Cutaneous Manifestation of Drug Allergy and Hypersensitivity

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KEYWORDS

• Drug allergy • Drug hypersensitivity • Cutaneous manifestations
• Cutaneous adverse drug reactions (CADR) • Photoallergy

KEY POINTS

- Cutaneous eruptions are the most common manifestation of both allergic and nonallergic drug hypersensitivity.
- Different medications may cause identical skin symptoms, and hypersensitivity to a single drug may manifest with various patterns of symptoms.
- Immediate drug reactions, developing within 1 hour of the drug intake, manifest with urticaria, angioedema, and/or anaphylaxis.
- Delayed type of drug hypersensitivity may manifest with virtually all other cutaneous drug eruptions.
- Analysis of morphology of drug-induced lesions as well as timing of reaction is critical for the final diagnosis

INTRODUCTION

Adverse drug reactions (ADRs) are responsible for about 6% of all hospital admissions and around 9% of hospitalization costs. Only a fraction of these reactions (less than 10%) can be defined as type B, that is, drug hypersensitivity reactions (DHRs), which are usually not predicable and occur in susceptible individuals.[1] However, DHRs may result in potentially fatal outcomes; thus, proper diagnosis and prompt, careful

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management is required. The pathomechanism of DHR may be either immunologic (allergy, allergic hypersensitivity) or nonimmunologic (nonallergic hypersensitivity). Although DHRs may manifest with various symptoms (organ specific or systemic), the skin is most commonly affected. Drug-induced skin symptoms are usually mild and self-limiting but may herald the development of a severe systemic and potentially lethal reaction. Drug reactions adopt many faces and should be taken into account in the differential diagnosis of numerous skin rashes. Careful clinical evaluation of visible skin lesions could greatly help in establishing a proper diagnosis.[2–4]

Allergic and Nonallergic Drug Hypersensitivity

DHRs have been defined as objectively reproducible signs or symptoms initiated by a drug at a dose usually tolerated by normal subjects and represent type B ADRs (**Fig. 1**).[5] DHRs with clearly defined immunologic (most often immunoglobulin E [IgE] mediated or T-cell mediated) mechanisms are referred to as drug allergy, whereas nonallergic drug hypersensitivity includes reactions with other, nonimmunologic pathogenic mechanisms (eg, aspirin hypersensitivity related to cyclooxygenase inhibition).[6,7] Similar drug-induced cutaneous symptoms may be evoked by both allergic and nonallergic mechanism, and a single drug can trigger reactions involving either an immunologic (allergic) or nonimmunologic mechanism. Furthermore, allergic DHRs may represent a type I, II, III, or IV drug-specific immune responses according to the Gell and Coombs classification. Distinguishing between these types of hypersensitivity reactions is important in deciding to propose alternative drugs. In drug allergy it may be possible to replace a culprit drug with a drug belonging to the same class but having a different chemical structure (eg, penicillin may be replaced by another antibiotic), whereas in the case of nonallergic hypersensitivity, the whole class of drugs should be avoided (eg, all nonsteroidal antiinflammatory drugs [NSAIDs], which are cyclooxygenase-1 [COX-1] inhibitors, will cross-react in the case of aspirin hypersensitivity).

Hypersensitivity reactions to drugs may manifest with organ-specific or systemic symptoms, ranging in severity from mild skin symptoms (eg, rash) to life-threatening reactions involving multiple organs and systems. Timing of reactions ranges from immediate symptoms, occurring within minutes (eg, penicillin allergy), to symptoms developing within several days after drug intake. Reactions occurring within the first 24 hours are called immediate or acute, whereas delayed reactions, by definition, usually appear more than 24 hours after drug intake.

Cutaneous eruptions are the most common manifestations of drug hypersensitivity and may include exanthematous eruptions, urticaria, angioedema, contact dermatitis,

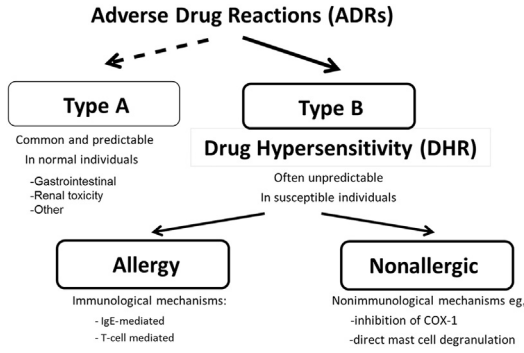

Fig. 1. Classification of ADRs and DHRs.