GeneXpert Captures Unstable Methicillin-Resistant Staphylococcus aureus Prone to Rapidly Losing the mecA Gene

Diana E. Ciardo, Sibylle Burger, Michael Payer, Christian Lee, and Nadine McCallum

Institute of Medical Microbiology, University of Zürich, Zurich, Switzerland; NeuroZentrum Hirslanden, Zürich, Switzerland; and Labormedizinisches Zentrum Dr. Risch, Schaan, Liechtenstein

Received 28 October 2009/Returned for modification 22 February 2010/Accepted 2 June 2010

A cefoxitin-susceptible Staphylococcus aureus strain was identified by the Cepheid GeneXpert as methicillin-resistant S. aureus (MRSA). This strain was highly unstable and rapidly lost SCCmec upon subculturing in vitro, indicating that unstable MRSA is best detected by gene amplification-based methods.

CASE REPORT

A 62-year-old woman underwent posterior lumbar decompression and stabilization L3 to L5 for intractable lumbar pain and neurogenic claudication due to severe stenosis and instability. One month after surgery, the patient experienced progressive lumbar pain; the wound area showed signs of inflammation without purulent secretion. The C-reactive protein (CRP) level was elevated to 98 mg/dl, and body temperature was elevated up to 40°C. Computer tomography showed correct decompression and placement of transpedicular screws and intervertebral cages, with no signs of loosening or abscess formation. A postoperative superficial and potentially deep wound infection was diagnosed. Blood cultures were taken, and empirical intravenous antibiotic therapy with vancomycin, flucloxacillin, and rifampin was administered for 4 days. Fever subsided, blood cultures became positive for Staphylococcus aureus, and intravenous therapy was continued with only flucloxacillin and rifampin for 13 days. The patient was then discharged with levofloxacin and rifampin per os, which was followed up 1 week after initial antibiotic treatment, and local pain subsided, blood cultures became positive for S. aureus, and intravenous therapy was continued with only flucloroxacin and rifampin for 13 days. The patient was then discharged with levofloxacin and rifampin per os, which was continued for a total of 6 weeks. The CRP level normalized 3 weeks after initial antibiotic treatment, and local pain subsided within 2 months. Further follow-up over 1 year with CRP and clinical and radiological controls was uneventful, and the patient fared well.

The initial S. aureus isolate appeared to be susceptible to methicillin, with an oxacillin MIC of 0.38 mg/liter, as tested by Etest (bioMérieux). The Xpert MRSA (GeneXpert system; Cepheid) performed according to Rossney et al. (17), however, identified a methicillin-resistant S. aureus (MRSA). The presence of the mecA gene was confirmed by a specific PCR amplification used as a control in SCCmec typing (14; data not shown). In addition, the strain showed very weak, inconclusive PBP2a production by latex agglutination upon β-lactam induction (MRSA-Screen; Denka Seiken Co., Ltd., Tokyo, Japan) (16). Such extremely-low-level methicillin resistance can occasionally occur in community MRSA (cMRSA) strains (12), although PBP2a agglutination remains positive, despite low-level resistance.

Published ahead of print on 9 June 2010.

* Corresponding author. Present address: Viollier AG, Spalenring 145/147, Postfach, 4002 Basel, Switzerland. Phone: 41 61 486 14 45. Fax: 41 61 486 14 87. E-mail: diana.ciardo@viollier.ch.
clones were closely related despite the slightly larger SmaI-E band of subclone 4, differences in the frequency of rifampin resistance formation, and variability in colony morphotype.

The variants were very likely to have evolved due to rearrangements arising during storage. Nonhemolytic variants within *S. aureus* are known to occur under laboratory and clinical conditions. They can arise by slipped mispairing, a replication error in the *agr* operon, which also controls hemolysin production. Loss of methicillin resistance from clinical isolates has been reported previously, and instability of the SCCmec element in specific strains has been described (4, 7). It is also known that the genetic background of a strain can determine the stability of SCCmec in *S. aureus* (11). Certain MRSA strains seem to be more prone to losing SCCmec or the mecA gene upon storage (6, 7, 9, 19). Isolates without the mecA gene but positive by Xpert MRSA have previously been described (18), but in this isolate, the GeneXpert test also became negative after storage, as did the mecA-specific PCR.

The very weak PBP2a agglutination in the initial culture, which is unusual even for low-level-resistant cMRSA, suggested that the majority of the bacteria in the original sample must have had already lost mecA and that the proportion still producing PBP2a was just above detection levels. Neverthe-
REFERENCES


