Immediate and Delayed Reactions to Radiocontrast Media: Is There an Allergic Mechanism?

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Radiocontrast media (RCM) are administered more than 75 million times per year for performing diagnosis and treatment of vascular disease and enhancement of radiographic contrast. Adverse reactions after RCM administration are common. Symptoms after RCM exposure may be regarded as hypersensitivity reactions or toxic reactions related to the well-defined toxicity of the compounds, or may be caused by factors unrelated to RCM, such as chronic idiopathic urticaria (Fig. 1). Hypersensitivity reactions to RCM may present clinically as anaphylaxis with the potential to result in fatalities or as delayed occurring exanthemas, not unlike those to other drugs. They have been classified in regard to the time interval between administration and the first appearance of symptoms as immediate when they occur within 1 hour after RCM administration or nonimmediate when they occur 1 hour to 10 days after iodinated RCM injection. Recently, positive skin tests have been described in case reports and in a multicenter study in patients with RCM hypersensitivity. In addition, laboratory data in favor of an allergic mechanism have been published. This review is focused on the current understanding of the mechanisms of immediate and nonimmediate hypersensitivity reactions to RCM and how this translates into recommendations concerning diagnostic procedures.

RADIOCONTRAST MEDIA

All RCM are highly concentrated solutions of tri-iodinated benzene derivatives. There are currently four types of contrast media commercially available: ionic monomers, nonionic monomers, ionic dimers, and nonionic dimers. The ionic contrast media are highly water soluble by means of their carboxylate group. The nonionic
products are made water soluble by introducing long side chains rich in hydroxyl groups. The majority of RCM marketed are nonionic monomers, whereas ionic monomers have been continuously withdrawn in most countries, at least for intravenous use. All compounds are nonreactive, have low protein-binding capacity, and are excreted unmetabolized in urine within 24 hours after injection.

EPIDEMIOLOGY

The frequency and mechanisms of hypersensitivity reactions differ between the different types of RCM. Mild immediate reactions have been reported in 3.8% to 12.7% of patients receiving intravenous injections of ionic monomeric RCM and in 0.7% to 3.1% of patients receiving nonionic RCM. Severe immediate adverse reactions to ionic RCM have been reported in 0.1% to 0.4% of intravenous procedures, whereas reactions to nonionic RCM are less frequent (0.02% to 0.04%). Fatal hypersensitivity reactions may occur in 1 to 3 persons per 100,000 contrast media administrations and are not related to one particular type of RCM. The frequency of nonimmediate reactions varies from 0.5% to 23.0%. This large variation may be due to the difficulty in verifying whether symptoms occurring days after exposure are, in fact, caused by the RCM. Various types of exanthema account for the majority of RCM-induced nonimmediate hypersensitivity reactions. Such exanthemas have been reported to affect 1% to 3% of RCM-exposed patients. Unlike immediate reactions, there seems to be a higher incidence of nonimmediate exanthemas associated with dimeric nonionic RCM but not to other types of RCM.

The main risk factor for immediate as well as nonimmediate hypersensitivity reactions is a previous reaction. Previous reactors have a 21% to 60% risk of a repeat immediate reaction when re-exposed to ionic RCM. When patients with

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Fig. 1. Classification of adverse side effects after RCM administration. (Adapted from Brockow K, Christiansen C, Kanny G, et al. Management of hypersensitivity reactions to iodinated contrast media. Allergy 2005;60:157; with permission.)