case report

Successful desensitization to radiocontrast media in two high-risk cardiac patients

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Hypersensitivity reactions to radiocontrast media (RCM) are common and in severe cases may present a challenge for treating physician in cases when premedication fails or the patient presents with severe comorbidities. We describe two cases in need of radiocontrast media after a severe reaction on previous exposure to iohexol. One presented anaphylactic reaction to RCM despite premedication and another presented with angina. Both cases were treated with a desensitization protocol to iodixanol. In conclusion, desensitization to radiocontrast media may be considered in patients with previously unsuccessful premedication and/or severe acute comorbidities.

SIMILAR CASES PUBLISHED: 1[4]

Hypersensitivity reactions to iodinated radiocontrast media (RCM) are common in daily practice. Reactions to RCM can be related to their chemical properties and are therefore dose-dependent (chemotoxic) or related to mast cell release of mediators (anaphylaxis IgE/non-IgE).[1] While American guidelines consider all reactions as anaphylaxis IgE/non-IgE, European studies show a possible role for Ig-E and skin testing.[1]

Management of patients with a previous anaphylactic reaction to RCM includes pretreatment regimes that may reduce, although not fully prevent severe reactions.[1,2] Rapid desensitization is a procedure that allows the gradual reintroduction of first-line medications to patients by providing a temporary tolerance to the drug. This is used solely in cases where no alternative of similar efficacy is available. This procedure has been proven effective for Ig-E mediated reactions where in vitro studies have determined a role for desensitization in avoidance of FcεRI receptor internalization and therefore mast cell activation.[3] Although the exact pathophysiology of the immediate type reaction to RCM is not clearly understood as an IgE-mediated reactions, few successful examples of desensitization to RCM have been published.[4]

CASE 1

A 79-year-old non-atopic middle-eastern female was referred to the allergy department for evaluation of an anaphylactic history to radiocontrast media (RCM). History was significant for metastatic endometrial carcinoma under treatment with taxol, carboplatin and radiotherapy, and severe aortic stenosis requiring valve replacement. Despite several asymptomatic previous exposures to RCM, five months prior she underwent a routine CT chest scan and within two minutes of the RCM, iohexol infusion, presented with sudden of shortness of breath, wheezing, diffuse flushing and urticaria. She received intravenous fluids and hydrocortisone, oxygen therapy and a bronchodilator through a nebulizer. The reaction resolved within few hours. Three months later, a second CT scan of the chest was planned, and the patient was premedicated with oral prednisolone 60 mg a day for two days, then 20 mg 1 hour prior to the procedure, along with ranitidine 150 mg, and cetirizine 10 mg. Within two minutes of RCM infusion (50 mL iohexol), she presented shortness of breath and wheezing with sudden decrease of O_2 saturation to 87%, increased heart rate to 134 bpm and blood pressure of 156/74 mm Hg (from previous 124/48) along with

dizziness and flushing in the back and shoulders that required admission to the intensive care unit and ventilation via continuous positive airway pressure (CPAP). She was resuscitated with intravenous hydrocortisone 200 mg, oxygen therapy and nebulized bronchodilator and then discharged from the intensive care unit after 2 days. Serum tryptase was not taken during any of the reactions. Two months later, her cardiac status progressed, and she was referred for evaluation of RCM hypersensitivity prior to a transcatheter aortic valve implantation (TAVI), and coronary angiography, requiring about 300 mL of RCM administration. Because the patient had failed premedication, desensitization was proposed and a protocol was generated.

CASE 2

A 66-year-old middle-eastern female was referred to the allergy department for evaluation of an anaphylactic history to RCM. History was significant for bronchial asthma under control, chronic urticaria, type II diabetes, and hypertension. Ten years before, a coronary angiography was performed with iohexol, and presented after 2 hours with flushing, facial angioedema, throat tightness, and shortness of breath followed by loss of consciousness which was treated in the emergency department with fluid therapy, bronchodilators and corticosteroids. At the time of referral, the patient was in need of new coronary angiography due to Canadian Cardiovascular Society class IV angina. Due to the severity of the previous reaction in a symptomatic patient requiring urgent coronary angiography, desensitization was proposed and a protocol was generated.

