P2055

Abstract (poster session)

Methicillin-resistant Staphylococcus aureus harbouring mecA-LGA251, a new mecA-homologue: limited impact on the outcome of infective endocarditis treated with flucloxacillin in a rat model

F. Laurent*, J.M. Entenza, A. Tristan, M. Giddey, J. Vouillamoz, F. Vandenesch, P. Moreillon (Lyon, FR; Lausanne, CH)

Background: S. aureus remains a leading cause of infective endocarditis worldwide. Penicillin-M is recommended as the antibiotic of choice for the treatment of methicillin susceptible S. aureus (MSSA) whilst vancomycin is the antibiotic of choice in case of endocarditis caused by mecA-encoded methicillin resistant S. aureus (MRSA). Recently, MRSA harboring a brand new and highly divergent mecA homologue (named mecA-LGA251, located in a novel SCCmec) have been reported. However the clinical impact of this new resistance mechanism on the outcome of clinical infection is unknown. The aim of the present study was to assess the efficiency of penicillinase-resistant betalactam antibiotic in a rat model of S. aureus endocarditis using strains harboring the classical mecA gene or the mecA-LGA251 variant. Methods: S. aureus strain Mu50 was used as reference for mecA-positive strains, and strain NCTC13552 as reference for mecA-LGA251-positive strains (MRlgaSA). Two clinical MRlgaSA isolates were tested, one from a human specimen (SA820) and one from a veterinary sample (SA1100) isolated in France in 2007 and 2008, respectively. The presence of the mecA-LGA251 gene was confirmed by specific PCR. Oxacillin (OXA) MIC (E-test) and OXA population analysis profile (PAP) were determined. Rats with catheter-induced aortic vegetations (---) were treated for 3 days with doses simulating the kinetics after intravenous administration in humans of the standard dose of flucloxacillin (FCX) of 2 g every 6 h. Animals were killed 8h after the end of the last dose and vegetations were cultured. Results: OXA MICs for Mu50, NCTC13552, SA820 and SA1100 were >32, 0.125, 0.38 and 0.5 mg/L, respectively. PAP revealed highly heterogeneosus OXA resistance for the three MRIgaSA isolates, without secondary increasing of OXA MICs for the most resistant selected colonies. At sacrifice, all vegetations from untreated animals (n= 5) as well as those infected with Mu50 and treated with FCX (n= 6), were infected. In contrast, FCX treatment successfully cured 6/8 (75%) and 9/9 (100%) vegetations of animals infected with strain SA820 and SA1100, respectively ($p<0.05$). Conclusion: Although resistant to cefoxitin and harboring additional PBP, the MRlgaSA isolates responded quite well to a humanized FCX treatment in the rat endocarditis model. Since mecA-LGA251 may be miss-diagnosed, it is not unlikely that cases of MRlgaSA infections, even severe, are currently treated successfully with beta-lactams.