

Hospital Drug Allergy & Intraoperative Anaphylaxis: A Challenging Case

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Outline

- Case HPI
- Introduction
- Background
- Case Presentation
- Discussion
- Conclusion

HPI

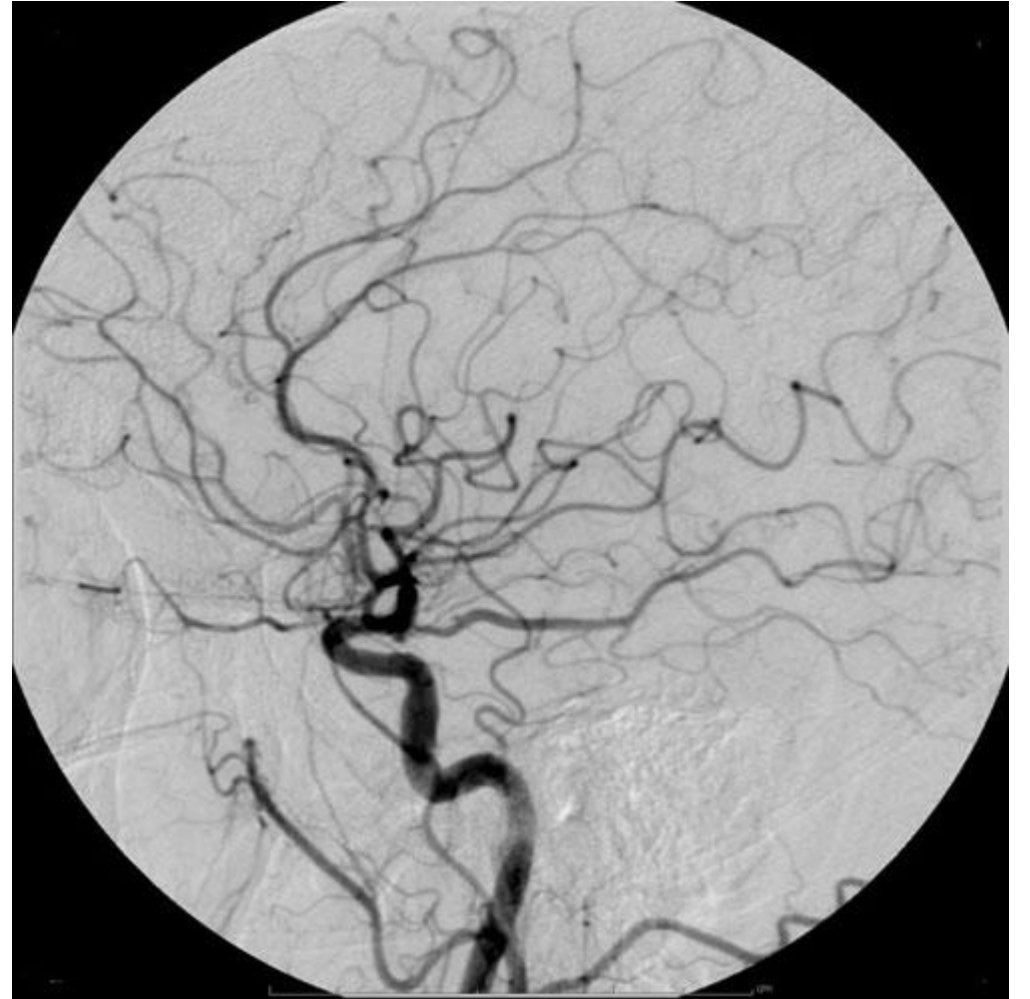
- 67 y/o male with history of non-obstructive coronary artery disease, pacemaker placement for complete heart block, asthma and bladder cancer. Required urgent heart catheterization, however was found to have significant history of allergic reaction to contrast media despite pre treatment.

