

Successful Graded Dose Challenge to Iodixanol Radiocontrast Media in a Patient With Delayed Anaphylaxis to Iohexol

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Gary Soffer, MD¹, Barrie Cohen, MD², Jennifer Toh, MD¹,
Devorah Edelman, MD¹, Karan Garg, MD³, and Sunit Jariwala, MD¹

Abstract

We present a case of an 82-year-old male with known radiocontrast media (RCM) hypersensitivity who was admitted to our hospital with gangrene of his right toe. The plan for revascularization of his lower extremity required an angiogram. This presented a management challenge as the patient had experienced 2 episodes of delayed anaphylaxis to Omnipaque (iohexol) RCM, and based on a literature review, there was no known or established precedent on a safe procedure in these situations. The patient was premedicated and given a graded dose challenge of an alternative RCM (iodixanol) prior to the radiographic study. He was given 1% of the total expected dose 1 hour before to the procedure and an additional 10% for the 30 minutes prior. He was then given the final dose in the operating room. Following angiogram, the patient was monitored for 18 hours in the post-anesthesia care unit, with no adverse reactions. He was placed on a prednisone taper for 1 week, with daily diphenhydramine. The patient remained asymptomatic throughout the hospital course. This novel approach to RCM hypersensitivity management lends itself to a hope that graded dose challenges may play a greater role in the management of these patients.

Keywords

radiocontrast media, graded dose challenge, iodixanol, delayed anaphylaxis

Radiocontrast media (RCM) is known to cause both immediate (<1 hour) and delayed (>1 hour) hypersensitivity reactions. While these reactions are generally mild in nature, approximately 1% to 3% of patients who receive ionic RCM and 0.05% of patients who receive nonionic RCM have severe reactions and most are immediate.^{1,2} Most delayed reactions are mild cutaneous eruptions and rarely anaphylactic. The current management of patients with known RCM hypersensitivity who require RCM studies involves using nonionic and iso-osmolar RCM and premedication with antihistamine and systemic corticosteroids. However, despite these measures, reactions still occur and the fatality rate from RCM is approximately 1 to 2 in 100 000.^{3,4}

It has been previously thought that RCM hypersensitivity was a non-immunoglobulin E-mediated reaction, but recent studies have demonstrated that at least 50% of RCM hypersensitivity reactions are triggered through an immunological mechanism; skin testing may be helpful in selecting a safe product in patients that have previously reacted.⁵ Graded challenges that are commonly performed after negative skin testing for drug testing such as penicillin have been rarely used in the setting of RCM hypersensitivity. We describe a case of delayed anaphylaxis to Omnipaque (iohexol) RCM who tolerated a graded challenge to Visipaque (iodixanol) RCM.

An 82-year-old male with known RCM hypersensitivity and multiple drug allergies was admitted to our hospital with gangrene of his right toe. His past medical history included coronary artery disease requiring a coronary artery bypass graft and 2 stents, cerebrovascular accident, peripheral vascular disease, hypertension, and inflammatory arthropathy treated with oral prednisone 7.5 mg daily for several years. He required an angiogram of the right lower extremity to evaluate the extent of peripheral vascular disease in order to plan for revascularization, and our allergy service was consulted.

Our evaluation revealed that he had 2 hypersensitivity reactions to iohexol RCM in the past. Approximately 2 months prior to admission, he had developed an erythematous and pruritic rash (legs, arms, and back), facial flushing, and nausea

¹Division of Allergy and Immunology, Montefiore Medical Center, Bronx, NY, USA

²Department of Pediatrics, Children's Hospital at Montefiore, Bronx, NY, USA

³Department of Vascular Surgery, Montefiore Medical Center, Bronx, NY, USA

Corresponding Author:

Barrie Cohen, Department of Pediatrics, Children's Hospital at Montefiore, 3415 Bainbridge Avenue, Bronx, NY 10467, USA.

Email: barrcohe@montefiore.org

and vomiting 4 hours following the administration of a high load of iohexol contrast for a cardiac catheterization. Twelve hours following the administration of RCM, his flushing persisted, the rash spread to his abdomen, and he became hypotensive to 75/40 with no changes in electrocardiogram or cardiac enzymes to suggest a cardiac event. A year prior to admission, the patient had experienced similar symptoms several days after his first cardiac stent was placed in the setting of iohexol administration.

