Clinical Pharmacology & Toxicology Pearl of the Week

~ Life-threatening Contrast Allergy ~

Case:

- ✓ A 63-year-old female with a history of hypertension, dyslipidemia and type 2 diabetes presented to hospital via EMS with 2 hours of retrosternal chest pain. The pain started while washing dishes at home and was associated with nausea and diaphoresis. Her ECG showed deep, inverted symmetrical T-waves in V1-V4. Her initial troponin was 423.
- ✓ Cardiology was consulted and the patient was admitted for urgent revascularization for refractory chest pain, however on further assessment she describes a history of anaphylaxis to IV contrast approximately 2-3 years ago.
- ✓ A risk-benefit analysis was performed to determine if the patient could safely undergo PCI.

Background:

- ✓ The rate of adverse reactions generally decreases in concert with osmolality. Ionic, high-osmolar contrast (e.g. Isopaque) is associated with a 15% incidence of adverse events, whereas low-osmolar contrast (e.g. Omnipaque) is associated with a 3% incidence. Adverse reactions related to non-ionic contrast media are estimated at 5-10%.
- ✓ The biggest risk factor for an adverse reaction to contrast media is a prior reaction. However, increased risk is associated with higher volumes (>100mL), intraarterial administration and patients with atopy and asthma.
- ✓ Patients with active malignancy are also at increased risk due to increased circulating histamine. Those with multiple myeloma are at increased risk because of interactions between contrast media and free light chains.
- ✓ Adverse reactions may be predictable and dose dependent (type A) or unpredictable and independent of dose (type B), these are also known as hypersensitivity reactions.
- ✓ The mechanism of contrast allergy is poorly understood with only a small minority being attributed to IgE mediated mechanisms.
- ✓ Non-IgE mediated pathways can produce histamine release and cause anaphylactoid-like reactions.

Clinical features:

- ✓ Immediate hypersensitivity reactions occur within one hour of administration. However, reactions can occur several hours to days after exposure.
- ✓ Reactions may range from mild to severe or life-threatening and are outlined in Table 1.

Table 1
A summary of mild, moderate, and serious anaphylactoid and nonanaphylactoid reactions [7]

Severity	Type	Reaction
Mild	Anaphylactoid	Limited urticaria/pruritus, limited cutaneous oedema, limited itchy/scatchy throat, nasal congestion, sneezing, conjunctivitis, rhinorrhea
	Nonanaphylactoid	Limited nausea/vomiting, flushing/warmth/chills, headache, dizziness, anxiety, altered taste, mild hypertension, self-limited vasovagal reactions
Moderate	Anaphylactoid	Diffuse urticaria/pruritus, diffuse erythema with stable vitals, facial oedema without dyspnea, throat tightness or hoarseness without dyspnea, wheezing/bronchospasm, mild or no hypoxia
	Nonanaphylactoid	Continuous nausea/vomiting, hypertensive urgency, isolated chest pain, vasovagal reaction reaction that requires and responds to treatment
Severe	Anaphylactoid	Diffuse oedema, facial oedema with dyspnea, diffuse erythema with hypotension, laryngeal oedema with stridor and/or hypoxia, wheezing/bronchospasm, significant hypoxia, anaphylactic shock (hypotension with tachycardia)
	Nonanaphylactoid	Vasovagal reacting resistant to treatment, arrhythmia, convulsions, seizures, hypertensive emergency

Morzycki et al. *Canadian Association of Radiologists 2017*

Management:

- ✓ Prophylactic antihistamine and steroid administration reduce the risk of anaphylaxis and anaphylactoid reactions.
- ✓ The most widely used premedication regimen involves prednisone 50mg given orally at both 13h and one hour before contrast administration with diphenhydramine 50mg IV or IM also administered one hour prior to imaging.
- ✓ Shortening the interval between corticosteroid administration to 5 hours and one hour before contrast administration is not inferior to 13-hour protocols and may improve time to diagnosis and shorten time in the emergency department.
- ✓ Rapid IV desensitization protocols which introduce escalating increments of contrast media have been used in patients with refractory anaphylactoid reactions despite premedication protocols. This should be performed in consultation with expert advice. One example of a rapid desensitization regimen is described in the Figure below.
- ✓ If a desensitization protocol is used, it is typically effective for 24 to 48 hours and patients should receive repeat desensitization prior to subsequent exposures.
- ✓ Reactions should be managed according to severity. Mild reactions can be managed with antihistamines orally or intravenously, while severe reactions may require the addition of epinephrine, steroids, and close monitoring.

Table 1. Visipaque® Contrast Desensitization.

