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Clinical Pearls

Clinical Pearls help prepare residents for the future by providing them with top tips from experts about what they should know about specific, key subject areas by the time they complete their residency.

DRESS syndrome

By José Dario Martinez, MD, IFAAD

1. Etiology, epidemiology, and HLA relationship

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a hypersensitivity syndrome triggered by multiple drugs. It can be produced by enzyme deficiency to detoxify, and it is associated with several HLA antigens as well as reactivation of human herpes virus 6/7. Among HLA antigens, DRESS is associated with HLA B58:01 (allopurinol) and HLA B15:02 (carbamazepine). It affects children and adults, has no gender predilection, occurs after 2-6 weeks after starting the culprit drug (first exposure), and is not dose related. It is a delayed hypersensitivity reaction with eosinophils activation and elevation that causes hepatic and cardiac damage.

2. Drugs and target organs

Multiple drugs can cause DRESS syndrome: antiepileptics (carbamazepine, phenytoin), antibiotics (vancomycin, minocycline, ampicillin, dapsone), and allopurinol, among many more. Allopurinol targets the kidney; carbamazepine the kidney; ampicillin the heart; dapsone liver and kidney; minocycline liver, lung, and heart; and phenytoin the liver. Mortality is around 10% and most of the cases are due to fulminant hepatitis.

3. Clinical skin and laboratory features; differentiate minor and major forms of DRESS; Dx criteria

Clinically, a widespread rash (97.6%), typical facial edema (53.6%), maculopapular rash (84.8%) or exfoliative rash (47.2%), and mucosal involvement (32.8%) are the most common skin features. Skin manifestations of DRESS exhibit a wide range of skin lesions and can vary according to the culprit drug.

Severity predictor with a sensitivity of 96% and a specificity of 100% include: BSA > 35%, eosinophils > 6%, absolute eosinophil count > 450 cells/mm3, CRP: > 5 mg/L, ALT > 92 U/L.

Distinguishing minor and major forms of DRESS: A major form has high fever, short latency, persistent reaction, and facial edema — this means a severe case of DRESS and the culprit drugs are sulfas, carbamazepine, vancomycin, allopurinol, and phenytoin.

Diagnosis of DRESS include Boquet´s et al criteria, RegiSCAR study group, and Japanese consensus group, all of them are useful for Dx.

4. DDx, poor prognostic factors, and long-term sequelae

Differential diagnoses include: drug eruptions, SJS/TEN, erythroderma, viral infections, angioimmunoblastic T-cell lymphoma (AITL).

Poor prognostic factors include high eosinophil count, thrombocytopenia, pancytopenia, renal failure, and involvement of various organs. Associated co-morbidities are crucial in the prognosis of these patients.

The long-term autoimmune aftermath of DRESS syndrome includes Graves' disease, Hashimoto's thyroiditis, type 1 diabetes mellitus, systemic lupus erythematosus, and alopecia areata.

5. Management and therapy

Management includes supportive therapy and skin care, systemic therapy includes dexamethasone IV (pulsed), then tapering with prednisone: 1-2 mg/kg/day PO or deflazacort PO, anti-TNF-α (etanercept), antihistamines, and antivirals (valacyclovir) as needed. The disease process of DRESS includes development and activation of drug-specific T-cells — cyclosporine inhibits the activation and proliferation of these T-cells. A small study showed quicker symptom resolution resulting in a reduced hospital stay and less Rx duration than corticosteroids, using cyclosporine (5 mg/kg/day) PO for 2-4 weeks.

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