Silverman JA, Oliver N, Andrew T, Tongchuan. He was receiving dialysis for 39.4 years. The patient was a 43-year-old man receiving vancomycin treatment. The isolate, a Staphylococcus aureus strain with reduced susceptibility to vancomycin (SARV; MIC, 4 μg/mL), was obtained from a patient residing in the United States that was associated with vancomycin treatment failure. The isolate was intermediately susceptible to vancomycin (MIC, 16 μg/mL) and produced luxurious growth on vancomycin-screening agar containing 6 μg/mL of vancomycin (Becton Dickinson). Isolate 2 was susceptible to vancomycin and oxacillin, by the Vitek test, but produced scant growth on oxacillin-screening agar containing 6 μg/mL of oxacillin (Becton Dickinson). Isolate 3 was susceptible to both vancomycin and oxacillin. On the basis of these findings, vancomycin therapy was discontinued, and the patient was treated with cefazolin and linezolid therapy. After this therapeutic course and surgical intervention, the patient’s bacteremia resolved and the condition of the wound improved.

The most remarkable finding in this case was the elevated vancomycin MIC for isolate 1. In-hospital vancomycin susceptibility testing was performed in accordance with the current Centers for Disease Control and Prevention (CDC)–recommended algorithm [2], which led to the finding of an MIC of 6 μg/mL by use of the E-test (AB Biodisk). Following the manufacturer’s recommendation for E-test MIC values that fall between 2-fold dilutions, we rounded up to the next 2-fold value before categorization; this yielded an MIC of 8 μg/mL, which is interpreted as intermediate level resistance. Although confirmatory broth microdilution testing by the CDC yielded an MIC (4 μg/mL) for this isolate classified as susceptible, on the basis of current Clinical Laboratory Standards Institute (CLSI) breakpoints [3], this elevated MIC of vancomycin is uncommon presently among clinical S. aureus isolates. Similar to the findings of Woods et al. [1], our patient’s prior exposure to vancomycin and experience of clinical failure of vancomycin therapy may have contributed to the emergence of SARV infection. Despite having an elevated MIC to vancomycin, isolate 1 had a low MIC to oxacillin, a finding confirmed by the Massachusetts Department of Public Health and the CDC. This phenomenon is consistent with a previous report of an S. aureus strain with intermediate resistance to vancomycin that was obtained from a patient receiving hemodialysis and showed an inverse relationship between vancomycin and oxacillin MICs [4].

To our knowledge, this is the first published report of infection due to an S. aureus strain with reduced susceptibility to vancomycin in Massachusetts. It is likely that the frequency of SARV infection will continue to increase and will pose challenges to clinicians worldwide, especially in situations where antistaphylococcal treatment failures are common (such as in cases of infective endocarditis and dialysis graft infections). Considering the variability associated with different antimicrobial susceptibility testing methods and the fact that SARV strains are only one 2-fold dilution away from being characterized as “true” vancomycin-intermediate S. aureus strains by CLSI interpretive criteria, the report of recent clinical failure due to SARV strains in the United States requires a reexamination of the current CLSI vancomycin breakpoints for staphylococci. It seems reasonable to consider

Str—With regard to the study by Woods et al. [1], we describe what we believe to be another case of infection with Staphylococcus aureus with reduced susceptibility to vancomycin (SARV; MIC, 4 μg/mL) in the United States that was associated with vancomycin treatment failure. The patient was a 43-year-old man receiving long-term renal dialysis who was admitted to the hospital with a body temperature of 39.4°C and a presumed right axillary graft infection. He was receiving dialysis through a right brachial artery to axillary vein graft. There was an abscess in the right axilla prior to admission that did not respond to localized wound care and antibiotic treatment. The patient had recently completed a course of gatifloxacin and vancomycin therapy. His past medical history was remarkable for multiple bilateral grafts and multiple courses of vancomycin therapy.

At the initial physical examination, a firm indurated area over the right axilla with purulence draining from a recent incision was observed. Samples for culture were obtained, and vancomycin therapy was initiated. Subsequently, the axillary graft was excised. Initial blood cultures grew S. aureus resistant to only ampicillin and penicillin. Wound culture of specimens from the graft grew 3 morphologically distinct isolates of S. aureus with different susceptibility patterns, as determined with the Vitek susceptibility test system (bioMérieux). One of the wound isolates (isolate 1), was intermediately susceptible to vancomycin (MIC, 16 μg/mL) and produced luxurious growth on vancomycin-screening agar containing 6 μg/mL of vancomycin (Becton Dickinson). Isolate 2 was susceptible to vancomycin and oxacillin, by the Vitek test, but produced scant growth on oxacillin-screening agar containing 6 μg/mL of oxacillin (Becton Dickinson). Isolate 3 was susceptible to both vancomycin and oxacillin. On the basis of these findings, vancomycin therapy was discontinued, and the patient was treated with cefazolin and linezolid therapy. After this therapeutic course and surgical intervention, the patient’s bacteremia resolved and the condition of the wound improved.