We performed skin prick testing to the 2 nonionic, isomolar RCM agents available at our hospital that were adequate for angiogram: iohexol (350 mgI/mL) and iodixanol (320 mgI/mL). Both skin tests were negative with an adequate histamine response. The patient had declined further testing with intradermals but agreed to a graded dose challenge to RCM prior to angiogram. We selected iodixanol as he had previously reacted both times to iohexol, and iodixanol is slightly less osmolar. He was premedicated with intravenous (IV) methylprednisolone 60 mg at 13 hours, 7 hours, and 1 hour prior to challenge and 50 mg of IV diphenhydramine 1 hour prior to the procedure.

Graded dose challenge was performed in the postanesthesia care unit (PACU) and the final dose of iodixanol was given in the operating room (OR) for the angiogram. He was given 1% of the total expected dose of iodixanol (0.15 mL of 320 mgI/mL concentration) 1 hour prior to the procedure and was then monitored for 30 minutes. He then received 10% (1.5 mL) of the total expected dose and monitored for 30 minutes. He was then brought to the OR and was given the final dose of iodixanol (15 mL) for the angiogram. The study required 28 mL of contrast, which was almost double the expected dose. Following the angiogram, the patient was monitored for 18 hours in the PACU, with no adverse reactions. He was placed on a prednisone taper for 1 week, with daily diphenhydramine 50 mg, until reaching his home dose of 7.5 mg. The patient remained asymptomatic throughout the hospital course.

This is the first case report of delayed anaphylaxis from iohexol RCM in a patient who tolerated an alternative RCM (iodixanol) with premedication and a graded dose challenge prior to the radiographic study. Although skin prick testing to the RCM was negative, previous studies have revealed that skin testing does not always accurately predict a hypersensitivity reaction to RCM.⁴⁻⁶ In the past, pretesting with a small dose of RCM was given 2 to 5 minutes before a radiological procedure, although the RCM agent could elicit a hypersensitivity reaction.⁶ Prieto-Garcia et al recently evaluated and skin tested 106 patients with immediate hypersensitivity reactions to RCM. This study identified 11 patients who had positive skin testing to the RCM agent to which they had previously reacted

and received a graded challenge with an alternate RCM (ie, skin test negative to this agent). Five of the 11 patients tolerated the graded challenge, and most reactions were mild and all were immediate.⁷

Radiocontrast media is widely used in diagnostic and therapeutic procedures, and clinicians must be aware of RCM hypersensitivity management strategies. As technology develops, and the use of RCM becomes more prevalent, it is imperative that we find a strategy to overcome hypersensitivities. Providers should recognize that delayed hypersensitivity reactions to RCM can occur and can be as severe as anaphylaxis. Our approach is a novel one, and while it warrants trial on a much larger scale, it lends itself to a hope that graded dose challenges may play a greater role in the management of patients with hypersensitivity reactions to RCM.

Declaration of Conflicting Interests

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References

1. Coleman WP, Ochsner SF, Watson BE. Allergic reactions in 10,000 consecutive intravenous urographies. *Southern Med.* 1964;57(12):1401-1404.
2. Wolf GL, Mishkin MM, Roux SG, et al. Comparison of the rates of adverse drug reactions: ionic contrast agents, ionic agents combined with steroids, and nonionic agents. *Invest Radiol.* 1991; 26(5):404-410.
3. Caro JJ, Trindade E, McGregor M. The risks of death and of severe nonfatal reactions with high- vs low-osmolality contrast media: a meta-analysis. *AJR Am J Roentgenol.* 1991;156(4):825-832.
4. Fischel HW, Doust VL. An evaluation of pretesting in the problem of serious and fatal reactions to excretory urography. *Radiology.* 1972;103(3):497-501.
5. Brockow K, Romano A, Aberer W, et al. Skin testing in patients with hypersensitivity reactions to iodinated contrast media—a European multicenter study. *Allergy.* 2009;64(2):234-241.
6. Yocum MW, Heller AM, Abels RI. Efficacy of intravenous pretesting and antihistamine prophylaxis in radiocontrast media-sensitive patients. *J Allergy Clin Immunol.* 1978;62(5):309-313.
7. Prieto-Garcia A, Tomás M, Pineda R, et al. Skin test-positive immediate hypersensitivity reaction to iodinated contrast media: the role of controlled challenge testing. *J Investig Allergol Clin Immunol.* 2013;23(3):183-189.