Introduction

- 70 million diagnostic radiographic examinations using contrast per year in world
- 10 million in US
- Allergic reaction to contrast media is a frequently reported complication of coronary angiography

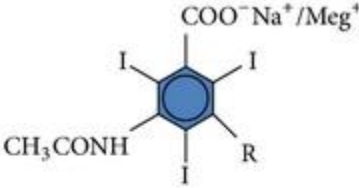
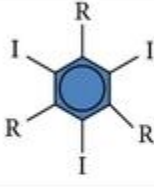
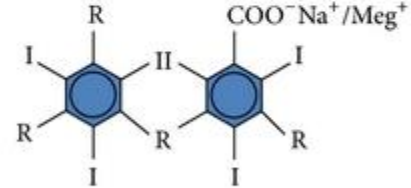
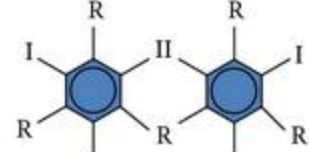
RCM classification

- Charge of the iodinated molecule
 - Ionic
 - nonionic
- Molecular structure
 - Monomeric
 - dimeric
- Osmolality of the injected prep
 - Hyperosmol >1400 mosm/kg
 - Low osmol 500-900
 - iso-osmol 290



Based on iodinated molecule

- Ionic monomers
 - Highest osmolality
 - Used mostly in extravascular procedure
 - Cheap
- Ionic dimer
 - Ioxaglate only available in US
 - 600 mosm/kg
- Nonionic monomers
 - Second generation agents
 - Low osmolality, 500-850
- Nonionic dimer
 - Iso-osmolar, 290
 - As with lowest rates of immediate reactions
 - Most expensive

Molecular structure	Era	Examples	Comment
	1950s	Ionic monomer Diatrizoate Iothalamate	High osmolality, 5-8x blood
	1980s	Nonionic monomer Iopamidol Iohexol Ioversol	Low osmolality, 2-3x blood, improved hydrophilicity
	1980s	Ionic dimer Ioxaglate	Low osmolality, ~2x blood
	1990s	Nonionic dimer Iodixanol (iotrolan)	Isoosmolality Osmolality = blood

Types of reactions

- Mild to moderate immediate hypersensitivity
 - 5-13% occur with ionic high osmolar
- Life threatening
 - 0.04-0.22 % with ionic hyperosmolar
 - 0.004%-0.04% with nonionic low osmolarity
 - No difference in mortality

Symptoms

Mild	Moderate	Severe
Self-limited without evidence of progression	Reactions which require treatment but are not immediately life-threatening	Life-threatening with more severe signs or symptoms
<ul style="list-style-type: none">• Nausea/vomiting• Altered taste• Sweats/Cough• Itching/Rash/Hives• Warmth (heat)• Pallor• Nasal stuffiness/Headache• Flushing /Swelling• Dizziness• Chills• Anxiety/Shaking	<ul style="list-style-type: none">• Tachycardia/bradycardia• Hypotension• Bronchospasm/Dyspnea/wheezing• Laryngeal edema• Pronounced cutaneous• Pulmonary edema• Hypertension	<ul style="list-style-type: none">• Laryngeal edema• Profound hypotension• Unresponsiveness (severe or progressive)• Convulsions• Cardiopulmonary arrest• Arrhythmias

Risk Factors

- Prior history
- Persistent Asthma
- Female Sex
- Atopy



**CONTRAST
ALLERGY**



Myth: Correlation of iodine sensitivity in seafood rich in iodine is related to iodine contrast allergy

- Schabelman, in 2010 debunked this myth showing:
 - Risk of reaction in patients with a seafood allergy is similar to that in patients with other food allergies or asthma
 - Allergy to shellfish, in particular, do not increase the risk of reaction to intravenous contrast any more that of other allergies
 - Also these patients would tolerating iodine-containing surgical scrubs



Case

- 67 Year old male
- History of:
 - Non-obstructive Coronary Artery Disease (CAD)
 - Pacemaker for Complete heart block
 - Asthma
 - Bladder Cancer
- Patient noted transient chest pain following a planned cystoscopy/retrograde pyelogram

Case continued

- Electrocardiogram (ECG) remained unchanged from baseline
- 1st Troponin was 0.18, peak 0.2, started on beta-blocker and statin
- Previous coronary angiogram two years prior noted 50% stenosis of mild left anterior descending artery (LAD)
- Urgent revascularization was scheduled for the next morning.....