The most remarkable finding in this case was the elevated vancomycin MIC for isolate 1. In-hospital vancomycin susceptibility testing was performed in accordance with the current Centers for Disease Control and Prevention (CDC)–recommended algorithm [2], which led to the finding of an MIC of 6 μg/mL by use of the E-test (AB Biodisk). Following the manufacturer’s recommendation for E-test MIC values that fall between 2-fold dilutions, we rounded up to the next 2-fold value before categorization; this yielded an MIC of 8 μg/mL, which is interpreted as intermediate level resistance. Although confirmatory broth microdilution testing by the CDC yielded an MIC (4 μg/mL) for this isolate classified as susceptible, on the basis of current CLSI breakpoints [3], this elevated MIC of vancomycin is uncommon presently among clinical S. aureus isolates. Similar to the findings of Woods et al. [1], our patient’s prior exposure to vancomycin and experience of clinical failure of vancomycin therapy may have contributed to the emergence of SARV infection. Despite having an elevated MIC to vancomycin, isolate 1 had a low MIC to oxacillin, a finding confirmed by the Massachusetts Department of Public Health and the CDC. This phenomenon is consistent with a previous report of an S. aureus strain with intermediate resistance to vancomycin that was obtained from a patient receiving hemodialysis and showed an inverse relationship between vancomycin and oxacillin MICs [4].

To our knowledge, this is the first published report of infection due to an S. aureus strain with reduced susceptibility to vancomycin in Massachusetts. It is likely that the frequency of SARV infection will continue to increase and will pose challenges to clinicians worldwide, especially in situations where antistaphylococcal treatment failures are common (such as in cases of infective endocarditis and dialysis graft infections). Considering the variability associated with different antimicrobial susceptibility testing methods and the fact that SARV strains are only one 2-fold dilution away from being characterized as “true” vancomycin-intermediate S. aureus strains by CLSI interpretive criteria, the report of recent clinical failure due to SARV strains in the United States requires a reexamination of the current CLSI vancomycin breakpoints for staphylococci. It seems reasonable to consider...
lowering the intermediate range to include isolates with MICs of 4 μg/mL, or, perhaps, to consider all staphylococcal isolates with vancomycin MICs of ≥4 μg/mL to be nonsusceptible.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

Rocco J. Perla, Eric L. Knutson, and John L. Fontana

HealthAlliance Hospital, Leominster, and Massachusetts Department of Public Health, Jamaica Plain, Massachusetts

References


Epidemiologic versus Genetic Relatedness to Define an Outbreak-Associated Uropathogenic Escherichia coli Group

Sir—France et al. [1] reported that a recently described clonal group of uropathogenic Escherichia coli appears to be distantly clonal and is not an outbreak-related group. They used a variety of strain-typing methods (enterobacterial repetitive intergenic consensus sequence 2 [ERIC 2] PCR, fumC C288T single-nucleotide polymorphism [SNP] analysis, PFGE, virulence profile, and mechanism of resistance) to show that a group of E. coli strains defined as clonal group A (CGA) by ERIC 2 PCR analysis was considerably more diverse than would be expected for an outbreak-related clone. Their conclusion, based on the analysis of their collection of 45 trimethoprim-sulfamethoxazole–resistant CGA isolates obtained from patients with cases of urinary tract infection (UTI) from 1996–1999, is valid and not surprising. However, their conclusion may lack external validity.

We feel that a collection of only 45 isolates spread over 3 years, by definition, is not likely to reveal any UTI outbreak. E. coli O157:H7 that causes outbreaks of hemorrhagic colitis is also distantly clonal [2, 3]. If PFGE analysis were applied to a small collection of E. coli O157:H7 strains from a single geographic site over a 3-year period, they would also be found to be diverse, even though this E. coli serotype is implicated in well-recognized outbreaks. The authors cannot generalize from a single collection of CGA that CGA does not constitute an outbreak-associated group.

The earlier study suggesting that CGA constituted an outbreak-related group was based on a collection of 55 trimethoprim-sulfamethoxazole–resistant isolates obtained over a 3.5-month period at 1 college campus [4]. Their genetic relatedness was assessed by multiple techniques, including ERIC 2 PCR, virulence factor profiling, serotyping, and PFGE. With use of the most discriminating method—PFGE—several of the isolates were indistinguishable. The conclusion that these genetically related strains comprised an outbreak group was based on the observation that they clustered in time at 1 geographic site.

We agree with France et al. [1] that ERIC 2 PCR is a highly condition-dependent typing method. ERIC 2 PCR should not be used to define a clone. However, it is an excellent tool with which to screen a large number of isolates to provisionally identify a clonal group. Once such a provisional group is identified, other, more-discriminating methods can be applied to define a clone. However, one cannot then go on to conclude that the strains within a clonal group do not constitute an outbreak group. Outbreaks of diarrhea caused by mixed Salmonella serotypes, phage types, drug-resistance types, or genotypes do occur. In the report by Manges et al. [4], geographic comparison isolates obtained from 2 other college campuses did identify E. coli isolates that belonged to the same serogroup and had the same ERIC 2 PCR pattern, but those isolates had distinct PFGE patterns. However, the difference in PFGE patterns does not necessarily exclude the possibility that some of the comparison strains belonged to an outbreak-related group.

The conclusion that a collection of strains constitutes an outbreak group is based on epidemiologic information, which, in diseases like community-acquired UTI, may not be easily obtained. This is why, in performing molecular epidemiologic studies, strain typing techniques must be applied to isolates that were appropriately collected with regard to place and time. Genotype data do not define an outbreak. They are only used to support the epidemiologic data that ultimately define an outbreak.

Acknowledgments

Potential conflicts of interest. LWR, and A.R.M.: no conflicts.

Lee W. Riley and Amee R. Manges

1School of Public Health, University of California, Berkeley, and 2Department of Epidemiology, Biostatistics, and Occupational Health, McGill University, Montreal, Quebec, Canada

References

