Paper - Basic Science

Paper Session: PTOA

Articular Fracture in the Knee of T-Cell-Deficient Mice Results in More Severe Posttraumatic Arthritis

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Purpose: Posttraumatic arthritis (PTA) is responsible for a significant portion of osteoarthritis (OA) cases in the US. Acute inflammatory synovitis has been implicated in studies of articular fracture and PTA. The synovium may play a role in regulating the immune response and mediating joint inflammation following trauma. Recent findings suggest that modulation of the immune response could be a novel treatment for PTA. T cells are critical effector cells in adaptive immunity. Overall, the influence of T cells is unclear, as their role in response to intra-articular fracture (IAF) has not been investigated. The purpose of this study was to determine how the loss of T-cell regulation would affect the severity of PTA following joint trauma utilizing an IAF model. T cells contribute to long-term inflammation in a variety of settings. We hypothesized that IAF in animals without T-cell function would result in a reduced severity of PTA.

Methods: T-cell-deficient, athymic, nude mice (NU:J) and wild-type mice (C57BL/6NJ) underwent closed IAF as previously described. Mice were sacrificed at 8 weeks post-fracture, and hind limbs were harvested for assessment of bone morphology via microCT and histologic assessment of arthritis via Mankin grading (safranin O/fast green) and synovitis (hematoxylin and eosin). Immune cell subsets were identified in whole blood via polychromatic flow cytometry and in joint tissues via immunohistochemistry.

Results: The absence of T cells exacerbated PTA following IAF with nude mice having significantly greater arthritic changes on the medial side of the knee joint ($P = 0.036$) and greater synovial inflammation laterally ($P = 0.027$). Higher levels of natural killer (NK) cells were detected in nude mice whole blood samples ($P = 0.113$) and significantly higher levels were found in the synovial tissue ($P = 0.029$).

Conclusion: Our hypothesis was not supported. The data instead support a role for T cells in regulating inflammation in PTA after IAF, possibly via regulatory T cells (Tregs). This is consistent with studies reporting the population of Tregs, a subset of CD4+ T cells, are decreased in the blood of OA patients compared to healthy controls and decreased Tregs were associated with impaired bone healing in patients and mice. Immune cell populations in whole blood were reflective of the immune cell phenotypes seen in synovial findings following fracture. Without T cells, NK cells had a larger role in the immune response, and more severe degenerative joint disease was observed. Therefore, targeting of Tregs or the NK axis may provide new areas to explore for prevention of PTA following articular injury.