

Foreword

The Complexity of Drug Hypersensitivity



Rafeul Alam, MD, PhD
Consulting Editor

Drug allergy remains one of the most important contributors to iatrogenic morbidity and mortality. Significant progress has been made in understanding the immunopathogenesis of allergy to certain drugs. The identification of specific HLA loci that predispose to drug hypersensitivity has greatly contributed to our knowledge about drug hypersensitivity. The association of HLA-B5701 with Abacavir¹ and HLA-B1502 with Carbamazepine² is now well established. Structural studies have demonstrated the binding of these drugs to the MHC antigen-presenting groove. The screening for these HLA genotypes prevents serious drug allergic reactions. However, our knowledge remains incomplete as only 55% of patients with positive HLA-B5701 treated with Abacavir develop hypersensitivity reaction. Similarly, only 3% to 7% of patients with positive HLA-B1502 treated with Carbamazepine develop Stevens-Johnsons syndrome and toxic epidermal necrolysis.² It is likely that a complex of a self-peptide associated with the drug in the MHC groove is the ultimate trigger for T-cell activation. This hypothesis needs identification of the self-peptide and demonstration of the trimolecular complex. Viral reactivation in the context of drug reaction with eosinophilia and systemic symptoms (DRESS)/drug-induced hypersensitivity syndrome is an intriguing subject, which could account for some of the manifestations and complications.

When a patient presents with an allergic skin rash, especially a delayed maculopapular rash, and is on multiple medications, the identification of the causative drug remains a challenge. A number of diagnostic approaches are being pursued. They include skin test, delayed-read intradermal test, patch test, lymphocyte proliferation test, and ELISPOT. Although progress has been slow, standardization and validation of these tests will greatly aid the diagnosis and proper management of drug allergy. An initial approach was to reach a consensus on definition, diagnostic approaches, and management of drug hypersensitivity reactions. An international consensus has

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recently been published, which will greatly facilitate this process.³ To update us on this important topic, I have invited Dr Pascal Demoly, who is a leader in the field. He has brought together an outstanding group of scientists and clinical investigators, who present the latest in the field.

Rafeul Alam, MD, PhD
Division of Allergy and Immunology
National Jewish Health and
University of Colorado Denver
1400 Jackson Street
Denver, CO 80206, USA

E-mail address:
alamr@njhealth.org

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