CXCL12 AND CXCR4 AS NOVEL BIOMARKERS IN PATIENTS WITH GOUTY ARTHRITIS

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Background: CXCR4 binds to its ligand CXC chemokine CXCL12 and plays a role in induction of recruitment of inflammatory cells including leukocytes and endothelial cells. The CXCL12/CXCR4 axis has been implicated in the pathogenesis of some types of inflammatory arthritis and autoimmune diseases including rheumatoid arthritis, osteoarthritis, systemic lupus erythematosus, and ankylosing spondylitis. Evidence of the pathogenic role of CXCR4 and CXCL12 in uric acid-induced inflammation has not been presented.

Objectives: The aim of this study is to evaluate the expression of chemokine receptor CXCR4 and its ligand CXCL12 in patients with gout and uric acid-induced inflammation.

Methods: Forty patients with intercritical gout and 27 controls were consecutively enrolled. Serum levels of interleukin-1β (IL-1β), IL-18, CXCL12, and CXCR4 were assessed using enzyme-linked immunosorbent assay. Gene and protein expression for these target molecules were measured in human U937 cells incubated with monosodium urate (MSU) crystals using real-time reverse transcription polymerase chain reaction and Western blot analysis.

Results: Patients with intercritical gout showed higher serum IL-1β, IL-18, and CXCL12 levels than those in controls, but not serum CXCR4 level. Serum CXCR4 level in gout patients was associated with serum IL-18 level, uric acid level, and uric acid/creatinine ratio (r = 0.331, p = 0.037; r = 0.346, p = 0.028; r = 0.361, p = 0.022, respectively). U937 cells incubated with MSU crystals significantly induced CXCL12 and CXCR4 mRNA and protein expression, in addition to IL-1β and IL-18. In cells transfected with IL-1β siRNA or IL-18 siRNA, CXCL12 and CXCR4 expression was down-regulated compared to non-transfected cells in MSU crystal-induced inflammation. Receiver operator characteristic (ROC) curve analysis showed that serum CXCL12 for the diagnosis of gout was an area under roc curve (AUC) of 0.690 (p = 0.009).

Conclusion: This study reveals that CXCL12 and CXCR4 are involved in the pathogenesis of uric acid-induced inflammation and gouty arthritis.

REFERENCES: