Drug reaction with eosinophilia and systemic symptoms in a child with *N*-methyl-D-aspartate receptor encephalitis

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ABSTRACT

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a rare but potentially life-threatening disorder that can be seen as a side effect of commonly used medications, particularly those in the anti-epileptic classes. Described here is a 10-year-old boy with newly diagnosed *N*-methyl-D-aspartate receptor encephalitis who presented for inpatient rehabilitation and developed a sudden-onset rash with coagulopathy. Cessation of the offending agents resulted in resolution of the symptoms.

KEYWORDS DRESS syndrome; pediatric rehabilitation; rash; seizure

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a severe, distinctive reaction to a medication characterized by a prolonged latency period, typically developing 2 to 8 weeks following initiation of the triggering medication. The most common anti-epileptic medications associated with DRESS include phenytoin, carbamazepine, and phenobarbital, with an incidence of roughly 1 per 5000 exposures.¹ Dermatologic manifestations typically present with an urticarial maculopapular eruption and occasionally include bullae, vesicles, purpura, facial edema, and/or cheilitis.² The rash is typically accompanied by fever, lymphadenopathy, hematologic abnormalities (lymphocytosis, eosinophilia), and abnormal liver function tests.³ Visceral organs can also be affected, causing hepatitis, pneumonitis, myocarditis, pericarditis, nephritis, or colitis.⁴ Though some cases are relatively self-limited with cessation of the medications, DRESS has a relatively high mortality rate, estimated to be around 10% of patients, typically in those with profound end-organ damage and pancytopenia,⁵ and those in whom the culprit medication is promptly discontinued fare best.⁶ DRESS is diagnosed by utilizing either the RegiSCAR criteria or Bocquet's criteria (*Table 1*).⁷ Identification and high clinical suspicion are imperative in identifying DRESS, because outcomes improve with earlier cessation of the medication. Topical steroid creams are recommended for use on symptomatic rash, and systemic steroids may be considered in severely affected patients.

CASE DESCRIPTION

A 10-year-old boy presented to the emergency department with a 4-day history of fever, headaches, and fatigue with acute onset of seizure-like activity, characterized by lip smacking, right arm clenching, and extensor posturing of both legs. He underwent basic laboratory testing and magnetic resonance imaging of the brain, which was normal. He was initially diagnosed with new-onset epilepsy and given a referral for outpatient neurology follow-up. He continued to have an increasing frequency of seizures and some unusual behaviors, such as repetitive statements that were nonsensical and hallucinations of auras. He was taken to a larger academic institution for a second opinion of his presentation, where a lumbar puncture revealed anti-*N*-methyl-D-aspartate antibodies. He was treated with five doses of intravenous methylprednisolone followed by seven doses of plasma exchange. Video electroencephalogram showed ongoing epileptiform activity throughout his hospitalization, requiring escalating treatment with valproic acid, oxcarbazepine, phenobarbital, topiramate, and clobazam. After a 3-week hospital admission, he was discharged to inpatient rehabilitation for ongoing care, because he had difficulty with balance, endurance, coordination, safety awareness, and impulsivity control.

Roughly 48 hours after presentation to the rehabilitation facility, he developed a maculopapular pruritic rash on the distal extremities, which migrated to include his trunk and neck, and new-onset oral ulcers that were painful. He

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Table 1. Criteria for diagnosis of drug reaction with eosinophilia and systemic symptoms

Source	Criteria
RegiSCAR (requires three of four criteria marked by asterisks)	Fever $>38^{\circ}\text{C}^*$ Enlarged lymph nodes at minimum of two sites* Involvement of at least one internal organ* Blood count abnormalities (lymphocytosis, eosinophilia)* Hospitalization Reaction suspected to be drug related Acute rash Lymphocytes above or below normal limits Eosinophils above the laboratory limits Platelets below the laboratory limits
Bocquet's (requires all three criteria)	Cutaneous drug eruption Adenopathies >2 cm in diameter or hepatitis (liver transaminases more than two times upper limit of normal) or interstitial nephritis or interstitial pneumonitis or carditis Hematologic abnormalities: eosinophilia $> 1.5 \times 10^9/\text{L}$ or atypical lymphocytes

developed a fever with T_{max} of 102°F , prompting an infectious workup, including a complete blood count and comprehensive metabolic panel. Laboratory findings revealed elevated eosinophil count, thrombocytosis, and elevated transaminases. The patient was diagnosed with DRESS, prompting cessation of the most likely offending agents: oxcarbazepine, phenobarbital, and topiramate. His clobazam and valproic acid doses were adjusted for optimal seizure control. His rash was treated with topical steroid ointment, and his mouth ulcers were treated with an oral lidocaine solution as needed. With discontinuation of some anti-epileptics, his rash began to abate, and his laboratory findings normalized. He was ultimately discharged home with ongoing outpatient therapies, no further seizures, and resolution of his aberrant blood work.

DISCUSSION

Patients in inpatient rehabilitation frequently arrive with new diagnoses, requiring a vast array of new medications. Clinicians are responsible for monitoring effectiveness and potential adverse reactions, many of which can be vague and involve minimal risk. This is not the case with DRESS syndrome, with an $\sim 10\%$ mortality rate and potentially months-long recovery process. Patients with a history of DRESS are at risk of future flares and can experience symptoms within other classes of medications, such as antibiotics or antipsychotics.⁸ DRESS syndrome can be caused by many medications that are frequently used within the inpatient rehabilitation patient population and should be on the differential diagnosis list of any patient with new symptoms of rash, swelling, and abnormal laboratory findings.

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