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Clarifying drug allergies

Story From the Front Lines

A woman in her 60s presented to an ED with acute on chronic diarrhea. She was found to have AKI and was admitted. The cause of her diarrhea was determined to be C Diff colitis. Upon medication review, she was discovered to have been diagnosed with cellulitis at an urgent care a week prior, for which she completed a 5 day course of clindamycin. Of note she had a reported history of allergy to penicillin. When asked about her reaction to penicillin, she stated penicillin caused a rash when she was a child.

Teachable Moment

About 1 in 10 patients has a reported penicillin allergy in their medical record.¹ More often than not, these reactions are rashes caused by a virus. Even in those with true IgE mediated hypersensitivity to penicillin--only 20% of these patients remain intolerant to penicillin after 10 years.¹

There are wide-reaching clinical consequences of being labeled with a penicillin allergy.² First, antibiotics given may be less effective. The most common clinical scenarios where this occurs is:

1. Methicillin Sensitive Staph Aureus Bacteremia (nafcillin is well-studied to be superior to vancomycin)³
2. Gram-negative bacteremia (avoiding cephalosporins due to concern for cross-reaction)
3. Syphilis (penicillin is agent of choice)
4. Gonorrhea (ceftriaxone is agent of choice)
5. Prophylaxis for skin and soft tissue infections (prior to dental or surgical procedures)²

There are other clinical implications for those with penicillin allergy. These include increased risk of developing C diff colitis or vancomycin resistant enterococcus, as well as increased risk for more adverse events and drug reactions. Simply having a label of penicillin allergy greatly increases healthcare costs for these patients as well.⁴

Unfortunately, most of the 32 million people in the United States that report a penicillin allergy do not undergo any further evaluation to determine if true allergy exists.¹ Given the potential consequences, it is critical to do a complete and thorough evaluation of all our patients with penicillin allergy.

A 2019 review in JAMA Clinical Review and Education recommends risk stratifying into high, medium, and low risk groups.² Risk stratification is nearly entirely based on history, emphasizing the importance of taking a thorough history for these patients.

Low risk patients are those with isolated reactions considered unlikely to be allergic (GI symptoms, headache, etc.), those with pruritus without any rash, isolated family history of penicillin allergy, or (probably the largest group), or unknown reactions > 10 yrs prior without typical IgE features (urticaria/angioedema, flushing/bronchospasm, etc.). For these patients, an amoxicillin challenge is considered most appropriate.

Medium risk patients are those with urticaria with rash, or other IgE features, but no features of anaphylaxis (generally skin features (urticaria/angioedema, etc) with either respiratory dysfunction or hypotension). These patients are recommended to get skin testing, followed by amoxicillin challenge in those with negative skin testing results.

High risk patients are those with anaphylactic reactions, previous positive skin testing results, and those with recurrent reaction to penicillins. For these patients, referral to allergy/immunology referral is appropriate where they can receive desensitization therapy. This may be the best solution as these patients are considered higher risk for cross reactivity with cephalosporins as well, and desensitization is the only way considered safe for them to receive this group of antibiotics, which they may likely require. Additional high-risk patients who should not receive re-trial of beta lactam drugs are those who previously experienced severe, non IgE based reactions such as serum sickness, SJS, AIN or DRESS.

Increasing awareness of this issue is important to patient care and healthcare costs in a significant way, considering the numbers of patients with penicillin allergy in the United States. In the case of our patient, evaluation of penicillin allergy could have likely prevented true harm. And as hindsight often seems so clear, again it is shown the importance of providers acting proactively with a preventive mindset, that may make the difference in patient outcomes.

References

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2. Shenoy ES, Macy E, Rowe T, and Blumenthal KG. Evaluation and Management of Penicillin Allergy: A Review. *JAMA: Clin Review and Ed.* 2019; 321 (2): 188-199.

3. McDanel JS, Perencevich EN, Diekema DJ, et al. Comparative effectiveness of beta-lactams versus vancomycin for treatment of methicillin-susceptible *Staphylococcus aureus* bloodstream infections among 122 hospitals. *Clin Infect Dis.* 2015;61(3):361-367.

4. Mattingly TJ II, Fulton A, Lumish RA, et al. The cost of self-reported penicillin allergy: a systematic review. *J Allergy Clin Immunol Pract.* 2018;6(5): 1649-1654.