Linezolid-Resistant Staphylococcus epidermidis, Portugal, 2012

To the Editor: Linezolid is a therapeutic option for skin and soft tissue infections and pneumonia caused by multidrug-resistant gram-positive bacteria (e.g., Staphylococcus spp.), which occur at higher rates in Portugal than in other European countries (www.ecdc.europa.eu/en/publications/Publications/annual-epidemiological-report-2013.pdf). Staphylococcus epidermidis are skin and mucosal commensal bacteria; infections in humans are mostly linked to indwelling medical devices. The ability of S. epidermidis to acquire resistance to antimicrobial drugs and to produce biofilm can seriously compromise the success of therapy; in many institutions worldwide, rates of methicillin resistance are >70% (1).

Rates of S. epidermidis linezolid resistance on various continents have been low and are associated with mutations in the central loop of 23S rRNA V domain and in genes (rplC, rplD and rplV) encoding the L3, L4, and L22 ribosomal proteins (6–8). Clonal relatedness was determined by pulsed-field gel electrophoresis (macrogenetic based on Smal) and by multilocus sequence typing (MLST) (www.cdc.gov/mlst/mlstnet). S. epidermidis from patient 1 was searched for in vitro adherence to abiotic surfaces by using a biomass quantification assay (9) and strain ICE9 as a positive control.

All isolates were resistant to multiple drugs, including linezolid (MIC > 32 mg/L), cefoxitin, chloramphenicol, cotrimoxazole, ciprofloxacin, clindamycin, and aminoglycosides, and susceptible to vancomycin (MIC = 2 mg/L) (Table). To characterize linezolid resistance, we compared the study isolates with linezolid-susceptible S. epidermidis RP62A/American Type Culture Collection 35984 sequence (GenBank accession no. CP000029). Study isolates contained the mutations T2530A, T2504A, and G2631T, although T2504A and G2631T were also present in linezolid-susceptible S. epidermidis RP62A (1,2). The most commonly reported G2576T mutation was not detected (1,2). We also compared study isolates with S. epidermidis RP62A and observed nucleotide mutations consistent with L94V (L101V from S. epidermidis American Type Culture Collection 12228, not associated with linezolid resistance) and G152D amino acid changes (2,8) and amino acid changes in the new D159E and A160P in L3 ribosomal protein. Mutations in this protein were linked to linezolid resistance, although definitive conclusions are not available (8). The cfr gene and mutations in ribosomal proteins L4 or L22 were not detected in the study isolates.

All isolates recovered had the same pulsed-field gel electrophoresis type and belonged to sequence type (ST) 2/clonal complex (CC) 5 (ST2 formerly belonged to CC2) (10) also detected among linezolid-resistant S. epidermidis from Europe, Brazil, and the United States (1–3). S. epidermidis from patient 1, considered representative of the observed clone, revealed a high ability to adhere to abiotic surfaces and grow in the biofilm form, which can facilitate infections associated with indwelling medical devices. This strain was classified as strongly adherent and had higher optical density (OD570nm = 2.33 ± 0.34) than a blank sample (culture medium: Luria Bertani broth + glucose; OD570nm = 0.2 ± 0.03). The OD570nm of the positive-control was 2.69 ± 0.44.

S. epidermidis ST2/CC5 is disseminated in hospital settings worldwide and is characterized by a high level of genetic diversity, an increased recombination/mutation rate, biofilm production ability, and acquisition of a high number of staphylococcal cassette chromosome mec elements (10). In Portugal, S. epidermidis ST2/CC5 has been observed in the community (10). We report emergence of methicillin- and linezolid-resistant S. epidermidis in a hospital in Portugal and its persistence for at least 7 months. Identification of the successful multidrug-resistant S. epidermidis ST2/CC5 clonal lineage highlights the need for strict infection control.
control procedures and revision of therapeutic strategies (e.g., linezolid use for the treatment of methicillin-resistant *Staphylococcus* spp. only when vancomycin is not a treatment option because of elevated MIC or clinical failures) to preserve therapeutic effectiveness of linezolid. Effective control of linezolid-resistant *S. epidermidis*, including among hospital-discharged patients who had received linezolid, is critical for preventing the potential for an epidemic in this hospital, and, on a larger scale, in Portugal, as has occurred for other gram-positive methicillin-resistant *S. aureus* and vancomycin-resistant enterococci.

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Composite SCCmec Element in Single-locus Variant (ST217) of Epidemic MRSA-15 Clone

To the Editor: Since early epidemiologic studies of methicillin-resistant Staphylococcus aureus (MRSA) were published, it has been clear that the majority of nosocomial MRSA infections worldwide are caused by isolates derived from a few highly epidemic MRSA (EMRSA) clones. These are thought to have emerged through acquisition of the staphylococcal cassette chromosome mec (SCCmec) element by successful methicillin-susceptible S. aureus strains, within 5 major lineages or clonal complexes (CCs) including CC22 (1). Although epidemic clones are found worldwide, shifts of the predominant clones over time in which the emerging and usually more antibiotic drug–susceptible clones replace the older ones have been noted in countries, in small regions within countries, and in single hospitals (2). The reasons and mechanisms of such replacement as well as the epidemiologic dynamics leading to the success of a particular epidemic clone are largely unknown.

In Italy, isolations of classical EMRSA clones such as ST8-MRSA-I, ST247-MRSA-I, and ST239-MRSA-III decreased from the 1990s to the 2000s; during the same period ST228-MRSA-I increased, became established, and turned into the predominant clone in Italy (3). The genesis of other clones, such as ST8-MRSA-IV and ST22-MRSA-IV, which were associated with a tendency towards decreased multidrug resistance, was documented during 2000–2007 (3). Similar to occurrences in other European countries, the gentamicin-susceptible Panton-Valentine leukocidin–negative ST22-MRSA-IV clone, also known as EMRSA-15 (1), is now becoming predominant in Italy, replacing ST228-MRSA-I in hospital settings (4).

As part of another investigation, we recently isolated a MRSA strain from the nasal swab samples of a 5-year-old boy and his parents. The 3 isolates shared the same antibacterial drug resistance pattern (oxacillin and ciprofloxacin resistance) and proved to be identical by pulsed-field gel electrophoresis, SCCmec typing, and agr typing. Remarkably, 2 months earlier, the child had been admitted to a pediatric hospital for 10 days to be evaluated and treated for behavioral problems. A MRSA isolate, which was identified in a nasal sample obtained and analyzed just before discharge in the absence of clinical symptoms and was not further investigated, showed the same antibacterial drug resistance pattern as the 3 isolates collected later. In the absence of an epidemiologic history of exposure outside the hospital, it seems reasonable to assume that the strain was acquired by the child in the hospital and then transmitted to his parents.