

Erythema multiforme to vancomycin

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• SERIOUS cutaneous reactions to glycopeptide antibiotics are uncommon (1). We report two patients with severe delayed cutaneous reactions to vancomycin, and we suggest possible allergic cross-reactivity between vancomycin and teicoplanin in one of these patients.

Patient 1 was a 68-year-old woman undergoing hip surgery who began intravenous cefazolin therapy after surgery.

Two cases of severe delayed cutaneous reactions.

Staphylococcus epidermidis sensitive to vancomycin and teicoplanin grew in blood cultures, and the patient was treated with intravenous vancomycin. Two weeks later, she developed pruritus and a nongeneralized erythematous rash. Because we suspected the development of "red-man syndrome", we continued vancomycin infusion at a lower rate. Nevertheless, the patient showed a generalized maculopapular skin rash 24 h later. Vancomycin was withdrawn in favor of treatment with prednisolone. Three days later, intravenous teicoplanin therapy was initiated. After 1 week, the patient developed general malaise, fever, conjunctival injection, more extensive rash, and later blisters on the legs. The teicoplanin was withdrawn, and treatment with steroids and fluid therapy was resumed for 2 weeks. Laboratory analyses, including biochemistry and blood count, showed normal results. The prick test (10 mg/ml) and intradermal skin test (1 mg/ml) with cefazolin were negative. Patch tests with cefazolin, vancomycin, and teicoplanin (15%

in vaseline) were negative. The challenge test with cefazolin, performed with the patient's authorization, was negative. Therefore, we believe this was a case of toxic epidermal necrolysis due to teicoplanin in a patient allergic to vancomycin.

Patient 2 was a 70-year-old woman allergic to β -lactam antibiotics who underwent hip surgery, and treatment with vancomycin was instituted during the postoperative period. On day 5, sudden fever began; therefore, blood cultures were made and vancomycin was discontinued. One day later, the fever disappeared, but the patient developed generalized urticarial rash with oral and vaginal mucous-erosive lesions, which were treated with steroids and antihistamines. The clinical diagnosis of erythema multiforme major was confirmed by skin biopsy that showed a perivenular lymphocyte dermal infiltrate. Patch testing with vancomycin was negative. Laboratory studies were normal, but *S. epidermidis* grew in blood cultures and was sensitive only to vancomycin and teicoplanin. Due to generalized staphylococcal sepsis and the severity of the symptoms induced by vancomycin, increasing doses of teicoplanin (12, 25, 50, and 113 mg) were administered cautiously and successfully every 30 min until the therapeutic dosage was reached (200 mg).

Treatment with vancomycin is not usually associated with severe reactions, but may be a problem when a patient has serious staphylococcal infection. In some cases, an IgE-mediated immediate reaction to this antibiotic group may occur (2), but the pathogenesis of severe delayed cutaneous reactions related to drugs is poorly characterized, although an immune reaction is suspected. In our second patient, the skin biopsy specimen showed lesions consistent with an immune cellular reaction. It has been reported that in peripheral blood a subpopulation of T cells express the cutaneous lymphocyte-associated antigen

that is increased in patients with delayed cutaneous reactions to drugs (3).

Nevertheless, it is not clear whether teicoplanin can be administered safely to patients who are allergic to vancomycin. Although the evidence of allergic cross-reactivity between teicoplanin and vancomycin remains controversial, several reported cases suggest that this can happen (4, 5). After the severe reaction that appeared in our first patient in relation to the use of glycopeptide antibiotics, we suggest that, as in our second patient, teicoplanin should be used cautiously in patients with previous evidence of allergy to vancomycin when there is no satisfactory alternative antibiotic.

Further *in vitro* studies with these drugs are necessary for a final assessment of such possible cross-reactivity.

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