Severe anaphylaxis following administration of radiocontrast in patient undergoing coronary intervention

Bishal KC1, Samir Gautam1, Sachin Dhungel1, Mazhar Khan1, Binesh Shakya2
1 Department of Cardiology, Gautam Buddha Community Heart Hospital
2 Department of Anesthesiology, Gautam Buddha Community Heart Hospital

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Abstract
Radiocontrast material is among the common drugs causing allergic reaction. Mostly it is well tolerated. The symptoms range from mild with urticaria to fatal anaphylaxis, developing rapidly. Anaphylaxis is the most severe form of radiocontrast media (RCM) induced hypersensitivity reaction. With more use of diagnostic and therapeutic procedure, the use of the radiocontrast media is increasing. We report here two cases of severe anaphylactic reaction that occurred during the coronary intervention for myocardial infarction.

Introduction:
Recent advances in medicine have led to various diagnostic and therapeutic techniques and most of these requires frequent use of radiocontrast media. These agents in interventional cardiology can localize and characterize the coronary lesion helping in further management of the patient. The use of these agents though comes at a price of various side effects including the hypersensitivity. Mild reaction to contrast media is common with patient complaining of chills and urticaria however serve anaphylaxis with shock occurs in less than one percent1.

The precise mechanism is still debatable with both immunological and non-immunological factors coming into play. It could be due to the release of the histamine from the mast cells or IgE mediated reaction. During the life-threatening situations, it becomes

*Corresponding Author:
Bishal KC
Department of Cardiology,
Gautam Buddha Community Heart Hospital
Email: bishalk@gmail.com
ORICID ID No: 0000-0002-9028-8209
impossible to identify the mechanism and also the subsequent management does not depend on the mechanism. The adverse reactions are not so uncommon as millions application of RCM occurs worldwide every year. 

CASE 1:
A 76 years old male presented in emergency with complaint of central chest pain of 18 hours duration with radiation to left arm and jaw. He was hypertensive with no other risk factors. On examination his vitals were stable with crepitations on bibasal lung fields. His ECG in emergency revealed ST segment depression in the anterior leads suggestive of posterior wall MI.

His Investigations were:
- RBS: 104mg/dl
- Serum creatinine: 0.9mg/dl
- Troponin I: positive
- ECG: normal sinus rhythm with ST segment depression on V1-V5, Fig 1.
- ECHO: hypokinetic inferior and inferolateral region, left ventricular ejection fraction 40-45%  

He immediately underwent coronary angiogram which revealed total occlusion of mid left circumflex artery Fig 2. He was then planned for coronary angioplasty. Subsequently the procedure started with routine wiring of the lesion with BMW guidewire, predilatation was done and stenting was completed with DES. Fig 3.

To begin with he was in stable condition with good orientation. His vitals were:
- Blood Pressure: 100/70mmHg
- Heart rate: 80/minute
- SpO2: 95%

After few shots of contrast during coronary angiogram, he became restless and agitated. He persistently tried to get up with his speech becoming more incoherent and he refused to follow the command. After balloon dilatation of the coronary lesion, he was much violent and started resisting the procedure. His vitals were:
- O2 saturation: 92%
- Pulse: 130/min
- BP: 80/60 mmHg

After that the stent was deployed quickly. Then he woke up violently. He was cyanosed and his SpO2 was 85%. He had this suffocating feeling and was to holding his neck trying hard to inspire with noisy breathing sounds.

On further examination of chest, breath sounds were barely audible. So provisional diagnosis of contrast media induced severe anaphylactic shock was made. He was given IM epinephrine and the patient was shifted to CCU. As his condition deteriorated, he was intubated with intravenous midazolam and succinylcholine and kept in mechanical ventilation. He developed ventricular tachycardia and immediate DC shock of 200joules was given twice, which reverted to sinus tachycardia. He was started on inotropic supports.

Next day his vitals stabilized and he was finally extubated.

Total time for development of symptoms: 40 minutes
- Type of contrast: iohexol
- Volume of contrast: 100ml

CASE 2:
A 57 years gentleman presented with complaints of central chest pain for four days in OPD. The pain was moderate to severe radiating to let arm and jaw and was associated with profuse sweating. He was chronic smoker and took occasional alcohol.
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On examination his vitals were stable and the systemic examination revealed normal findings.

His Investigations were:
RBS: 109mg/dl
Serum creatinine: 1.4mg/dl
Troponin I positive
ECG: normal
ECHO: normal

So, a diagnosis of NSTEMI was made and was admitted. Next day he underwent coronary angiogram, which revealed total occlusion of mid left circumflex artery. Subsequently angioplasty with stenting was planned.

Suddenly he became agitated and increasingly confused. He became cyanosed and his saturation dropped to 80%. He developed diffuse wheeze. The diagnosis of contrast media induced allergic reaction was made. The procedure was stopped and the patient was shifted to CICU. There he developed silent chest. Immediate artificial manual breathing was started and he was sedated. His condition gradually improved with the oxygen saturation gradually improved.

Total time for development of symptoms: 25 minutes
Type of contrast: iohexol
Volume of contrast: 60ml

**DISCUSSION:**
Chronologically reactions to RCM occurs as an immediate hypersensitivity (IHR) reaction occurring within 1 hour like in our cases or non-immediate hypersensitivity reactions (NIHR) occurring > 6 h, mostly 1–3 days and up to 10 days after RCM application 1.