Desensitization

Both patients were informed and signed consent for the desensitization procedure. The procedure was done in the intensive care unit, 4 hours before coronary angiography and TAVI procedures. In both cases, premedication was given after consultation with treating cardiologist and included an oral prednisolone 50 mg, ranitidine 150 mg and cetirizine 10 mg tablets at 24, 13, 7, and 1 hour before the procedure, montelukast 10 mg at 24 hour, and 1 hour before the procedure. A skin prick test with undiluted iohexol (Omnipaque GE healthcare, Cork, Ireland), and iodixanol (Vispaque, GE healthcare, Cork, Ireland) was negative as well as intradermal testing with 1/10 dilution. The desensitization protocol was performed as shown in **Table 1**. Neither patient reported symptoms during the entire protocol receiving a total of 16.67 grams iodixanol (320 mg/mL) with stable vital signs. In case 1 surgery was delayed for 4 hours and the patient received 320 mL of iodixanol in several boluses for a total of 370 mL. The aortic valve was successfully replaced and the patient was extubated 8 hours later. In case 2 coronary angiography was performed after 30 minutes and the patient received 300 mL of iodixanol with stent placement. Tryptase was drawn before the desensitization protocol and additional samples were taken in case 1 after 30 minutes, 5 hours and 8 hours, and in case 2 after 1 hour, without significant changes for both patients. Repeated skin testing 4 months after desensitization with 1/10 and 1/1 concentration to iodixanol and iohexol was negative.

DISCUSSION

RCM hypersensitivity reactions can be immediate or a delayed. Following the introduction of nonionic low-osmolarity RCM in the 1970s, the rates of reactions to RCM with non-ionic low-osmolar agents use have been reduced from 3.8-12.7% to 0.7-3.1%, and ten-fold reductions from 0.1-0.4% with severe reactions, but reactions including death are still reported.[2,5]

We describe one case that, where despite premedication, the patient presented with anaphylactic reactions to RCM and one case of a patient with angina present at rest in need of RCM after anaphylaxis. Both patients tolerated a successful desensitization protocol, and underwent a coronary angiogreaphy, followed by transaortic valve implantation surgery or stent with no complications.

Reports of positive skin, basophil activation tests (BAT), RCM specific Ig-E and mast cell release of mediators like histamine and tryptase support a role for Ig-E mediated mechanisms in some patients.[2] An in vivo role for complement activation and bradykinin activation remains unclear. The pathophysiologic mechanisms may resemble the ones involved in the reactions following administration of taxanes, where a mechanism remains to be established and skin testing shows controversial results.[6] Recently, there was a report of an 81-year-old female who presented with anaphylaxis to iodixanol despite intensive pretreatment. She was desensitized to iodixanol in 1 hour and 50 minutes via an 11-step doubling dose protocol up to a final step of 5 mL undiluted iodixanol.[4]

Rapid desensitization is a procedure that can be used to provide a temporary tolerance to a first-line drug when no alternative is available. There is high cross-reactivity between different types of RCM agents in patients presenting with anaphylaxis, and a positive skin test.[7] In a recent meta-analysis,[8] cross reactivity between iohexol and iodixanol was reported as 10% (5-23%) based on results of skin test-positive patients, but data is scarce regarding cross-reactivity between

Table 1. Iodixanol desensitization protocol.

Step	Solution	Rate (mL/hr)	Time (min)	Volume (mL)	Dose step (mg)	Cumulative (mg)
1	1	2.5	15	0.625	0.104	0.104
2	1	5	15	1.25	0.208	0.312
3	1	10	15	2.5	0.416	0.729
4	1	20	15	5	0.833	1.562
5	2	2.5	15	0.625	2.082	3.644
6	2	5	15	1.25	4.164	7.808
7	2	10	15	2.5	8.329	16.137
8	2	20	15	5	16.658	32.794
9	3	5	15	1.25	41.644	74.438
10	3	10	15	2.5	83.288	157.726
11	3	20	15	5	166.575	324.301
12	3	40	15	10	333.150	657.451
13	4	10	15	2.5	800.002	1457.453
14	4	20	15	5	1600.005	3057.458
15	4	40	15	10	3200.010	6257.468
16	4	80	24.3	32.5	10400.032	16657.500

Solution 1: 0.167 mg/mL; Solution 2: 3.332 mg/mL; Solution 3: 33.315 mg/mL; Solution 4: undiluted iodixanol (320 mg/mL)

iohexol and iodixanol in patients with negative skin testing. Therefore, it is difficult to determine the role of performing desensitization with iodixanol instead of the initial culprit agent, iohexol. Despite incomplete understanding of the mechanisms involved in RCM anaphylactic reactions, desensitization can be considered where no alternative is available to the use of RCM.

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