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Successful infection control for a vancomycin-intermediate *Staphylococcus aureus* outbreak in an advanced emergency medical service centre

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SUMMARY

Background: A vancomycin-intermediate *Staphylococcus aureus* (VISA) (vancomycin minimum inhibitory concentration: 4 mg/L) outbreak occurred in an advanced emergency medical service centre [hereafter referred to as the intensive care unit (ICU)] between 2013 and 2014.
Aim: Our objective was to evaluate the infection control measures that were successful.
Methods: Seventeen VISA strains were isolated from the sputum of 15 inpatients and the skin of two inpatients. Fourteen VISA strains were recognized as colonization. However, three VISA strains were isolated from the sputum of three inpatients with pneumonia. Environmental cultures were performed and VISA strains were detected in five of 65 sites. Pulsed-field gel electrophoresis (PFGE) and multi-locus sequence typing (MLST) was performed on 21 VISA strains.
Findings: Molecular typing including PFGE and MLST showed that the patterns of 19 VISA strains were identical and those of the other two VISA strains were possibly related. This meant that a horizontal transmission of VISA strains had occurred in the ICU. In August 2013, the infection control team began interventions. However, new inpatients with VISA strains continued to appear. Therefore, in October 2013, the ICU was partially closed in order to try to prevent further horizontal transmission, and existing inpatients with the VISA strain were isolated. Although new cases quickly dissipated after the partial closure, it took approximately five months to eradicate the VISA outbreak.
Conclusion: Our data suggest that despite the employment of various other infection control measures, partial closure of the ICU was essential in terminating this VISA outbreak.

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Introduction

Meticillin-resistant *Staphylococcus aureus* (MRSA) is a major causative organism of hospital-acquired infection. MRSA strains easily colonize hosts, particularly immunodeficient patients, and can cause a variety of serious infections.[1–4] The principal mode of transmission is via the transiently colonized hands of hospital personnel.[5,6] Outbreaks of MRSA in intensive care units (ICUs) or neonatal intensive care units are often prolonged and may result in substantial morbidity and mortality.[7,8] Vancomycin is used widely as treatment for MRSA infections.[9,10] In 1997, however, the first vancomycin-intermediate *Staphylococcus aureus* (VISA) (vancomycin MIC: 8 mg/L) strain was isolated from the surgical wound of a Japanese infant whose infection did not respond favourably to long-term vancomycin therapy.[11] Furthermore, a decrease in the effectiveness of vancomycin for the treatment of MRSA has subsequently been reported in both the USA and Japan.[12–14] After the report of the first VISA patient, cases emerged in many countries.[15–19] However, to the best of our knowledge, no other VISA outbreaks have been reported thus far. In this report, we describe a VISA outbreak in our advanced emergency medical service centre (hereafter referred to as the ICU) and the stepwise infection control measures, along with our evaluation of them.

Methods

Ethical approval

All studies described herein were approved by the Human Ethics Review Boards of Kurume University (14121).

Setting and outbreak description

In the Kurume University Hospital, there are 25 diagnosis and treatment departments that serve 24 wards with 1025 beds, including an ICU with 43 beds. The ICU accepts many severe patients from ambulance and helicopter emergency medical services. A VISA strain was first detected from the sputum of an inpatient in the ICU in January 2013. Private room isolation and the reinforcement of direct or indirect contact infection measures were performed for the inpatient with the VISA strain. However, additional inpatients with VISA strains subsequently emerged. The simultaneous identification of three new inpatients with VISA at the beginning of August 2013 led to the identification of an outbreak, and interventions by the infection control team (ICT).

Bacterial strains and patients

Twenty-two VISA isolates from the 17 inpatients and five environments in the ICU between January and September 2013 were enrolled in this study.

Minimum inhibitory concentration

The minimum inhibitory concentrations (MICs) of vancomycin, oxacillin, cefazolin, cefepime, imipenem, erythromycin, clindamycin, levofloxacin, gentamicin, sulfamethoxazole–trimethoprim, rifampicin, and linezoid were determined in reference to MicroScan (Siemens Healthcare Diagnostics Inc., Tokyo, Japan) via the broth-dilution method, in accordance with the guidelines of the Clinical and Laboratory Standards Institute.[20] The vancomycin MIC of VISA was defined as 4–8 mg/L. When the strains of VISA were detected, a second antimicrobial susceptibility method was employed to confirm that these strains were in fact VISA isolates, the drug sensitivity of which was measured using MicroScan (Pos Combo 3.2J Panel and Pos MIC 3.3J Panel) (Siemens Healthcare Diagnostics).

Molecular typing

Pulsed-field gel electrophoresis (PFGE) against 21 VISA strains (16 from inpatients and five from environments) was performed as described previously.[1,6] The DNA was digested with *Sma*I (Takara Shuzo Co., Shiga, Japan). CHEF Mapper pulsed-field electrophoresis systems (Bio-Rad Life Science Group, Hercules, CA, USA) were used for the electrophoresis, with a potential of 6 V/cm, with switch times of 0.47 and 63 s, and run times of 20 h and 18 min. After staining with ethidium bromide, the PFGE patterns were interpreted based on the criteria described by Tenover *et al.*[21]

Multi-locus sequence typing (MLST) of the seven housekeeping genes (*arcC*, *aroE*, *glpF*, *gmk*, *pta*, *tpi*, *yqiL*) was performed as previously described by Enright *et al.*[22] Briefly, to prepare template DNA for polymerase chain reaction (PCR), genomic DNA was purified from each *S. aureus* strain using a Cica Geneus DNA extraction reagent (Kanto Chemical Inc., Tokyo, Japan) according to the manufacturer's protocol. PCR amplifications of MLST loci were performed with an ExTaq DNA polymerase (Takara Shuzo Co.) according to the protocol recommended by the manufacturer. The PCR profile included denaturation at 96°C for 2 min, followed by 35 cycles of denaturation at 96°C for 20 s, annealing at 55°C for 30 s, and extension at 72°C for 30 s, with a final extension at 72°C for 10 min. The amplified fragments were purified with a QIAquick PCR purification kit (Qiagen, Hilden, Germany) and sequenced with a Big Dye terminator cycle sequencing ready reaction kit v2.0 (PE Biosystems, Foster City, CA, USA) using an ABI PRISM 3100 Genetic Analyzer (PE Biosystems) according to the supplier's protocol. The sequence of each amplicon was assigned to an allele by reference to the MLST database (http://saureus.mlst.net/).[23]

Results

Bacterial strains and patient characteristics

Seventeen VISA strains were isolated from the sputum of 15 inpatients and the skin of two inpatients between January and September 2013 (Figure 1). The ages of the 17 inpatients (13 males and four females) ranged from 30 to 89 years with a mean of 65.6. The diagnoses on admission included trauma in six cases; cerebral haemorrhage, severe burn, and haemorrhagic or septic shock (two cases of each); plus pancreatitis, aortic dissection, panperitonitis, gastrointestinal perforation, and myocardial infarction (one case of each). The mean detection period of the VISA strain after admission was 19.2 days, ranging from seven to 43 days, and four of the 17 inpatients had previously been treated with vancomycin. Fourteen VISA strains were recognized as colonization, and three VISA strains were isolated from the sputa of three inpatients