Clinical manifestations of IHR differ from NIHR with IHR symptoms mostly cutaneous to full blown anaphylaxis while NIHR mostly presents with exanthems, mostly maculopapular exanthems6.

Among the various allergic manifestations of RCM use, anaphylaxis is the most serious form and can be life threatening. World Allergy Organization (WAO) define anaphylaxis as “a severe, life-threatening generalized or systemic hypersensitivity reaction”4.

The classical mechanism of immune mediated HSN reaction is IgE mediated reaction but usually the IgE response occurs after the mechanism of sensitization which usually occurs after the prior exposure to the known allergen and during the second exposure there is hyper response causing anaphylaxis.

In this RCM induced reaction the mast cell degranulation can also play significant role which does not requires sensitization with prior exposure so the previous exposure to contrast media is not necessary for this. Past studies have also supported that around 90% of cases the histamine release was the major cause for the anaphylaxis and the IgE mediated mechanism in minority of case 1.

The incidence of RCM induced allergic reaction varies and depends upon various factors such as type of contrast, timing of onset, use of premedication. The occurrence of mild IHR to new modern nonionic low osmolar RCM is around 0.5-2% and severe reaction occur in about 0.02–0.04%6.

Ionic monomeric contrast media are more likely to be associated with adverse reactions and nowadays has been withdrawn from the markets6.

The major risk factor for development of RCM induced allergic reaction both IHR and NIHR is the prior exposure to the radiocontrast. In one of the case control studies done showed that the IHR to RCM was less frequently observed after intra-arterial administration that with other modes and they reason that it could be related to the delayed and diluted arrival of the media to the lungs2.

**Clinical manifestation:**
The clinical manifestations range from mild urticaria to fatal anaphylactic shock.

The fatal reaction is rare and the fatality is about 1 to 2 per 100,000 procedures

Anaphylaxis mostly presents as a cutaneous reaction with urticaria and mucosal lesion however can affect any organ system most notably the lungs are affected with bronchospasm occurring initially and can lead to silent chest if not addressed initially and quickly as both the patients developed. The further progression leads to the development of hypotension known as anaphylactic shock which has high mortality as one of our patients did develop. Various arrythmias are also common and our patient developed ventricular tachycardia (VT) which could also be because of prolonged hypoxia. The VT was reverted with DC shock twice.

**Assessing the severity:**
The severity of anaphylaxis can be classified according to the clinical presentation of the patients which are as follows:

- **Mild**
  - Reaction is self–limited, does not progress, and rarely requires treatment
  - Limited pruritus or urticaria, localized edema of the skin
  - Limited itchy/scratchy throat
  - Nasal congestion/rhinorrhea/sneezing, and/or conjunctivitis

- **Moderate**
  - Reaction usually requires treatment and may progress to a severe reaction if untreated.

- **Severe**
  - Reaction is life-threatening and can cause significant morbidity

**Moderate and severe reaction:**
- Widespread pruritus or urticaria, or diffuse skin erythema
- Facial edema (moderate - without dyspnea, severe - with dyspnea)
- Throat tightness or hoarseness (moderate - without dyspnea, severe - with dyspnea)
- Wheezing/bronchospasm/cough (moderate - minor or no hypoxia, severe - with hypoxia)
- Anaphylactic shock (hypotension plus tachycardia) in severe reactions

**Management:**
Management depends upon the clinical scenario of the patient and the severity of the patients.
UNRESPONSIVE:
An unresponsive patient should be resuscitated according to the ACLS guidelines.

MODERATE OR SEVERE reaction:
The steps in the management are as follows:

1. Stop the administration of contrast media
2. Call for help
3. Initiate oxygen
4. IV access if not in place already
5. Continuous log of all intervention and medication of the patients
6. Keep the patient flat
7. Commence CPR if required
8. Epinephrine administration
   • There is no absolute contraindication for the use of epinephrine in emergency situation
   • It can be given in patients with severe respiratory symptoms like hoarseness of voice, stridor or in case of anaphylactic shock
   • Intramuscular route is preferred over IV route as this is associated with fewer dosing errors and cardiovascular complication
   • Can be repeated 5-15 minutes depending upon the severity
   • In adults and adolescents >25kg, IM 0.3ml epinephrine drawn up at 1mg/ml is given with preferred site over the anterolateral thigh
9. Hypotension and tachycardia
   • Immediate administration of epinephrine
   • Administration of 1-2 liters of normal saline as fast as possible
10. Laryngospasm
    • Immediate epinephrine
11. Bronchospasm
    • Immediate epinephrine
    • Inhaled beta 2 agonist such as albuterol via metered dose inhaler or nebulization by face mask

Conclusion:
This case report highlights the fact that we must be aware of all the adverse outcomes during any intervention involving the radiocontrast media including life threatening anaphylactic shock. This can happen all of a sudden in patient without any history of allergic reaction or any prior exposure to the offending agent. Appropriate identification and management will certainly improve outcome and can be lifesaving in emergency situation. We must be vigilant during the procedure requiring RCM and all possible emergency drugs must be kept ready for the emergent use. Those patients who had the reaction are at increased risk almost five-fold in next exposure so must be well documented and written in patient discharge. Unfortunately, techniques such as skin sensitivity test prior to the use of RCM has minimal role.

Conflict of interest:
The authors declare no conflicts of interest regarding the publication of this paper.

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