Problem: Patient with History of Contrast Allergy

- 1st episode two years prior: Patient had Nausea and an erythematous, pruritic rash to IV contrast for a CT scan
- 2nd episode one year after 1st reaction: Patient was pretreated for contrast allergy with:
 - Prednisone 50mg (13, 7 and 1 hour prior to coronary angiography)
 - Diphenhydramine 1 hour prior to procedure
 - Allergic reaction was noted to have more severe nausea, pruritus, and developed bullae. Admitted to ICU for 2 days
- 3rd episode about 6 months after 2nd reaction:
 - CT scan of abdomen

Desensitization to IV contrast – When Pretreatment Fails.

- Non-ionic, iso-osmolar contrast helps to decrease the risk of allergic reaction
 - Visipaque is currently the best choice
- Patient still undergoes pretreatment with prednisone, diphenhydramine and ranitidine prior to starting desensitization
 - Epinephrine and glucagon must be at bedside at during desensitization
 - IM epinephrine is preferred over IV

Desensitization Protocol

- Visipaque every 10 minute with two additional dilutions from the published starting point.
- Patient started to develop pruritus on the 3rd dose, resolved with IV Benadryl
- 4th dose, dry staccato cough and return of pruritus
 - IM epinephrine, IV methyl prednisone and diphenhydramine
 - Repeat 3rd and 4th doses after resolution of anaphylaxis
- 30 minutes till completion of desensitization

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- 30 minutes till completion of desensitization
 - Cath lab calls: will not be ready for the patient for another hour at least

What to do?

- No study has ever looked at how long contrast desensitization's will last. All procedures completed within 30 minutes of desensitization
- Visipaque's half life is 2 hours, with peak time of 2 minutes
- We are almost at full concentration contrast

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- Visipaque's half life is 2 hours, with peak time of 2 minutes
- We are almost at full concentration contrast
- There is a max daily dose of Visipaque: We used about half of it already and the cath lab needs to use Visipaque for procedure.

Solution

- Currently on dose 11 of 13. Halted advancement.
- Returned to dose 4, slowed down dosing to every 15 minutes
- Cath. Lab ready about 1.5 hours later. Resumed advancement, going straight to dose 12.
- Last dose given in the cath. Lab

Outcome

- Found severe stenosis of the LAD
- Successfully underwent Percutaneous coronary intervention with a drug eluding stent (DES)
- No complications occurred during the procedure and he was symptom free the next day

Discussion

- 2 types of contrast media exist, both of which are associated with a risk of allergic reactions
- 2 Types of reactions are possible
 - Ionic
 - Nonionic

