A Review of Cutaneous Drug Eruptions

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KEYWORDS

• Drug eruption • Adverse cutaneous reaction • Drug reaction

KEY POINTS

- Drug eruptions are a common cause of morbidity and even mortality in the geriatric population.
- The specific pattern of the eruption can provide clues to the culprit medication.
- Most commonly, drug eruptions present 7 to 21 days postadministration of the offending medication, but this can vary based on the type of reaction and whether or not patients have been previously sensitized.
- The cornerstone of treatment is drug discontinuation and supportive care, although it may occasionally be possible to treat through the eruption.
- Administration of systemic steroids has limited benefit for many drug eruptions and should be considered on a case-by-case basis.

INTRODUCTION

Cutaneous drug eruptions can range from an asymptomatic rash to a life-threatening emergency. Because of the high frequency, morbidity, and potential mortality associated with drug eruptions, it is important to be able to promptly recognize, work up, and treat patients with possible drug reactions.[1] The geriatric population is at particular risk for drug eruptions. A 2006 study by Yalcin and colleagues found the prevalence of cutaneous adverse drug reactions to be 1.4% during a 5-year period when analyzing 4099 geriatric patients.[2,3] It is unclear if the increased risk is due to polypharmacy alone or also to changes in drug metabolism and/or excretion with age.[4,5]

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EPIDEMIOLOGY

Studies have shown varying rates of cutaneous drug reactions in hospitalized patients. In a 2006 prospective study, researchers found that a prevalence of only 0.7% of hospitalized adult patients developed a drug rash; this is considerably lower than figures from other studies.[6] One reason may be the exclusion of cutaneous eruptions after blood or blood products were administered, which is a major cause of reaction in other studies.[6] The Boston Collaborative Drug Surveillance Program analyzed 15,438 consecutive inpatients from June 1975 to June 1982 and concluded that 2.2% of hospitalized patients developed allergic drug reactions.[7,8] Other studies have suggested that approximately 3% of all hospital admissions were secondary to various adverse drug reactions.[9–11] The rates of drug reactions are higher in patients who are immunosuppressed, such as those with HIV, systemic lupus erythematosus, and lymphoma. The severity of the reaction can be correlated with the stage of their disease. Patients with AIDS are at least 8.7 times more likely to develop cutaneous drug reaction compared with the average population.[6] The elderly are also at an increased risk of developing drug eruptions.[12,13] The rate of hospitalization for adverse drug reactions in the elderly has been reported to be as high as 16.6% to 24% compared with 4.1% in younger patients; these percentages refer to all adverse reactions, not simply cutaneous reactions.[14,15]

Costs associated with adverse drug reactions make up a substantial portion of hospital admission expenditures. A 1998 study by Moore and colleagues[11] found that 5% to 9% of hospital admission costs were associated with adverse drug reaction.

PATHOPHYSIOLOGY

The precise mechanism of adverse drug reactions is unknown but most are likely the result of immune-mediated reactions. The development of drug eruptions depends on a patient's inherited drug-metabolizing enzyme profile; acquired factors, such as viral infection; and host factors, such as age and gender.[16,17]

Different immune responses cause distinct cutaneous reaction patterns. Type I hypersensitivity is defined by the cross-linking of IgE receptors that results in mast and basophil degranulation, releasing chemical mediators, such as histamine and leukotrienes. This type of hypersensitivity manifests as urticaria, angioedema, and anaphylaxis. Type III hypersensitivity involves antigen-antibody complexes that form and deposit in the skin and small vessels. Examples include serum sickness and vasculitic drug eruptions. Type IV or delayed-type hypersensitivity is defined by sensitized T cells that are reintroduced to an antigen, resulting in a release of cytokines, which then activate monocyte and macrophages. Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are manifestations of type IV hypersensitivity reactions.[17]

Despite the differences in rates of drug eruptions, virtually all studies have found morbilliform and urticarial reactions the most common types of drug eruptions; accounting for approximately 94% of drug eruptions.[6–8] A vast number of medications has been implicated in cutaneous drug eruptions but the probability of any particular drug causing a reaction varies considerably. Antibiotics are notorious offenders. Overall, the most common offending drugs that cause cutaneous drug eruptions include amoxicillin, trimethoprim-sulfamethoxazole, ampicillin, semisynthetic penicillins, blood, and blood products.[18] Drug eruptions can be classified by clinical and histologic characteristics particular to each type of reaction, and each category of eruption has multiple likely culprit medication offenders. Specific drug eruptions, broken down by morphology, are discussed.