Beta-Lactam Hypersensitivity Reaction: CROSS-REACTIVITY

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Beta-Lactam Hypersensitivity Reactions

Immediate-type
- IgE mediated
- Symptoms
- Urticaria
- Anaphylaxis
• First encounter: silent sensitization
• Re-exposition: rapid occurrence of the symptoms

Delayed-type
- T cell mediated
- Symptoms:
  • Maculo-papular Erythema
  • Skin-Rash
  • Severe reaction: Bullae, SJS / TEN, DRESS, AGEP
  • Lesions in intern organs
- Occurance after 8-12 days after starting the therapy
Immediate Hypersensitivity

- First Encounter: silent sensitization
- Reposition: rapid occurrence of symptoms

Delayed-type Hypersensitivity

- Occurrence after 8-12 days therapy
- Expansion of drug reacting T cells

β-lactam Antibiotika
Core Structure Defines The Class

Penicillin G
Penicillin V
Amoxicillin

Aztreonam
Azactam *

Imipenem Tienam *
Meropenem Meronem *
Ertapenem Inva *

Core-structure and Side-chain
Antigenic determinant in β-Lactams

- Antigenic determinant for T cells
  - Core structure (Cephem)
  - Total structure

![Antigenic determinant for IgE](image)
- Side chain
  - Total structure

Possible cross-reactivity between different classes

Antibodies (IgE) are able to recognize very tiny determinants on a molecule.

- Amoxicillin
- Cefadroxil

Cave: Possible cross-reactivity between penicillin and cephalosporin due to identical side chain

Possible cross-reactivity between different classes

High affinity, but low cross-reactivity
Crossreactivity

• Concepts
  – Type of the involved immune mechanism
    T cell mediated? IgE mediated
  – Analysis of the chemical structure of the culprit β-lactam
    Identical core structure?
    Delayed type DHR → Switch to another β-lactam class
    Identical side chain?
    Immediate reaction → Choose a molecule with another side chain

• Clinic
  – Skin test
  – By negative skin test → Provocation test
  – Cave anaphylaxis!

Cephalosporin Challenges in Penicillin ST-Positive (IgE) Patients

<table>
<thead>
<tr>
<th>Reference (Year)</th>
<th># of Patients</th>
<th># (%)</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Girard (1968)</td>
<td>23</td>
<td>2 (8.7)</td>
<td>Both reactions to cephaloridine*</td>
</tr>
<tr>
<td>Assem (1974)</td>
<td>3</td>
<td>3 (100)</td>
<td>All reactions to cephaloridine*</td>
</tr>
<tr>
<td>Warrington (1978)</td>
<td>3</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Solley (1982)</td>
<td>27</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Saxon (1987)</td>
<td>62</td>
<td>1 (1.6)</td>
<td>Specific cephalosporin not noted</td>
</tr>
<tr>
<td>Blanca (1989)</td>
<td>16</td>
<td>2 (12.5)</td>
<td>Both reactions to cefamandole*</td>
</tr>
<tr>
<td>Shepherd (1993)</td>
<td>9</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Audicana (1994)</td>
<td>12</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Novalbos (2001)</td>
<td>23</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Macy (2002)</td>
<td>42</td>
<td>1 (2.4)</td>
<td>Reaction to cefixime</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>220</strong></td>
<td><strong>9 (4.1)</strong></td>
<td></td>
</tr>
</tbody>
</table>

* These cephalosporins have R-group side chains similar to benzylpenicillin.

Cross-reactivity
Penicillin - Cephalosporin

• Cross-reactivity between Penicillin and Cephalosporin is probably over-evaluated
• Cross-reactivity is rare (only 4.1% of skin tests with positive IgE)
  – z.T. bedingt durch Kontaminationen des Cephalosporins mit Penizillinen
  – z.T. bedingt durch gleiche Seitenkette
Case # 1

• Patient mit Urtikaria 2 hr nach Amoxicillin:
• Kann er Cephalosporine 3. Generation haben?

Hautteste prick/i.d.
- mit PPL +++
- mit Amoxicillin ++
- Cephadroxil -

Case # 2

• Patient with a severe exanthem after 7 days of Amoxicillin treatment
• May he receive a Cephalosporine of 3rd generation?

Skintest i.d. Epicutan
- PPL - nd
- Amoxicillin - ++
- Cephadroxil nd -
- Kefrol (Cefazolin) nd -

Aknowledgements

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