CHALLENGES IN THE MANAGEMENT OF DRUG ALLERGY

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Consultant Respiratory Physician
with an interest in Allergy
• Image of the week (who, where, when, why and what happened next?)
• Case presentation 1 (SUI)
• Case presentation 2 (classic referral)
PENICILLIN CURES GONORRHEA
IN 4 HOURS
SEE YOUR DOCTOR TODAY
Beta-Lactam Ring Structure
Mr SV born 1935

- Admitted UHL 02/03/2013 aortic dissection for surgery
- Previous AAA repair, CVA, COPD
- Good Ex Tolerance
- Allergy to penicillin (‘severe D and V’)
- AICU admission ‘?true allergy’
11/03/13

• ?chest sepsis (WCC, CXR and pyrexia)
• FY2 planned to administer meropenem
• Dw micro SpR ‘since patient has side effects and not true allergy’ administer coamoxiclav
• Reconfirmed with patient ‘no rash or anaphylactic reaction’
• 1<sup>st</sup> dose administered by Staff nurse
• Patient coughed and c/o chest pain
• Became unresponsive, PEA, VF……
• Mast cell tryptase (80, 60 and 20)
• Penicillin IgE normal (next day)
21st March 2013

• CT shows parietal and bilateral occipital infarction
• Transferred to Pilgrim hospital
Context/Discussion
Allergy to penicillins

• Most common reported medication allergy
• Majority of self reported allergy could be disproved
Nice and Drug allergy (consultation complete) 2014

- Immediate, rapidly evolving reactions
  - Anaphylaxis, urticaria/angioedema without systemic features, asthma (NSAIDs)
  - Within 1 hour, previous exposure not necessary
Nice 2014

- Non immediate reactions without systemic involvement
  - Exanthem like or fixed drug reaction like
  - Day 2 to day 10 depending on previous exposure
Non immediate reactions with systemic involvement

- DRESS, DHS
- TEN, SJS

- 2 days to 6 weeks depending on previous exposure
Nice 2014

• ‘Reaction is less likely to be caused by drug allergy if
  – Gastrointestinal symptoms only’
Accuracy of history

• Presence of IgE-mediated allergy cannot be predicted
• Patients with convincing histories are more likely to be allergic
NICE - documentation

- Name of drug
- Date and time of episode
- Indication
- Description
- Number of doses and relationship to symptoms
- Route of administration
Time elapsed since reaction

- 50% loss of sensitivity over 5 years
- 80% over 10 years
Referral to a drug allergy specialist

- Consider in anyone with a history of allergy
- Patients requiring beta-lactams or other regular antibiotics
- Patients who report reactions to two or more classes of antibiotic
Penicillin skin testing and graded challenge
In vitro tests

• IgE
• BAT
Risk of cephalosporin administration

- Up to 10% in historic studies (patients not proven to be allergic, penicillin contamination and nature of reactions inconclusive)
- Approx 2% in more recent studies in skin test positive (to penicillin) patients
Administration of a cephalosporin to a patient with a history of penicillin allergy

- Patient with past reaction to penicillin requires a cephalosporin
  - Skin testing to penicillin
    - NOT AVAILABLE
      - Risk stratification
        - Low risk
          - Penicillin reaction occurred >10 years ago
            - AND/OR
              - Penicillin reaction did not include features of IgE-mediated reactions
            - Give cephalosporin directly:
              - Reaction (within 24 hours) may occur in <1 percent of patients, but risk of anaphylaxis is very small
          - Moderate risk
            - Penicillin reaction occurred within past 10 years
              - AND/OR
                - Penicillin reaction included features of IgE-mediated reaction
            - Give cephalosporin by graded challenge:
              - Reaction (within 24 hours) may occur in <1 percent of patients, but risk of anaphylaxis is very small
          - High risk
            - Patients with probable anaphylaxis to penicillin based on clinical history
              - Densensitize to cephalosporin
        - Options:
          - 1. Give alternate drug
          - 2. Give cephalosporin by graded challenges; less than 2 percent will react in 24 hours, but reactions may be anaphylactic
          - 3. Desensitize to cephalosporin
    - Positive
      - Give cephalosporin:
        - Less than 1 percent will have mild reactions within 24 hours
    - Negative

IgE: immunoglobulin E.

