Induction of Vascular Endothelial Growth Factor (VEGF) in septic joint disease

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INTRODUCTION:
Bacterial arthritis is a progressive joint disease which includes rapid destruction of articular cartilage even in the absence of a causative factor. The resulting periinfectious arthropathy is mainly characterized by a self-perpetuating joint destruction and an extensive angiogenesis in the emerging pannus-like synovial membrane, but the underlying molecular mechanisms remain incompletely understood. This study was conducted to elucidate the role of angiogenic and cartilage-destructive vascular endothelial growth factor (VEGF) in septic arthritis.

METHODS:
Aspirates of synovial fluid from patients with pyogenic arthritis were examined for intraarticular released VEGF-levels by ELISA. In vitro studies with primary and C28/I2 chondrocytes were performed to study the inducibility of VEGF after challenge by gram-positive and -negative bacteria by using real-time RT-PCR, ELISA and immunohistochemistry. Activation of the transcription factors AP-1 and SP-1 after microbial stimulation was assessed by EMSA-experiments. The necessity of the TLR, ERK-1/-2, AP-1- and SP-1-pathway for infectious VEGF-induction was examined by using specific antibodies.

RESULTS

Figure 1 A-C: A: ELISA experiments revealed a strong expression of VEGF in osteoarthritic (OA) and septic cartilage (PA) but neglectable amounts in healthy tissue samples. Immunohistochemistry confirmed these results and showed an increased VEGF staining in tissue sections of septic cartilage (C) compared to healthy control samples (B).

Figure 2: VEGF is induced in primary bovine chondrocytes after challenged by bacterial supernatants. PAS: Pseudomonas aeruginosa supernatant; SAS: Staph. aureus supernatant, TSB: growth medium.

Figure 3: VEGF is induced in chondrocytes after bacterial challenge. Blocking experiments revealed that the induction is mediated via the AP-1/SP-1 and ERK-1/-2 pathway. Using TLR-specific antibodies, bacteria mediated VEGF expression was partly suppressed in cultured chondrocytes.

DISCUSSION:
In summary our findings indicate a role of cartilage-derived VEGF in perpetuating destructive arthropathy after intraarticular infections by enhancing catabolic processes in the articular cartilage itself (Pufe et al. 2004) or by stimulating neoangiogenesis in the emerging pannus-like synovial membrane (Nagashima et al. 1995). The elucidation of the infectious VEGF induction pathway may provide a therapeutic target in the future for prevention of periinfectious cartilage degradation in articular joints.

REFERENCES: