Bacteraemia due to meticillin-resistant *Staphylococcus aureus* carrying the *mecC* gene in a patient with urothelial carcinoma

María Pilar Romero-Gómez,† Marta Mora-Rillo,‡ Fernando Lázaro-Perona,† María Rosa Gómez-Gil† and Jesús Mingorance†

†Servicio de Microbiología Clínica, Hospital Universitario La Paz, IdiPAZ, Paseo de La Castellana, 261, Madrid 28046, Spain
‡Unidad de Enfermedades Infecciosas y Microbiología Clínica, Hospital Universitario La Paz, IdiPAZ, Paseo de La Castellana, 261, Madrid 28046, Spain

We present a case of bacteraemia due to meticillin-resistant *Staphylococcus aureus* (MRSA) carrying the *mecC* gene. The susceptibility to meticillin of *Staphylococcus aureus* was investigated directly from one blood culture bottle using GenomEra MRSA/SA (Abacus Diagnostica Oy) test. This test identified *S. aureus* but the presence of the *mecA* gene result was negative, and the isolate was reported as meticillin-sensitive *Staphylococcus aureus* (MSSA).

Susceptibility studies were done using VITEK 2 AST-P588 susceptibility cards (bioMérieux). The strain was identified as MRSA by the VITEK 2 system, although oxacillin MIC was low (0.5 µg ml⁻¹). In view of these results, the isolate was tested for the presence of the *mecC* gene by a specific PCR and was verified as MRSA carrying *mecC*. The emergence of this new *mecA* homologue could have important consequences for the detection of MRSA when routine PCR methods are used as an identification method or provisional detection of MRSA, as in the case reported in this article, because *S. aureus* carrying the *mecC* gene will be wrongly diagnosed as meticillin susceptible. Negative results must be interpreted with caution and should be followed by conventional culture, and antimicrobial susceptibility testing or detection of *mecC* gene by a specific PCR.

The first meticillin-resistant *Staphylococcus aureus* (MRSA) was described in the early 1960s, soon after the introduction of meticillin in human therapy, and since then it has become a major public health issue due to the worldwide spread of several clones. The genetic mechanism of meticillin resistance was identified as a gene called *mecA*, that codes for a specific meticillin-resistant transpeptidase (penicillin-binding protein 2a). The gene is inserted in a mobile genetic element known as the Staphylococcal chromosomal cassette (SCCmec) which is integrated into the *S. aureus* chromosome (Ito et al., 1999). The penicillin-binding protein 2a coded by *mecA* has a low affinity for β-lactam antimicrobial drugs; thus bacteria expressing this protein are resistant to almost all β-lactams (Ruimy et al., 2008).

A new divergent *mecA* homologue (*mecC* or *mecA_4GA251*) (García-Alvarez et al., 2011; Shore et al., 2011) has been recently described in a novel SCCmec type XI (Shore et al., 2011). The recent discovery of the SCCmec XI, which harbours this new *mecC* element with only 70% sequence similarity to *mecA* genes, raises concerns about the detection of MRSA carrying this element (García-Alvarez et al., 2011).

This new *mecC* was detected in milk samples from dairy cows in the UK and in human clinical samples in the UK, Germany, Denmark and Ireland (Cuny et al., 2011; García-Alvarez et al., 2011; Petersen et al., 2013; Shore et al., 2011). Prevalence studies of *S. aureus* isolates carrying *mecC* in Denmark indicate that the frequency could be as high as 4%.

Previous studies in animal and clinical human strains have shown that MRSA carrying *mecC* gene was identified as MRSA by VITEK 2 automated system (growth in the presence of 6 µg ml⁻¹ cefoxitin according to the VITEK 2 Advanced Expert System), although oxacillin MICs were low (0.5 µg ml⁻¹) or moderately high (≈ 4 µg ml⁻¹). The isolates were misidentified as *mecA*-negative, and therefore meticillin sensitive, by routine PCR (Cartwright et al., 2013; Walther et al., 2012).

We present a case of bacteraemia due to MRSA carrying the *mecC* gene. The patient was a 76-year-old man recently diagnosed as having urothelial carcinoma. He was without...
relevant epidemiological history, had not travelled abroad and had no known contact with livestock. In January 2013, laparoscopic radical cystectomy with lymphadenectomy and cutaneous transureteroureterostomy reconstruction was performed. After such urological surgery two catheters are placed temporarily on both urethers to aid healing. Usually these catheters fall down through ileostomy when ureter anastomosis has healed. A fortnight after discharge, the patient was admitted due to fever and anuria after the pigtail catheter spontaneously fell out.

On physical examination, his blood pressure was 135/75 mmHg, pulse rate was 70 beats min⁻¹ and body temperature was 37.7 °C. Laboratory tests showed a white blood cell count of 1200 cells mm⁻³ (neutrophils 82 %, lymphocytes 6 %), C-reactive protein 272.8 mg dl⁻¹ and creatinine 2.61 mg dl⁻¹. Urgent bilateral nephrostomies were performed on admission and empiric antibiotic treatment with meropenem was started.

Blood cultures taken during the patient’s febrile episode were incubated in an automated BACTEC FX system (Becton Dickinson). Both aerobic and anaerobic bottle cultures became positive after 3 days of incubation for Gram-positive cocci in clusters. The organism was identified directly from blood culture bottles as *S. aureus* by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry.

The meticillin susceptibility of *S. aureus* was investigated directly from one blood culture bottle by using the GenomEra MRSA/SA (Abacus Diagnostica). This test identified the *S. aureus* and did not detect the mecA gene; therefore, the isolate was reported as MSSA.

The organism was subcultured onto sheep blood and chocolate agar. The sheep blood and chocolate agar plates were incubated at 35 °C in an atmosphere containing 5% CO₂ for 48 h, and *S. aureus* was identified in pure culture.

The susceptibility studies were done using VITEK 2 AST-P588 susceptibility cards (bioMérieux). The strain was identified as MRSA by the VITEK 2 system although oxacillin MIC was low (0.5 µg ml⁻¹), and was confirmed by cefoxitin disk diffusion. The isolate was susceptible to other antimicrobial drugs tested.

After the first microbiological result of MSSA on blood cultures the empirical meropenem treatment was changed to targeted cloxacillin. Treatment was changed to daptomycin after the VITEK 2 result. Neither clinical complication nor metastatic seeding due to *S. aureus* bacteraemia was observed and the patient was discharged after 14 days of targeted treatment.

In order to confirm the diagnosis of MRSA, detection of the mecA gene by PCR and the agglutination of a penicillin-binding protein 2a assay were done, with both test results negative.

In view of these results, the isolate was tested for the presence of mecC by a specific PCR and was verified as MRSA carrying mecC (García-Álvarez et al., 2011). Molecular typing of the isolate showed that it belonged to ST1945 and was spa type t843. These characteristics matched those of the most prevalent clones described by García-Álvarez et al. (2011).

The discovery of mecC could have important consequences for the detection of MRSA when routine PCR or monoclonal antibody methods are used for the rapid detection of MRSA, because mecC *S. aureus* will be wrongly diagnosed as meticillin susceptible. Negative results must be taken carefully and should be followed by conventional culture and antimicrobial susceptibility testing.

The principal requirement for clinical microbiology and infection control is the accurate identification and characterization of isolates in a timely manner. PCR assays should be designed for simultaneous detection of mecA and mecC to afford the rapid identification and differentiation of MRSA (Pichon et al., 2012; Stegger et al., 2012).

### References


