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CASE REPORT

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# Successful Desensitization After Iohexol-Induced Anaphylaxis in a Patient with Peripheral Arteriovenous Malformation: A Rare Case Report

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## ABSTRACT

Radiocontrast agents (RCAs) are common triggers for hypersensitivity reactions, often presenting as urticaria, anaphylaxis, or exanthems. This case presents the successful desensitization of a patient requiring endovascular treatment for an arteriovenous malformation (AVM), who had a history of anaphylaxis related to iohexol.

An 18-year-old male patient was diagnosed with an AVM in the popliteal fossa. Grade 3 anaphylaxis was observed during the procedure, necessitating the administration of adrenaline, and the procedure was terminated early. The patient's AVM required endovascular treatment, which required the use of a low dose of iodinated contrast agent. The patient underwent a skin prick test with iohexol (1/1) and an intradermal test, starting with a dilution of 1/1000, followed by dilutions of 1/100 and 1/10, all of which were negative. Due to the lack of alternative contrast agents available in our country, iohexol desensitization was planned for the angiography. A premedication regimen was followed by an 11-step rapid desensitization protocol, and the endovascular treatment procedure was successfully completed under desensitization.

There are a limited number of protocols successfully applied in patients with contrast agent anaphylaxis in the literature, and desensitization protocols for contrast agents have not yet been included in drug allergy guidelines. In this case, successful peripheral angiography was performed following the application of a rapid desensitization protocol with iohexol. Desensitization for iohexol anaphylaxis is uncommon, and more cases are needed to confirm the efficacy of this protocol.

**Keywords:** Anaphylaxis, iohexol desensitization, arteriovenous malformation

## INTRODUCTION

Iohexol is a non-ionic iodinated contrast media (ICM) commonly used in procedures such as computed tomography (CT) and angiography, and the use of contrast media in CT has significantly increased over the years (1). Radiocontrast media (RCM) are frequent triggers of both immediate and non-immediate hypersensitivity reactions, manifesting predominantly as urticaria/anaphylaxis or exanthems, respectively. In the minority of patients with immediate hypersensitivity reactions to RCM, allergy is demonstrated by positive skin tests (2). Desensitization to allergens is a standard preventive measure for anaphylaxis in patients with a history of severe immediate hypersensitivity reactions to a drug, particularly when no therapeutic alternatives are available (3). In vitro studies have demonstrated that desensitization plays a role in preventing mast cell activation by internalizing the FcεRI receptor in IgE-mediated reactions (4). Although the exact pathophysiology of immediate reactions to RCM is not fully understood, a limited number of successful cases of desensitization to RCM have been demonstrated (5-7).

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We present a successful case of desensitization in a patient with anaphylaxis due to iohexol, who required peripheral angiography due to a peripheral arteriovenous malformation. There are only a few documented reports of desensitization for immediate hypersensitivity reactions to iohexol in the literature, and a validated protocol has not yet been published.

## CASE PRESENTATION

An 18-year-old male patient had been presenting to the hospital with complaints of intermittent left leg pain for 8 years. The patient had undergone several contrast-based CT scans using iohexol. Investigations revealed an arteriovenous malformation (AVM) measuring 7 cm in length and 2.5 cm in width, located proximally in the left crus and extending to the popliteal fossa. During the interventional procedure, which involved peripheral angiography and embolization with iohexol, the patient developed redness, shortness of breath, and a drop in peripheral oxygen saturation 20 minutes after the procedure. His oxygen saturation was 80% in room air, with a respiratory rate of 24 breaths per minute, while other vital signs remained normal. Intubation for airway management was not required. Anaphylaxis occurred periprocedurally, necessitating the administration of adrenaline, and the procedure was terminated early. The patient received treatment with intravenous dexamethasone, pheniramine, hydration, inhaled salbutamol, and intramuscular adrenaline. After treatment, his clinical status and vital signs returned to normal within two hours. Blood had not been drawn from the patient for tryptase level at the time of the reaction.

The patient was admitted to the adult allergy clinic 2 months after experiencing anaphylaxis due to iohexol. To rule out other possible causes, latex-specific IgE was tested at 0.01 kU/L (class 0), and chlorhexidine-specific IgE was 0.03 kU/L (class 0), both indicating negative results. The patient's baseline tryptase level was 4.37 µg/L, excluding mast cell disorders. The patient underwent a skin prick test with iohexol (1/1) and an intradermal test starting with a dilution of 1/1000, followed by dilutions of 1/100 and 1/10, all of which were negative. Due to the lack of alternative contrast agents available in our country, testing with an alternative contrast agent could not be performed. According to the Naranjo algorithm, the patient scored 8 points (Table I).

