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Enthesitis in seronegative spondyloarthropathies with special attention to the knee joint by MRI: a step forward toward understanding disease pathogenesis

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Abstract

Seronegative spondyloarthropathies are a unique group of disorders sharing similar clinical characteristics (e.g., inflammatory back pain, spondylitis, sacroiliitis, uveitis, inflammatory bowel disease, skin rashes, and enthesitis). Clinical and genetic similarities suggest that they also share similar causes or pathophysiologies. Rheumatoid factor (RF) is characteristically negative in this group of disorders, hence collectively termed seronegative spondyloarthropathies (SpA). They include psoriatic arthritis, ankylosing spondylitis, reactive arthritis, ulcerative colitis, and Crohn's disease. "Enthesitis", the term used to describe inflammation at tendon, ligament, or joint capsule insertions, is considered a common feature in this domain and was included in the European Spondyloarthropathy Study Group criteria for the classification of SpA. Evaluation of entheseal-related changes at different joints by MRI became an important item on the research agenda in both differentiated and undifferentiated arthritis. Most of the research focused on MRI findings in the hand and wrist joints among patients with RA and SpA and support two patterns of inflammation "RA" phenotype where synovial involvement is the primary target of inflammation and "SpA" pattern where enthesitis comes first followed by synovitis. In this review, we summarize the literature on enthesitis in SpA and focus on MRI findings in the knee joint in the SpA group of disorders and subclinical synovitis among patients with skin psoriasis. Keywords Enthesitis . Knee enthesitis . Knee joint . MRI imaging of en thesitis. Rheumatoid arthritis . Seronegative spondyloarthropathies.

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Correlations of Urinary Biomarkers, TNF-LikeWeak Inducer of Apoptosis (TWEAK), Osteoprotegerin (OPG), Monocyte Chemoattractant Protein-1 (MCP-1), and IL-8 with Lupus Nephritis

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Abstract

Objective This case-controlled study was designed to correlate urinary biomarkers, TNF-like weak inducer of apoptosis (TWEAK), osteoprotegerin (OPG), monocytes chemoattractant protein-1 (MCP-1), and interleukin-8 (IL- 8) levels, with renal involvement in a cohort of systemic lupus erythematosus (SLE) patients to examine their diagnostic performance.

Patients and Methods In 73 SLE patients, and in 23 healthy volunteers, urinary levels of TWEAK, OPG, MCP-1, and IL-8 levels were measured. Disease activity was assessed by total SLE disease activity index, and renal activity by renal activity index (rSLEDAI), and both were correlated with urinary biomarkers. Sensitivity, specificity, and predictive values of individual biomarkers to predict lupus nephritis were also calculated.

Results Significantly higher levels of urinary biomarkers were observed in SLE patients with lupus nephritis (LN) compared with those without LN (TWEAK, $p<0.001$; MCP-1, $p<0.001$; OPG, $p<0.001$; IL-8, $p<0.032$). Other significantly higher levels were observed in SLE patients with LN compared with control subjects (TWEAK, MCP-1, OPG, and IL-8 $p<0.001$). Positive correlations were observed between rSLEDAI and TWEAK ($r=0.612$ and $p< 0.001$), MCP-1 ($r=0.635$ and $p<0.001$), and OPG ($r=0.505$ and $p<0.001$).

Conclusions Urinary levels of TWEAK, OPG, and MCP-1 positively correlate with renal involvement as assessed by rSLEDAI with reasonable sensitivity, specificity, and predictive values to detect lupus nephritis while IL-8 was not significantly associated with global or rSLEDAI.

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STUDY OF THE C677T MUTATION IN THE METHYLENE TETRAHYDROFOLATE REDUCTASE GENE AS A GENETIC RISK FACTOR FOR METHOTREXATE-RELATED ADVERSE EFFECTS IN RHEUMATOID ARTHRITIS PATIENTS

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Methotrexate is a synthetic antifolate compound. It acts as a highly selective inhibitor of the enzyme dihydrofolate reductase enzyme. The current study examined the relationships between C677T polymorphism in the MTHFR gene and methotrexate related adverse effects in a cohort of RA patients at 6 and 12 moths duration. The study comprised 624 RA Caucasian patients who were recruited from 6 centers across the United Kingdom (UK). Of the 624 patients recruited 210 early RA patients had full data available at 6 months were selected to take part in this study and 272 early RA patients had data available at 12 months also were included. At 6 months analysis no significant differences were observed between RA patients with CC genotype compared to CT/TT genotype; in relation to bases line demographic features, disease characteristics and smoking status ($p>0.05$). a significant difference was observed in relation to systemic steroid use at base line being higher in RA patients with CT/TT genotype compared to those with CC genotype ($p =0.047$). At 6 months of the putative predictors of MTX toxicity, only DAS28-CRP was found to be significantly associated with the odds of experiencing side effects. While at 12 months, only the presence of radiographic erosions was found to be significantly associated with the odds of response to MTX monotherapy. We concluded that C677T polymorphism in the MTHFR gene is neither predictive of toxicity nor efficacy in RA patients treated with MTX. Further prospective clinical trials in larger cohorts are required to accurately evaluate whether or not MTHFR genetic polymorphisms could be a reliable predictors of efficacy and/or toxicity in RA patients treated with MTX.

Keywords: Methotrexate, C677T polymorphism, folic acid

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C677T POLYMORPHISM IN THE METHYLENETETRAHYDROFOLATE REDUCTASE GENE AND METHOTREXATE-RELATED ADVERSE EFFECTS AND RESPONSE TO THERAPY IN RHEUMATOID ARTHRITIS PATIENTS

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Rheumatoid arthritis (RA) is a chronic disease often having symmetrical polyarthritis of the diarthrodial joints. Methotrexate (MTX) is the most commonly used Disease modifying antirheumatic drugs (DMARDs) and has proven to reduce disease activity. The aim of the current study is to examine the relationships between C677T polymorphism in the MTHFR gene and MTX related adverse effects and response to therapy in a cohort of RA patients. The study comprised 624 RA Caucasian patients who were recruited from 6 centers across the United Kingdom (UK). Of the 624 patients recruited, 210 early RA patients had full data available at 6 months were selected to take part in this study. At 6 months analysis no significant differences were observed between RA patients with CC genotype compared to CT/TT genotype; in relation to bases line demographic features, disease characteristics and smoking status ($p>0.05$). A significant difference was observed in relation to systemic steroid use at base line being higher in RA patients with CT/TT genotype compared to those with CC genotype ($p=0.047$). At 6 months of the putative predictors of MTX toxicity, only DAS28-CRP was found to be significantly associated with the odds of experiencing side effects. In conclusion, C677T polymorphism in the MTHFR gene is neither predictive of toxicity nor efficacy in RA patients treated with MTX. Further prospective clinical trials are required to accurately evaluate whether or not MTHFR genetic polymorphisms could be a reliable predictors of efficacy and/or toxicity in RA patients treated with MTX.

Keywords: Rheumatoid arthritis, Methotrexate, Methylenetetrahydrofolate reductase genetic polymorphism, DAS28-CRP.

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