Considerations for cross-reactivity between vancomycin and other glycopeptides

To the Editor:

In the editorial by Kayode and Rutkowski entitled Vancomycin hypersensitivity: it is not always what it seems,¹ the authors highlight several important points about the broad range of immediate and delayed hypersensitivity reactions occurring in association with vancomycin. They refer to a theoretical possibility of cross-reactivity between vancomycin and other glycopeptides owing to structural similarity but draw attention to notable differences. These include a lack of association between teicoplanin and development of non–immunoglobulin E (IgE)–mediated mast cell activation sometimes called red man syndrome, citing in contrast to vancomycin, the inability of teicoplanin to induce mas-related G-protein–coupled receptor 2 (MRGPRX2) driven induction of laboratory of allergic diseases 2 mast cell degranulation.² Particularly with regards to delayed hypersensitivity reactions associated with vancomycin, they state that immunological cross-reactivity has not been demonstrated between vancomycin and other glycopeptides and that clinical reports are limited. Indeed, a previous report cited lack of cross-reactivity between vancomycin and dalbavancin based on a presumed IgE-mediated reaction to vancomycin and a negative ingestion challenge to the lipoglycopeptide dalbavancin; however, it is highly likely that the former represented a non–IgE-mediated (MRGPRX2) driven reaction associated with vancomycin.³,⁴

In discussing cross-reactivity between vancomycin and other structurally related drugs, it is important to distinguish between pharmacological cross-reactivity based on shared or lack or shared interaction with a known pharmacological receptor versus immunological cross-reactivity based on a shared adaptive immune response that includes a recognition of a shared or similar epitope. We draw attention to a recent report that supports a novel mechanism by which HLA class II complexes are recognized by CD8⁺ T cells based on a presumed IgE–mediated reaction to vancomycin and a negative ingestion challenge to the lipoglycopeptide dalbavancin; however, it is highly likely that the former represented a non–IgE–mediated (MRGPRX2) driven reaction associated with vancomycin.³,⁵

In a small but measurable subset of patients with HLA-A*32:01 restricted vancomycin-induced delayed-type hypersensitivity (DRESS). Thus, diagnostic tests such as ex vivo IFN-γ ELISpot and potentially intradermal skin testing in combination with HLA typing should be considered to detect the potential for this cross-reactivity to aid in the safe selection of ongoing or future treatments.

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REFERENCES