TITLE: WHOLE GENOME SEQUENCING OF METHICILLIN-RESISTANT *Staphylococcus aureus* FROM ST5 LINEAGE OF HUMAN AND CANINE ORIGINS PINPOINTS THE BACTERIAL TRANSMISSION DIRECTION

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ABSTRACT:

Methicillin-resistant *Staphylococcus aureus* (MRSA) are associated with both community- (CA-MRSA) and health-care-acquired (HA-MRSA) infections in humans. The capability of MRSA to infect pets has gained increasing attention. The majority of the isolates detected in pets were typical CA-MRSA isolates (i.e. Panton-Valentine leukocidin-PVL positives, carry SCC*mec*IV or V and display increased susceptibility to non-β-lactams). In the last 10-15 years, isolates from the CC5 lineage have entered Brazilian hospitals. Recently, we isolated ST5 (CC5)-SCC*mec*II MRSA—related to the HA-MRSA, New-York Japan clone—from dogs in Rio de Janeiro. This result motivated us to perform studies on the genomic epidemiology of CC5 MRSA from dog (strain SA112) and human origins (strains CR14-004, CR14-035, CR14-055 and CHU15-056) to get some clues to the evolutionary origin of the dog isolate, since typical HA-MRSA are not commonly reported in animals. Whole-genome sequencing was performed using Illumina MiSeq platform, and genomes were assembled (Velvet and Geneious softwares) and annotated (NCBI Prokaryotic Genome Annotation Pipeline). Phylogenetic analysis based on SNP calling—using these and other CC5-related genomes available on NCBI—grouped canine and the human strain CR14-035 in the same cluster. Specialized annotation using Patric tool revealed a very similar virulence profile for these two genomes. Typical *S. aureus* genomic islands were manually annotated using Local BLAST, and both strains carry νSAα, νSAβ and νSAγ. Resistance traits were identified with ResFinder tool and there was no difference between both genomes. A bacteriophage search, using the Phaster tool, detected important differences in the type of phages found and in its position on the bacterial chromosome. The virulence potential of the canine (SA112) and human (CR14-035) strains was assessed using a *Caenorhabditis elegans* model. Both MRSA were virulent to worms and there was no statistical significance between the survival curves using Kaplan-Meyer test. Despite the differences found in phage profiles all phages detected in the animal strain have already been detected in human *S. aureus* isolates. All together, these results suggest that the evolution of this canine strain has not probably occurred in animals, inferring a human-to-animal transmission. The circulation in community settings of a MRSA lineage commonly found in hospitals is an additional challenge for the public health surveillance authorities.

Key-words: HA-MRSA, CA-MRSA, canine infection, genomic epidemiology, MRSA phylogeny and evolution

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