Severe human bone infection due to methicillin-resistant Staphylococcus aureus carrying the novel mecC variant

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Sir, Staphylococcus aureus is a commensal bacterium capable of causing a wide range of opportunistic infections. Methicillin-resistant S. aureus (MRSA) emerged 50 years ago and has since disseminated worldwide in hospitals, in the community and, more recently, in livestock.1 Methicillin resistance is usually due to the expression of the mecA gene, and can be detected by both phenotypic methods (cefoxitin and moxalactam susceptibility) and genotypic methods targeting the mecA gene. We describe here a human case of invasive bone infection due to an unusual MRSA strain in which these classical diagnostic approaches yielded conflicting results that prompted further investigation.

A 48-year-old French gardener was admitted to Limoges Hospital (France) with severe sepsis in December 2010. His medical history included obesity, arterial hypertension, partial cryptogenic epilepsy for 20 years, a painful lesion of the tongue for 3 years, and otitis and sternal pain for 3 weeks. Written consent to publish this case was obtained from the patient. Physical examination revealed right parotitis fistulizing into the external auditory canal. CT of the chest showed anterior mediastinitis with sternal osteitis, while a facial CT scan showed a tympanic bone fracture.

Culture of ear fluid, blood and a retrosternal abscess yielded an S. aureus strain (LIM84). Antibiotic susceptibility was determined with the Vitek 2 system (bioMérieux, Marcy l’Étoile, France), and methicillin resistance was sought with the disc diffusion method using moxalactam and cefoxitin. The strain was susceptible to all tested antibiotics, except for β-lactam agents, which gave different results for the different methods: the Vitek 2 oxacillin MIC categorized the strain as susceptible (0.5 mg/L), whereas the Vitek 2 Cefoxitin Screen test and diameters for moxalactam (22 mm) and cefoxitin (24 mm) categorized the strain as resistant. Our in-house PCR method was negative for the mecA gene.2 We thus suspected that the LIM84 strain was exhibiting resistance to methicillin due to either a modified or a borderline S. aureus phenotype.

Eight months later, in August 2011, the French National Reference Centre for Staphylococci (FNRCs) issued an alert concerning the emergence of a new mecA variant, initially called mecA(LGA251), but later classified as mecC.3 This mecC gene had been first identified in the UK and Denmark in animal and human specimens.4–8 Other cases have been further described in other animals,4–8 and the MeC phenotype was difficult to detect.5,9 We thus sent the S. aureus LIM84 strain to the FNRCs, which detected mecC using a specific PCR method.10 Molecular characterization showed that LIM84 belonged to the agr3 allele type, spa-type 19280 and clonal complex CC130, which is reported to be the most prevalent clone harbouring mecC. Use of a microarray (Alere StaphyType DNA microarray; Alere Technologies GmbH, Jena, Germany) indicated that strain LIM84 harbouring no specific virulence factors, with an absence of scn, sak and cph (as previously reported by Harrison et al.11), suggesting that the clone was not adapted to humans; however, acquisition of other specific genes (unknown or not included in the microarray) indicating human adaptation cannot be excluded.
The patient was a gardener living on a farm that raised livestock and thus came into contact with cows, suggesting a possible contamination of the patient from an animal origin. The patient was initially treated with claxacinil, gentamicin and metronidazole for only 3 days and then switched to vancomycin, gentamicin and fosfomycin. After 2 weeks of this intravenous treatment, he was prescribed oral ofloxacin and rifampicin for 8 weeks. A CT scan of the chest 23 days after the initial hospitalization showed a marked decrease in the retrosternal collection and the patient’s parotitis, and the infection was considered cured at the end of treatment.

One year later, in February 2012, the patient was sampled at home to detect the possible persistence of mecC-MRSA carriage. Two different methicillin-susceptible Staphylococcus aureus strains were isolated from nose and throat swabs. mecC PCR was negative, and the genetic backgrounds of the two isolates differed from that of strain LIM84 on the basis of agr typing and DNA microarray results. This demonstrated the absence of long-term colonization with the mecC-positive strain.

This case illustrates the ongoing evolution of bacteria, requiring microbiologists to investigate atypical results of antibiotic susceptibility tests. It also shows that conventional phenotypic tests are still useful for detecting new or atypical resistance mechanisms, which cannot be detected by genotypic methods. This challenges the view that genotypic methods are now the gold standard for resistance studies of S. aureus. As mecC detection is crucial for optimal patient management, this capability should be added to commercial diagnostic tools.

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Author contributions
O. B. isolated the strain and wrote the report, F. L. and M. B. were responsible for genotypic analyses, B. F. and P. V. managed the patient and F. L. and M. C. P. reviewed the report.

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The bla<sub>CTX-M-1</sub> IncI1/ST3 plasmid is dominant in chickens and pets in Tunisia

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