6

Assessing the role of implant stability on the development of staphylococcal osteomyelitis in a murine fracture model

Sabaté Brescó Marina[1,2], Kluge Katharina[1], Moriarty Fintan[1], O'Mahony Liam[2], Richards, R. Geoff[1], Ziegler Mario[2]
[1] AO Research Institute, Davos, Switzerland
[2] Swiss Institute of Allergy and Asthma Research (SIAF), University of Zurich, Davos, Switzerland

Introduction: Implant instability is considered a risk factor for delayed healing of fractures and infection; however, little experimental data is available confirming this belief, or describing the underlying mechanisms. In this study, a murine model based upon the MouseFix™ system (RISystem AG, Davos)[1,2] was used to investigate immune response in bone when fractures are fixed with rigid or non-rigid (i.e. flexible) constructs. Implant associated osteomyelitis was developed in some groups using a clinical isolate of *Staphylococcus epidermidis*, one of the leading etiologic agents of orthopedic infections[3]. The development of infection and immune responses associated with either rigid or flexible implants was assessed.
Methods: Rigid and flexible MouseFix™ titanium plates, with or without *Staphylococcus epidermidis* (10^4 CFU) contamination, were used with a femoral osteotomy in C57bl/6 mice (female, 20-26 week old). Mice were sacrificed at 7, 14, and 30 days after surgery (n=6-9 per group). Live bacteria from the implant, bone, and soft-tissue were quantified. Bone and spleen cells were kept for mRNA analysis and stimulated to collect supernatants for cytokine and chemokine quantification. Lymph node and bone cells were characterized by flow cytometry.
Results: At each time-point over 30 days, unstable fractures had a higher infection rate compared to stable fractures. Monocytic lineage cells (F4/80+) increased in percentage over time in all four conditions, probably due to macrophage recruitment, but slightly more in animals with flexible implants suggesting a role of these cells. In lymph node, IL-17+ cells were increased at early time-points in infected animals, especially in those where bacteria were not detected. Levels of IL-10+ cells were similar between all groups at 7 days, increasing in not-infected animals later. When studying IL-17+/IL-10+ ratio in CD3+CD4+ cells, animals with flexible devices seemed to be skewed to a more anti-inflammatory response, which could explain differences observed.
(1) Grongroft, I., et al., Fixation compliance in a mouse osteotomy model induces two different processes of bone healing but does not lead to delayed union. J.Biomech., 2009. 42(13): p. 2089-2096. (2) Matthys, R. and S.M. Perren, Internal fixator for use in the mouse. Injury, 2009. 40 Suppl 4: p. S103-S109. (3) Montanaro, L., et al., Scenery of Staphylococcus implant infections in orthopedics. Future.Microbiol., 2011. 6(11): p. 1329-1349.