JOURNAL OF CLINICAL MICROBIOLOGY, Feb. 2006, p. 673 Vol. 44, No. 2
0095-1137/06/$08.00+0 doi:10.1128/JCM.44.2.673.2006

Letters to the Editor

De Novo Daptomycin Nonsusceptibility in a Clinical Isolate

We report a case of non-daptomycin-susceptible *Enterococcus faecium* bloodstream infection in a patient with no previous exposure to daptomycin. To our knowledge, this is the first report of de novo resistance to daptomycin in a clinical isolate.

An 84-year-old man was admitted to the hospital because of progressively debilitating weakness and fever. A past medical history of chronic renal insufficiency, compensated congestive heart failure, urinary incontinence, and anemia was elicited. Physical examination findings included a nonradiating systolic heart murmur and mild pitting edema in both lower extremities. There were no skin lesions or rashes and no stigmata of endocarditis. Serum bicarbonate, creatinine, and hematocrit were 19 mmol/liter, 3.2 mg/dl, and 32.5%, respectively. The remainder of his complete blood count and chemistry panel results were normal. Blood cultures were positive for vancomycin-resistant *Enterococcus faecium* and *Enterococcus gallinarum*. An echocardiogram revealed echogenic material on the aortic valve consistent with the presence of a vegetation.

Laboratory tests of an *E. faecium* isolate revealed a MIC for daptomycin as determined by an Epsilometer test (AB Biodisk, Sweden) of 6 μg/ml (a result indicating nonsusceptibility according to the susceptibility breakpoint of ≤4 μg/ml listed in the product package insert). The Epsilometer test was repeated and gave a result of 4 μg/ml. The *E. faecium* isolate was also resistant to penicillin, ampicillin, gentamicin, and vancomycin but was susceptible to linezolid. The *E. gallinarum* isolate was susceptible to ampicillin, gentamicin, and vancomycin and was not tested for susceptibility to daptomycin.

Options for treating vancomycin-resistant enterococcal infections remain limited. Promising alternatives include treatment with daptomycin, linezolid, and quinupristin-dalfopristin (for *E. faecium* only). Daptomycin is considered by many to be an attractive alternative to linezolid and quinupristin-dalfopristin (3, 6). Daptomycin in this patient would have been preferred due to its rapid bactericidal activity, cost considerations, and the absence of the bone marrow suppression that may be seen with linezolid (particularly associated with the longer duration of therapy needed for endocarditis) and because of once-daily dosing. Additionally, compared to linezolid there may be a lesser tendency for the accumulation of potentially harmful metabolites in the setting of renal failure (1).

Based on the recent introduction of daptomycin and the paucity of reports, the development of resistance to this drug in enterococci appears to be rare. Furthermore, spontaneous resistance in an isolate with no preceding exposure to daptomycin has not been previously reported, although there have been four recent reports of emerging daptomycin resistance (3, 4, 5, 7), one involved methicillin-resistant *Staphylococcus aureus*; all of the cases were associated with prolonged treatment with daptomycin. In a recent review of the world literature on vancomycin-resistant enterococcal endocarditis, (8) there were no instances or reports of daptomycin-resistant native or prosthetic valve endocarditis (8).

A unique aspect of the present case is that the patient had no previous exposure to daptomycin. Additionally, there were no risks known to be associated with the development of multidrug-resistant enterococcal infection, such as longer duration of hospitalization, prolonged stay in an intensive care unit, high APACHE II score, excessive exposure to vancomycin and other antibiotics, repeated abdominal surgeries, and immunosuppression associated with organ transplantation or hematologic malignancy (2, 9). There have been no previous reports of clinical enterococcal isolates initially nonsusceptible to daptomycin at our institution or, to our knowledge, in our community. We are hopeful that this case is not a harbinger of an emerging pattern.

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