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First nosocomial outbreak of *vanA*-type vancomycin-resistant *Enterococcus raffinosus* in France

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SUMMARY

Background: Vancomycin-resistant *Enterococcus raffinosus* has rarely been associated with nosocomial infection and outbreaks.
Aim: To report the successful control of a nosocomial outbreak of *vanA*-type vancomycin-resistant *E. raffinosus* in a surgical intensive care unit.
Methods: The investigation of the outbreak is reported with control measures taken. Molecular typing of vancomycin-resistant *E. raffinosus* isolates was performed by repetitive sequence-based polymerase chain reaction (PCR).
Findings: Between September and October 2014, vancomycin-resistant *E. raffinosus* isolates were isolated from four patients. The index patient had been hospitalized previously in Portugal, and was not found to be colonized by vancomycin-resistant enterococci on screening cultures obtained at admission. However, vancomycin-resistant *E. raffinosus* was isolated from a bile sample 19 days after hospital admission. All four isolates were resistant to both vancomycin and teicoplanin due to the presence of the *vanA* gene, while remaining susceptible to daptomycin and linezolid. Repetitive sequence-based PCR confirmed the spread of a single *vanA*-positive *E. raffinosus* clone. Infection control measures including direct PCR screening on rectal specimens, contact precautions, and cohorting of patients and personnel led to successful control of the outbreak.
Conclusion: This is the first reported outbreak of *vanA*-type vancomycin-resistant *E. raffinosus* in France in both clinical and screening specimens among hospitalized

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patients. The inability of routine selective screening media to detect the vancomycin-resistant *E. raffinosus* in the index case likely contributed to the outbreak.

Introduction

For the last two decades, vancomycin-resistant enterococci (VRE) have emerged as an important nosocomial problem worldwide, and are associated with increased healthcare-associated morbidity, mortality and costs.[1] VRE outbreaks are mainly caused by *Enterococcus faecium* and, less commonly, *Enterococcus faecalis*, with *vanA* and *vanB* being the two most important genotypes clinically.[2] Vancomycin-resistant isolates belonging to other enterococcal species appear sporadically. *Enterococcus raffinosus* was first described in 1989 by Collins *et al.*,[3] and has rarely been associated with human infections.[4–7] Thus, few vancomycin-resistant *E. raffinosus* have been reported among VRE clinical isolates.[8–11] To the authors' knowledge, only three clonal disseminations of vancomycin-resistant *E. raffinosus* have been reported from the USA, Poland and the UK.[12–14]

This article reports the first French outbreak due to *vanA*-type vancomycin-resistant *E. raffinosus*, affecting patients in a surgical intensive care unit (SICU), and describes the epidemiological investigation and characteristics of the single clone involved.

Materials and methods

Hospital setting and surveillance

The outbreak occurred in a 15-bed SICU housed in an 800-bed tertiary care teaching hospital in the Paris area. According to French guidelines, isolation precautions are applied to patients admitted from foreign hospitals at admission until rectal swab screening specimens are reported negative for multi-drug-resistant (MDR) micro-organisms (i.e. VRE and carbapenemase-producing Enterobacteriaceae).[15] VRE screening is usually performed by culturing a rectal swab on to selective media. The current outbreak of vancomycin-resistant *E. raffinosus* was managed similarly to vancomycin-resistant *E. faecium* outbreaks.[15]

Microbiology

During the outbreak, all contact patients were screened every week by performing the GeneXpert VRE assay (Cepheid, Toulouse, France) on rectal swab specimens, in accordance with the manufacturer's instructions. A rectal swab was also cultured on to selective chromID VRE agar (bioMérieux, Marcy-l'Étoile, France), incubated aerobically at 35°C, and read after 24 h and 48 h. Species-level identification was obtained by MALDI-TOF mass spectrometry (Microflex; Bruker Daltonics, Bremen, Germany).

Antimicrobial susceptibility testing

Minimum inhibitory concentrations were determined using the broth microdilution method as described by the guidelines of the Clinical and Laboratory Standards Institute. The following agents were tested: ampicillin, vancomycin, teicoplanin, rifampicin, gentamicin, erythromycin, clindamycin, tetracycline, tigecycline, ciprofloxacin, linezolid and daptomycin. Results were interpreted according to the 2014 European Committee on Antimicrobial Susceptibility Testing breakpoints (http://www.eucast.org/clinical_breakpoints/).

Genotypic analysis

Vancomycin (*vanA*, *vanB*, *vanD*), aminoglycoside [*aad6*, *aac(6′)-Ie-aph(2″)-Ia*, *aph(2″)-Ib*, *aph(2″)-Ic*, *aph(2″)-Id*; *aph(3″)-IIIa*, *ant(4′)-Ia*], tetracycline [*tet*(O), *tet*(L), *tet*(M)] and macrolide [*erm*(B), *mef*(A)] resistance genes were screened by PCR.

Molecular typing was performed following a commercialized semi-automated rep-PCR method (DiversiLab, bioMérieux) and using the *Enterococcus* DNA fingerprinting kit, as described previously.[16] The Pearson correlation distance method was used to create a similarity matrix, and a dendrogram was generated. Isolates sharing more than 95% of similarity with indistinguishable fingerprint patterns were grouped and designated as a rep-PCR cluster.

Results

Outbreak description and control measures

The index case (Patient 1) was a Portuguese patient, admitted to the hospital for liver surgery. His recent history included hospitalization in the preceding three months in a hospital in Portugal. He underwent a selective liver resection and was admitted to the 15-bed SICU at the study hospital. In accordance with national guidelines and local infection control policy, he was screened on admission for carriage of MDR bacteria, and placed on contact precautions. Rectal screening by culture was negative for VRE, and contact precautions were lifted. On day 19 of admission, a *vanA*-type vancomycin-resistant *E. raffinosus* was isolated from a bile sample of Patient 1. He was treated with linezolid, and contact precautions were immediately resumed. All contact patients present in the hospital were identified and screened for VRE intestinal carriage using the GeneXpert VRE assay and rectal swab cultures. Transfer of cases and contact patients to other units in and out of the hospital was stopped. During the following days, two additional patients from the SICU were identified as intestinal carriers of vancomycin-resistant *E. raffinosus* (Patients 2 and 3).

All patients infected or colonized by vancomycin-resistant *E. raffinosus* were placed on contact precautions, including the use of protective equipment and enhanced hand hygiene. Patients present in the unit were cohorted in three distinct areas with dedicated nursing staff: VRE patient section, contact patient section and VRE-free patient section. All SICU patients had screening swabs performed every week. Extensive cleaning of