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Delayed-Onset Anaphylactic Reaction With High Fever After Amoxicillin Oral Challenge And Negative Penicillin Skin Testing

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Background

- Immunologic adverse drug reactions can be categorized based on Gell and Coombs's classification system
- Anaphylaxis typically occurs independent of other reactions
- Literature on mixed hypersensitivity drug reactions is limited
- This case presents a child with features of type I and type III or IV hypersensitivity reactions after amoxicillin drug challenge

Gell and Coombs Classification

Type	Description	Examples
Type I	Immunoglobulin E-Mediated Reactions	Anaphylaxis
Type II	Antibody-Mediated Cytolytic Reactions	Hemolytic anemia, thrombocytopenia
Type III	Immune Complex-Mediated Reactions	Serum sickness, cutaneous vasculitis
Type IV	Delayed T Cell-Mediated Hypersensitivity Reactions	Drug reaction with eosinophilia and systemic symptoms, Stevens-Johnson syndrome

Case Description

Initial Presentation

- 12-year-old female developed sore throat and tested positive for streptococcal pharyngitis
- She was treated with amoxicillin and developed rash with features of:
 - Urticaria
 - Livedo reticularis
 - Scarlatina
 - Vasculitis
- Patient also developed:
 - Fatigue
 - Generalized edema
 - Joint swelling
 - Periorbital erythema
- Labs:
 - Low C4 level (8.5 mg/dl)
 - Eosinophilia (1350 cells/mcL)
 - Increased variant lymphocytes (16%)
 - Normal inflammatory markers
 - Normal tryptase level
- Penicillin skin prick and intradermal testing was negative

Presentation After Oral Challenge

- She underwent amoxicillin oral challenge
- Two hours after challenge she had:
 - Shortness of breath
 - Scratchy throat
 - Papular rash
 - Diffuse erythema and pruritus
- 0.3 mg intramuscular (IM) epinephrine was administered with prompt symptom resolution
- One hour later she developed:
 - Erythema/flushing
 - Periorbital and lip edema
 - Nausea
 - Lightheadedness
 - Delayed capillary refill
 - Fever of 103.1 degrees F
- IM Epinephrine and IVF were given
- Tryptase level was elevated at 10.3 compared to baseline of 4.9 ng/mL
- She was admitted overnight for observation and discharged asymptomatic the next day

Discussion

- This patient presented with delayed-onset, biphasic anaphylaxis
- The presence of high fever suggests a co-existing type III or IV reaction
- Rare cases of mixed hypersensitivity drug reactions that include multiple reaction types have been reported
- Recognition of this phenomenon is important when evaluating patients with adverse drug reactions involving mixed features

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