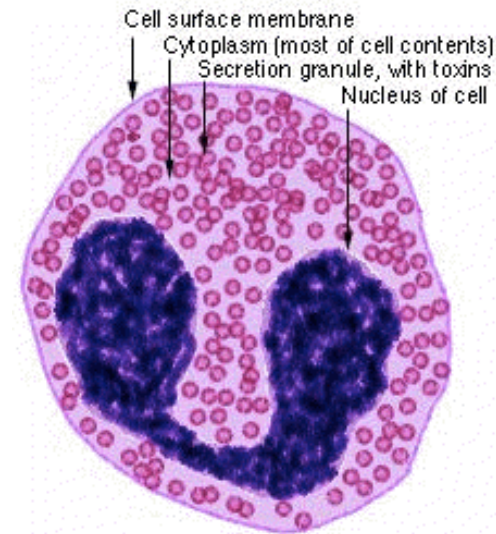
Patient with phenytoin induced DRESS

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

- 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:

- 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

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

[†] Necessary criteria for diagnosis according to RegiSCAR.

[‡] 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

- 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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