Telavancin is a potent, rapidly bactericidal antimicrobial that has a similar mechanism of action to vancomycin, but also causes bacterial membrane depolarization. To our knowledge, this is the first case using telavancin in mitral valve MRSA endocarditis.

Current expert opinion recommends consideration of alternative therapies for bacterial isolates with a vancomycin MIC of ≥2 mg/L, as the required higher doses may lead to an increase in toxicity over efficacy. For this reason, daptomycin was chosen over vancomycin. Initially, daptomycin was dosed (4 mg/kg) at 350 mg intravenously every 48 h—renally adjusted, but not at the recommended dose for endocarditis, 6 mg/kg. Over a period of 8 days, the dose was increased twice (secondary to noticed underdosing and improving renal function) to a final dose of 500 mg intravenously every 24 h. During this period the MIC for the isolate increased from 0.38 mg/L to 4 mg/L (daptomycin-non-susceptible S. aureus (DNSSA)).

Common reasons for daptomycin clinical failure reported in the literature include antecedent vancomycin therapy, exposure of an isolate to suboptimal concentrations of daptomycin and having a large inoculum of infection that is not or cannot be aggressively debrided. Higher doses of daptomycin (10 mg/kg/day) have been suggested for reducing the inoculum from endocardial vegetation, though we ultimately chose against this, as the data are conflicting.

This case demonstrates the efficacy and tolerability of telavancin as well as the importance of proper antimicrobial dosing to prevent the unintended emergence of bacterial resistance. As noted in the literature, prompt surgical intervention should be pursued (if warranted) to optimize clinical outcome. In conclusion, we report successful treatment of a patient with MRSA mitral valve endocarditis. While bacteraemia initially resolved with mitral valve annuloplasty, vegetation excision and linezolid monotherapy, telavancin was successful in completing this patient’s treatment for left-sided endocarditis, para-spinal abscess and forearm wound despite being exposed to vancomycin and subtherapeutic doses of daptomycin that led to development of DNSSA.

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Transparency declarations
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Life-threatening acute generalized exanthematous pustulosis induced by two different protease inhibitors in an HIV-1-infected patient

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Keywords: antiretroviral drugs, drug-related cutaneous reactions, adverse events

Sir,

Antiretroviral drugs can cause a variety of cutaneous adverse reactions in HIV-infected persons. To the best of our knowledge, no case of acute generalized exanthematous pustulosis (AGEP) has been reported in HIV-infected patients. We report a case of cross-protease inhibitor-induced life-threatening AGEP in an HIV-1-infected patient.

A patient was admitted for pancytopenia. Exhaustive clinical, biological, radiological and histological (lymph node biopsy) work-up revealed HIV-1 infection and Castleman’s disease. The HIV-1 plasma viral load was 4.4 log10 copies/mL and the CD4 count was 220 cells/mm3. HIV-1 belonged to subtype B with evidence of transmitted primary resistance to thymidine analogues and non-nucleoside reverse transcriptase inhibitors; the virus was CCR5-tropic. The patient was started on tenofovir,
emtricitabine and ritonavir-boosted darunavir. At day 10, the patient developed generalized pruritus and a pustular rash that spread rapidly over the dorsal surface of the trunk and neck. The pustules were tiny and non-follicular, and arose on a diffuse erythematous background. Body temperature was 40°C with hypotension and anaphylactic shock requiring immediate discontinuation of all drugs and admission to the intensive care unit. Serology suggested past exposure to Epstein–Barr virus and cytomegalovirus. The patient was discharged 48 h later, with dramatic skin improvement 48 h after discontinuation of antiretroviral drugs, with marked desquamation. Twenty days later, the patient was sequentially restarted on a triple combination with didanosine introduced first, then raltegravir and finally unboosted atazanavir. Nine days after atazanavir initiation, the patient again developed generalized pruritus and a pustular rash that spread rapidly over the dorsal surface of the trunk and neck, but the symptoms were less severe than in the first episode. All antiretroviral drugs were discontinued and the patient improved rapidly. We then decided to treat Castleman’s disease first with rituximab, which yielded significant improvement regarding splenomegaly and pancytopenia. After completion of the treatment with rituximab, dual therapy with raltegravir and maraviroc was initiated, with no sign of cutaneous intolerance.

AGEP is a well-known severe skin disorder, most cases of which are drug related. The main culprit drugs are antibiotics (such as aminopenicillins and pristinamycin), some diuretics, calcium inhibitors (diltiazem), azole antifungals and chloroquine. Viral infections can also trigger AGEP. Our patient had characteristic features of AGEP, including rapid and acute onset, a pustular eruption and fever above 38°C. The dramatic improvement and superficial desquamation observed twice when two distinct protease inhibitor-containing regimens were withdrawn and the absence of cutaneous adverse reaction with a protease inhibitor-sparing dual therapy suggest that protease inhibitors were responsible.

Two similar cases have been reported in HIV-seronegative subjects receiving protease inhibitor-based post-exposure prophylaxis. To the best of our knowledge, drug-related AGEP has never been reported in HIV-infected patients. This may be related to the rarity of AGEP disease. This also may be because of HIV-related immune deficiency with a reduced activation of drug-specific CD4+ and CD8+ T cells. If so, then earlier treatment initiation applied according to recent guidelines might lead to an increase in AGEP in coming years. Interestingly, our patient was not severely immunocompromised, and Castleman’s disease-related activation might have favoured the development of such a life-threatening cutaneous adverse event. Physicians dealing with HIV/AIDS should therefore be aware that AGEP can be caused by protease inhibitors such as ritonavir-boosted darunavir and atazanavir. The clinical diagnosis of AGEP should strive to identify the culprit drug, which must be withdrawn immediately, as AGEP is potentially severe. HIV protease inhibitors should be added to the list of drugs capable of triggering AGEP.

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**References**


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**Nationwide hospital antibiotic consumption in Slovenia**

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**Keywords:** antibiotic policy, drug monitoring, drug utilization

Sir,

Data on hospital antibiotic consumption at national, hospital and ward levels are scarce. Recently, France reported a first survey of...