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 risk of an adverse reaction to low osmolarity contrast media is ~1-3%. This is equivalent to about 1.5 events per 1000 doses administered, with 2.6% being reported as serious reactions.
- ✓ 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 as a result 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 very small minority being attributed to IgE mediated mechanisms.
- ✓ Non-IgE mediated pathways are capable of producing histamine release and causing 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 below.

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

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.
- ✓ 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.

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.

The Calgary Clinical Pharmacology physician consultation service is available Mon-Fri, 8am-5pm (excluding STAT holidays). The on-call physician is listed in ROCA. Clinical Pharmacology consultations are also available through the Netcare e-referral process and through Calgary Zone Specialist Link. Click HERE for more details.

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).

References:

1. Morzycki, A., et al. (2017). "Adverse Reactions to Contrast Material: A Canadian Update." Canadian Association of Radiologists Journal **68**(2): 187-193.
2. Schrijvers, R., et al. (2019). "Premedication for Iodinated Contrast Media Induced Immediate Hypersensitivity Reactions." Current Treatment Options in Allergy **6**.
3. Mervak, B. M., et al. (2017). "Intravenous Corticosteroid Premedication Administered 5 Hours before CT Compared with a Traditional 13-Hour Oral Regimen." Radiology **285**(2): 425-433.
4. Khan, S., et al. (2020). "Successful Coronary Angiography Following Rapid Intravenous Desensitization for Refractory Contrast Allergy." Can J Cardiol **36**(7): 1161.e1161-1161.e1162.