

Kids With Rash and Fever on Antibiotics May Have DRESS

BY BRUCE JANCIN

VAIL, COLO. — Drug rash with eosinophilia and systemic symptoms, or DRESS, needs to be included in the differential diagnosis when a patient presents with fever and a rash 1-8 weeks after starting a drug.

DRESS is a severe variant of cutaneous drug reaction with a mortality of 8%-10%, mainly due to multiorgan system failure or hepatitis. Hospital bills in survivors often exceed \$100,000, Heather R. Heizer said at a conference on pediatric infectious diseases sponsored by the Children's Hospital, Denver.

Hallmarks of DRESS include a high and long-lasting fever and a macular erythematous rash that usually begins centrally on the trunk and abdomen. The rash is typically itchy and may feature papules or pustules. Facial edema, particularly in the periorbital region, is common, said Ms. Heizer, a physician assistant at the hospital. Systemic involvement includes lymphadenopathy in three-quarters of cases, hepatitis in half, and eosinophilia or atypical lymphocytosis in up to about one-third. Aplastic anemia and hypogammaglobulinemia are not uncommon.

A key point is this: The severity of skin involvement bears no relationship to the extent of internal organ involvement, Ms. Heizer said.

Antibiotics are clearly the drug class most often associated with DRESS in children. Indeed, antibiotics account for up to 30% of all adverse drug reactions requiring hospitalization in children. Other drugs or drug classes that have precipitated DRESS include anticonvulsants, allopurinol, and heparin.

The pathogenesis of DRESS is not well understood. Several recent small studies have implicated human herpesvirus 6, although this needs confirmation, she said. Current thinking is that the clinical manifestations of DRESS are mediated by antiviral T cells that cross-react with the offending drug.

The most important aspect of the treatment of DRESS is prompt identification and withdrawal of the offending agent. Antihistamines and topical corticosteroids can be employed to manage symptoms. The use of systemic steroids is controversial. They help relieve some symptoms, although the rash and hepatitis may persist for weeks. The problem is that a rebound of symptoms can occur when the systemic steroids are stopped. Case reports suggest N-acetylcysteine may be useful as a detoxifying agent in the setting of DRESS, Ms. Heizer said. Disorders sharing features in common with DRESS include Stevens-Johnson syndrome, Kawasaki disease, toxic epidermal necrolysis, and Epstein-Barr virus infection.

Dr. Mary Glodé, professor of pediatrics at the University of Colorado at Denver, commented that DRESS and other drug fevers are diagnoses of exclusion, and therein lies the dilemma.

"It's hard to tell initially if the fever is

caused by the drug, since you're treating an infection. There can be dozens of things going on. The problem with a diagnosis of exclusion is nowadays you have so many expensive tests, and then those test results lead to lymph node biopsy and other procedures. It has really complicated life for our patients, their families, and ourselves," she said. ■

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^a Tdap = Tetanus, diphtheria, and acellular pertussis. ^b ACIP = Advisory Committee on Immunization Practices. ^c CPT = Current Procedural Terminology is a registered trademark of the American Medical Association.

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