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Carbapenem administration

• 99% of history and skin test positive patients will tolerate a carbapenem

• ‘Up to date’ still recommends ‘2 or 3 step graded challenge’
Mr SV

- Cephalosporin/carbapenem?
- Complete avoidance of beta lactams?
CASE PRESENTATION 2
Mrs GT born 1982

- EDU anaphylaxis pathway
- September 2013
- Day 7 of amoxicillin (for cellulitis), week 4 of diclofenac (for craniofacial pain)
Presentation

- Took both tablets at 8am with breakfast
- Midday stuffy nose, ‘prickly throat’, lacrimation
- Occupational nurse administered antihistamine but unable to swallow
- Pruritis, DIB, ‘voice change’
- LRI adrenaline etc
PMH

• Atopic (SPT 8mm to cat, 6mm to dog, 5mm to grass and 10*5mm to hdm)
• Childhood asthma
• ‘Occasional’ hay fever
• No regular medication
• Baseline MCT and penicillin IgE NAD
Diagnosis?/Plan

- Avoid beta lactams and NSAIDs
- Challenge to amoxicillin
- Challenge to naproxen
- Challenge to both
- ?
Management

• Amoxicillin challenge negative
Context/Discussion
NSAID allergy

• Pseudoallergic (related to COX-1 inhibiting properties of the drug)
  – Usually multiple NSAIDS

• Allergic (presumed IgE mediated)
  – Can be single or small number of NSAIDS
Pseudoallergy

- NSAID induced asthma and rhinositis
- NSAID induced urticaria/angioedema in patients with chronic symptoms
- NSAID induced urticaria/angioedema in asymptomatic patients
- AERD
Allergy (presumed IgE)

- Urticaria/angioedema
- Anaphylaxis

- Both allergy and pseudoallergy often follow apparent tolerance (careful history may indicate ‘warning signs’) and especially intermittent use
Diagnosis/Management

- History
- No in vitro or spt
- Definitive diagnosis requires challenge

- Avoidance
- Paracetamol/Codeine
- Selective challenge (aspirin)
- COX 2 inhibitor challenge
• Celecoxib challenge negative
Desensitisation (limitations)

- Known side effects of NSAIDS (GI upset)
- Require continuous treatment (as above)
Towards better management of drug allergy

• Audit of NICE guidance on documentation
Any questions?

Thank you for your attention
# KEY LEARNING POINTS

**Penicillin Allergy**

<table>
<thead>
<tr>
<th>Differentiate allergy from ADR</th>
<th>Self reported rate</th>
<th>Crossover allergy rates LOW</th>
<th>1. Not all reactions preclude the use of penicillin.</th>
</tr>
</thead>
<tbody>
<tr>
<td>(non allergic manifestations eg.GI upset, diarrhoea or vomiting)</td>
<td>0.7-10%</td>
<td>0.5% 1st gen ceph</td>
<td>2. <strong>NON-SERIOUS ALLERGY</strong> (e.g. rash alone, no anaphylaxis) cephalosporins/ carbapenems should still be used, when 1st line (monitor closely)</td>
</tr>
<tr>
<td>Document type of allergy &amp; temporal relationship</td>
<td><strong>Anaphylaxis</strong> 4-15 per 1000 treated patients</td>
<td>0.2% 2nd gen ceph</td>
<td>3. <strong>SERIOUS ALLERGY</strong> AVOID ceph/carbap &amp; use alternatives.</td>
</tr>
<tr>
<td></td>
<td><strong>Crossover allergy rates LOW</strong> 0.8% 3rd gen ceph</td>
<td>0.8-0.9% carbap</td>
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</tr>
</tbody>
</table>

1. **1st gen cephalosporin** - cefradine, cefalxine, cefradroxil, cefaclor
2. **2nd gen cephalosporin**
3. **3rd gen cephalosporin** - cefuroxime, cefotaxime, cefixime, ceftazidime, ceftriaxone
4. **carbapenems** - Imipenem, Ertapenem and Meropenem
Patients reporting an adverse reaction to penicillin are relatively common, 0.7 to 10%. Not all reactions preclude the use of penicillin. The different types of allergic reactions, depending on the time of onset. The reaction the patient actually has experienced should be endorsed in drug card allergy box.

**Anaphylactic reactions** to penicillins only occur in about **0.004% to 0.015% of treated patients.**

**Allergy** to penicillins. They may also have a crossover-allergy to other β-Lactams. **First generation cephalosporin** (e.g. cefradine, cefalxexin, cefradroxil and cefaclor). Cefotaxime, cefixime, ceftazidime, ceftriaxone) is near zero (0.2% and 0.8% respectively.

**Recommendations for treatment and prophylactic regimens.** Cephalosporins/ carbapenems should still be used, when 1st line and the patient closely monitored. Patients with serious allergic symptoms to penicillins (including previous anaphylaxis) should avoid cephalosporins and carbapenems, where possible, and alternatives agents be administered.