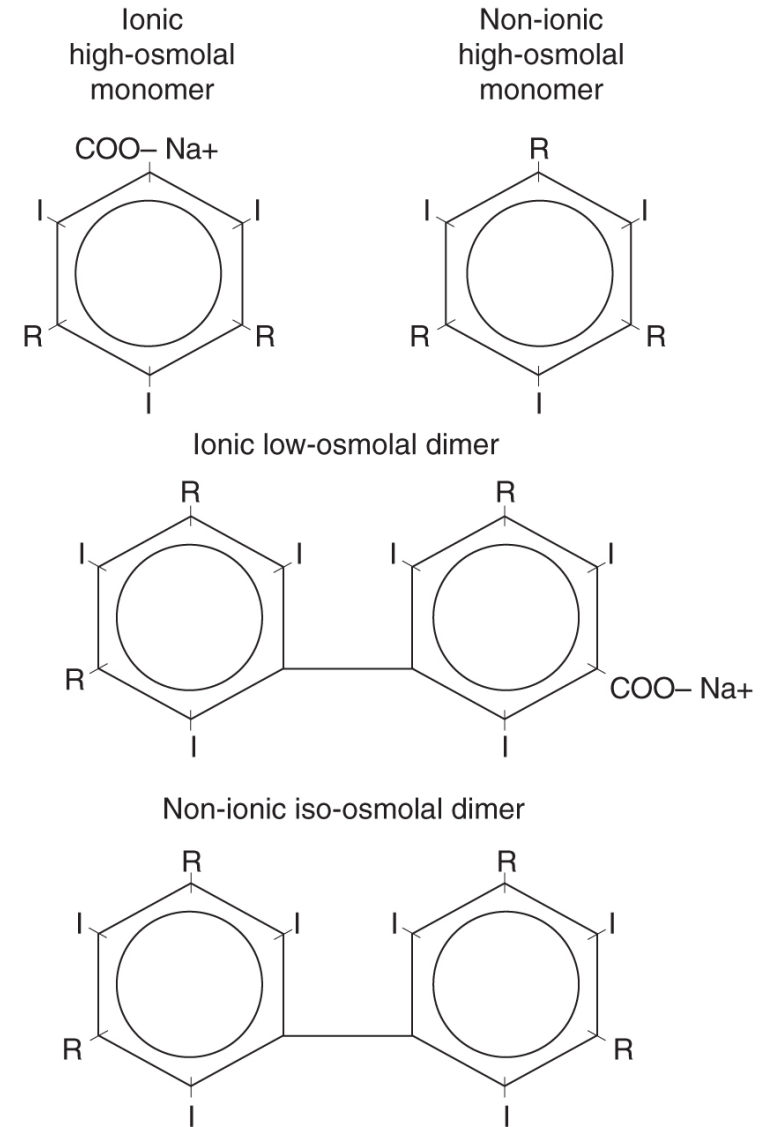


Figure 2. Molecular structure and ionicity of iodinated contrast media.

Iodinated Contrast Media – 2 Types of Reactions

Chemotoxic

- Symptoms: warmth, flushing, vasovagal
- Reaction influenced by **properties** of contrast such as **osmolality**, infusion **rate**
- **Directly dependent** on dose & concentration

Anaphylactoid (non-IgE mediated)

- **Mimics** allergic reaction, marked with nausea, vomiting, rash, hives, bronchial/laryngeal spasm, hypotension, shock
- **Independent** of dose & concentration of contrast **above threshold**
- MOA unclear:
 - ? Contrast may directly activate basophils/mast cells → release serotonin/ cytokines
 - ? Activation of complement/ coagulation/ fibrinolytic cascades → release of mediators

Contrast Agents - Review

IONIC

- High Osmolality (Higher risk of complications)
 - Diatrizoate sodium (Hypaque)
 - Iothalamate meglumine (Conray)

NON-IONIC

- Low Osmolality (Lower risk of complications)
 - Gadodiamide (Omniscan)
 - Iopamidol (Isovue)
 - Iopromide (Ultravist)
 - Ioversol (Optiray)
 - Iodixanol (Visapaque)
 - *Iso-osmolar*

Conclusions

- Contrast is used to evaluate the anatomy & pathology of the coronary vessels
- Complications with contrast used for catheterization are 0.23%
 - Mortality is 1/ 55,000
- Patients with known contrast allergy are at increased risk for repeat reactions
- Several other risk factors for contrast reactions exist, but the biggest is **HISTORY** of prior reaction
- Risks minimized with **nonionic contrast**, **low osmolar** contrast and **pretreating** with steroids, H1 & H2 blockers
 - Breakthrough symptoms still possible – not 100% effective

Conclusions

- Graduated exposure of the allergen can create a temporary state of tolerance to the agent → this is the definition of desensitization
 - Cannot be used for STEMI – takes too long
 - Can be used for NSTEMI patients who have a contrast allergy in need of urgent (vs emergent) PCI
 - Incremental doses given, side effects controlled with steroids, epi and H1/2 blockers in a controlled setting
 - Patients who undergo desensitization tend to tolerate contrast media without major adverse events
 - Desensitization is an underutilized process when it comes to contrast allergy

Summary

- Rapid contrast desensitization should be considered as a strategy in patients with **known** severe contrast allergy, or **continued breakthrough reactions**, despite premedication, who require IV contrast media for **non-emergent** therapeutic or diagnostic interventions.

Thank you!