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Original Completed Research

Characterization of the Intraarticular Cytokine Response in Children with Septic Arthritis

Walter Dehority, Kathryn Helmig, Scott Plaster, Nathan Huff, Andrew Parsons, Susan Tigert, Selina Silva

Background: Acute septic arthritis (ASA) is the most common pediatric orthopaedic infection, and may be associated with severe sequelae. An improved understanding of the intra-articular inflammatory response in ASA may facilitate the use of immunomodulatory agents to attenuate the deleterious effects of the host immunological response on synovial tissue, help monitor disease progression and differentiate ASA from non-infectious arthritides. To our knowledge, no study has characterized the intra-articular cytokine response in children with ASA in detail. Given this, we attempted to validate a multi-plex cytokine assay for use in the blood and synovial fluid of children with ASA.

Methods: Twelve children (8 controls undergoing orthopaedic surgery for non-infectious conditions and 4 with ASA) were prospectively enrolled over 14-months. Blood and synovial fluid were simultaneously collected intra-operatively from each subject, and the levels of 40 different cytokines were determined using a 40-plex assay (BioRad). Cytokines were grouped by function and structure into 12 different groups for analysis. Given the large number of comparisons undertaken, the Benjamini-Hochberg method was utilized to control for type 1 errors, with an *a priori* false discovery rate of 10% utilized.

Results: Subjects with ASA were all male (100.0% vs. 62.5%; $p=0.0398$), and were younger than controls (mean age 8.0 vs. 13.1 years, $p=0.0400$). Significant elevations were seen in interleukins with chemokine properties in the blood of children with ASA compared with controls (median 622.3 vs. 120.2 pg/mL, $p=0.0032$), while significant elevations in 6 different cytokine groups were seen in synovial fluid compared with controls, most notably interleukins with chemokine properties (median 1,625.7 vs. 88.1 pg/mL, $p=0.0001$) and IL-6 (median 8,294.3 vs. 10.7 pg/mL, $p=0.0066$).

Conclusions: Analysis of the cytokine response in children with ASA deserves further study in order to identify patterns of cytokine elevation with therapeutic and diagnostic potential.