Although the patient's AVM required endovascular treatment and was evaluated using $CO_2$ angiography, the use of a low dose of iodinated contrast agent was essential during the treatment. Due to the unavailability of alternative contrast agents in our country and the patient's previous Grade 3 anaphylactic reaction, the procedure was planned with desensitization. Methylprednisolone 40 mg was administered at 13 hours, 7 hours, and 1 hour prior to the procedure, and pheniramine was given 1 hour before. A rapid desensitization protocol consisting of 11 steps was

**Table I: Naranjo Algorithm Assessment**

| Question | Yes | No | Do Not Know | Score |
|---|---|---|---|---|
| 1. Are there previous conclusive reports on this reaction? | +1 | 0 | 0 | +1 |
| 2. Did the adverse event appear after the suspected drug was administered? | +2 | -1 | 0 | +2 |
| 3. Did the adverse event improve when the drug was discontinued or a specific antagonist was administered? | +1 | 0 | 0 | +1 |
| 4. Did the adverse event reappear when the drug was readministered? | +2 | -1 | 0 | 0 |
| 5. Are there alternative causes that could on their own have caused the reaction? | -1 | +2 | 0 | +2 |
| 6. Did the reaction reappear when a placebo was given? | -1 | +1 | 0 | +1 |
| 7. Was the drug detected in blood or other fluids in concentrations known to be toxic? | +1 | 0 | 0 | 0 |
| 8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased? | +1 | 0 | 0 | 0 |
| 9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure? | +1 | 0 | 0 | 0 |
| 10. Was the adverse event confirmed by any objective evidence? | +1 | 0 | 0 | +1 |
| | | | **Total Score: 8** | |

**Table II: Iohexol Desensitization Protocol (6).**

| Dose no | Dilution | Concentration (mg/ml) | Volume to administer (ml) | Time of administration (min) |
|---|---|---|---|---|
| **1** | 1: 1000 | 0.30 | 5 | 0 |
| **2** | 1: 500 | 0.60 | 5 | 10 |
| **3** | 1: 250 | 1.2 | 5 | 20 |
| **4** | 1: 125 | 2.4 | 5 | 30 |
| **5** | 1: 62.5 | 4.8 | 5 | 40 |
| **6** | 1: 32 | 9.6 | 5 | 50 |
| **7** | 1: 16 | 19.2 | 5 | 60 |
| **8** | 1: 8 | 38.4 | 5 | 70 |
| **9** | 1: 4 | 76.8 | 5 | 80 |
| **10** | 1: 2 | 153.6 | 5 | 110 |
| **11** | 1: 1 | 300 | | |

implemented with premedication (Table II). The first 10 steps of the desensitization process were conducted in the adult allergy clinic, while the 11th step was performed in the angiography unit, after which the patient was taken to the angiographic procedure. The endovascular treatment was successfully completed without any breakthrough reactions. After the endovascular treatment, the patient was observed for 24 hours in the intensive care unit for possible immediate allergic reactions. The patient was discharged without any complications.

## DISCUSSION

Immediate and nonimmediate hypersensitivity reactions to ICM have been reported to occur at a frequency of about 0.5%-3% in patients receiving nonionic ICM (8). These reactions are primarily diagnosed based on clinical findings. In a previous study, positive skin tests (STs) were observed in 26% of patients reporting ICM hypersensitivity reactions; 3% had a positive skin prick test (SPT) and 25% had a positive intradermal test (IDT) (1). A negative skin test for iodinated (radio-)contrast media does not exclude hypersensitivity in all patients experiencing ICM reactions (9,10). In our case, the history strongly suggested a reaction to the contrast agent despite negative skin tests, and alternative causes were excluded.

According to the guidelines, an alternative ICM is recommended if the culprit ICM is known in cases of moderate to severe immediate hypersensitivity reactions (fully developed anaphylaxis) (8). Recent guidelines do not recommend specific approaches for verified contrast medium hypersensitivity with immediate reactions when no alternative contrast agent is available. Additionally, no established protocol for contrast medium desensitization exists (8,11). Rare desensitization procedures have been reported based on case studies (3). In a previous study, iohexol desensitization was successfully applied to one patient (6). Saad et al. adapted an initial protocol for desensitization related to iodixanol allergy for use with iohexol (5,6). In the current case, we considered this protocol in managing our patient. Following the implementation of this protocol, the patient was able to undergo peripheral angiography.

This case presents certain limitations, including the unavailability of tryptase level measurement during the reaction and the absence of a provocation test, despite a clear clinical history suggestive of hypersensitivity to the contrast agent. Additionally, testing with alternative contrast agents could not be conducted due to the unavailability of alternative contrast media agents in our country. Desensitization could enable the use of radiocontrast media in urgent circumstances, such as those necessitating angiography (3). Our case is significant in demonstrating the successful application of iohexol desensitization in angiography. Since contrast media desensitization is rare, more cases need to be reported to confirm the desensitization protocol and to determine when to continue using iohexol.

## CONCLUSION

A case of severe anaphylaxis associated with iohexol was successfully managed, allowing the completion of endovascular treatment. This case is significant in confirming the effectiveness of the iohexol desensitization protocol previously used in a patient with iohexol hypersensitivity reactions.

**Conflict of Interest**

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**Author Contributions**

Hazal Kayıkçı contributed to the design and implementation of the case, to the analysis of the results, and to the writing of the manuscript. Melek Cihanbeylerden, Çise Tüccar, Ayşegül Pehlivanlar Ustaoğlu, Ebru Damadoğlu, Gül Karakaya and A. Fuat Kalyoncu contributed to the final version of the manuscript.

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