Dose[a]	Dilution	Concentration (mg/mL)	Dose (mg)	Volume (mL)
1	1:10 000	0.032	0.160	5
2	1:5000	0.064	0.320	5
3	1:1000	0.320	1.600	5
4	1:500	0.625	3.125	5
5	1:250	1.250	6.250	5
6	1:125	2.500	12.50	5
7	1:62.5	5.000	25.00	5
8	1:32	10.00	50.00	5
9	1:16	20.00	100.0	5
10	1:8	40.00	200.0	5
11	1:4	80.00	400.0	5
12	1:2	160.0	800.0	5
13	1:1	320.0	1600	5
14[b]	1:1	320.0	1600	5
15[c]	–	–	–	–

[a]10-minute intervals between dosages.
[b]Addition to protocol described in Uppal et al.; repetition of dose 13.
[c]Future dosage(s), if indicated.

From Sanan et al. Allergy & Rhinology. Volume 10: 1–3

Case resolution:

- ✓ The patient underwent rapid IV desensitization in the cath lab prior to undergoing successful angiography.
- ✓ She did not experience any anaphylactoid symptoms during her desensitization.

References:

1. Morzycki, A., et al. (2017). Association of Radiologists Journal 68(2): 187-193.
2. Schrijvers, R., et al. (2019). Current Treatment Options in Allergy.
3. Mervak, B. M., et al. (2017). Radiology 285(2): 425-433.
4. Khan, S., et al. (2020). Can J Cardiol 36(7): 1161.e1161-1161.e1162.

5. Uppal et al. Int Heart J 2018; 59: 622-625.
6. Sanan et al. Allergy & Rhinology Volume 10: 1–3

The Clinical Pharmacology (CP) physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA on the AHS Insite page. CP consultations are also available through Netcare e-referral and Specialist Link. You can also find us in the Alberta Referral Directory (ARD) by searching "Pharmacology" from the ARD home page. Click HERE for more details about the service.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK). Information about our outpatient Medical Toxicology Clinic can be found in Alberta Referral Directory (ARD) by searching "Toxicology" from the ARD home page.

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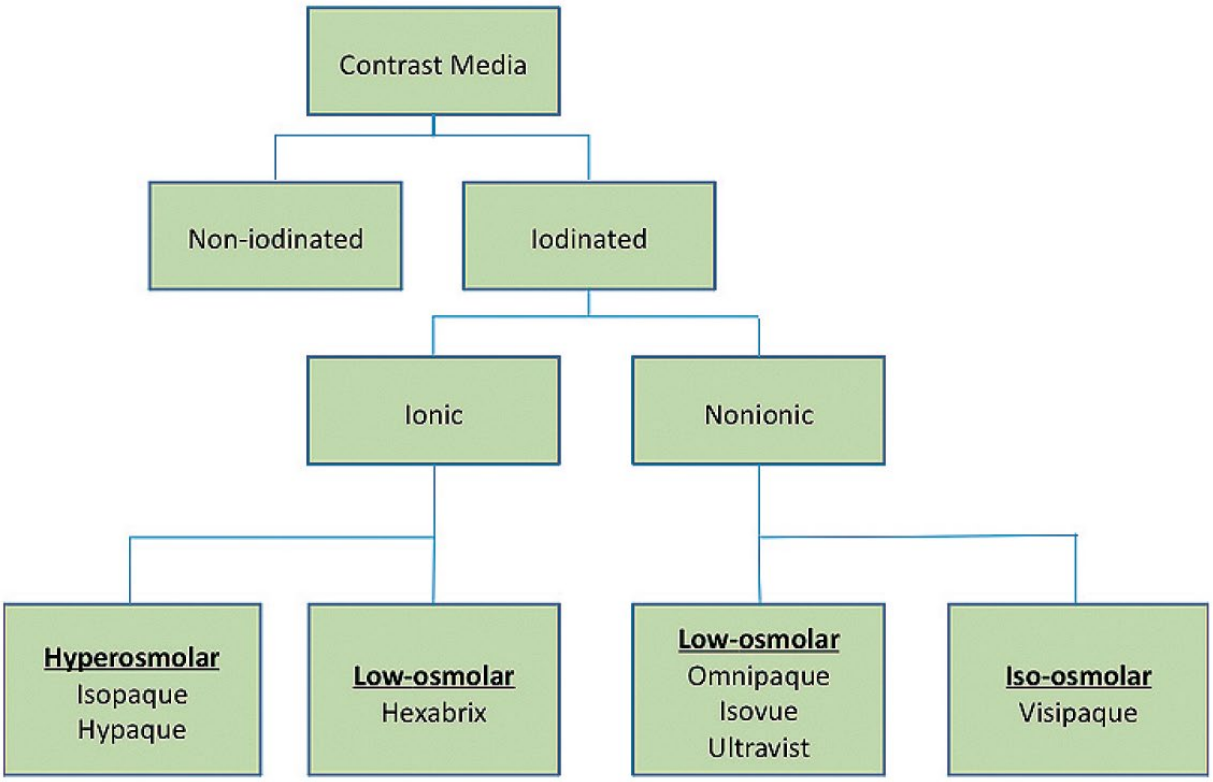

Figure. Types of contrast media.

From Uppal et al. Int Heart J 2018; 59: 622-625