27th ECCMID Vienna, Austria 22 – 25 April 2017

The congress of ESCMID

Session: P006 MRSA and MSSA: epidemiology and resistance

Category: 3a. Resistance surveillance & epidemiology: MRSA, VRE & other Gram-positives

22 April 2017, 15:30 - 16:30
P0125

Deciphering a rare methicillin-resistant Staphylococcus aureus strain: genome sequencing and molecular characterization of CC15-MRSA

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Background: The molecular epidemiology of methicillin resistant *Staphylococcus aureus* (MRSA) continues to evolve with the emergence and spread of new strains. CC15-MRSA has hitherto only been sporadically described in literature although methicillin sensitive *S. aureus* (MSSA) from this lineage are ubiquitous. Recently, we reported the first identification of this rare MRSA strain in retail meat products and nosocomial infection in the Middle East. With the emergence of CC15-MRSA in our setting we have carried out the whole genome sequencing of the identified isolates to gain insight into the genetic characteristic of this rare MRSA. While whole genome sequencing data have already been reported for CC15-MSSA, this has previously not yet been the case for CC15-MRSA.

Material/methods: Four isolates, three from retail camel meat and one from a nosocomial infection were studied. *S. aureus* identification and confirmation of methicillin resistance was performed using

standard laboratory techniques. Genomic DNA was extracted and whole genome sequencing was carried out using the Illumina HiSeq2500 genome analyzer. Reads were assembled and the resulting contigs were mapped on a similar Genbank entry AHVD00000000.1, derived from a ST15-MSSA. Due to presence of repeats, the SCC element could not be scaffolded into a single contiguous sequence.

Results: All the CC15-MRSA isolates had a new MLST profile 13-13-1-1-81-11-13, which is a single locus variant of ST15. These isolates comprised of pta=81 instead of pta=12 in canonical ST15. pta=81 differs from pta=12 by only 1 SNP. This SNP was present in all four isolates. Four copies of tnpIS256 (size 1200 nt) and five copies of tnpIS431 (size 700 nt) were present. There were two identical copies of a tnpIS256-based insertion element carrying *aacAaphD* with one copy presumably inserted between SCC and *fusC*, and the other copy disrupting the chromosomal outer surface protein gene *sasC*. The SCC element was spread over three contigs with each contig terminating in tnpIS431. One of these contig comprised of a recombinase gene *ccrAA* (deviant variant not in GenBank), *ccrC-PM1*, *fusC* and a helicase while another one included *mvaS*, *dru*, *mecA.* The third one comprised *yobV*. The overall constellation was interpreted as a novel SCC*mec*V /SCC*fus* composite element. The same element was also found by microarray hybridization in CC97-MRSA. CC15-MRSA had a different variant *of hsdM/hsdS* at the major pathogenicity island vSaα compared to the reference CC15-MSSA genome. One of the isolates carried a 30-kb plasmid packed with additional antibiotic resistance genes, namely *cadD*, *cadX*, *blaI*, *blaR*, *blaZ*, *lnuA*, *aadD* with three copies of the plasmid per cell.

Conclusions: We provide the first molecular characterization of a rare MRSA strain. The findings suggest the possibility of uptake of an SCC element from (or a transfer to) another clonal complex.