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TNFa AS PREDICTION OF EFFICACY OF COMBINED TREATMENT IN RHEUMATOID APTHRITIS

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Objective: To evaluate the benefit of TNF α measurement in patients with rheumatoid arthritis (RA) receiving methotrexate (MT) in combination with infliximab (IF) for prediction of the treatment efficacy.

Methods: 18 female RA patients were followed up for 30 weeks of treatment. Their mean age was 46±8.4 y, and mean duration of the disease was 13.2±5.3 y. RF positiveness was detected in 83.3%, and ACPA presence in 66.8% of patients. X-ray stages III and IV were most common (66.8%). Extra-articular manifestations of RA (mild anemia) were found in 66.8% of the subjects. All the patients received MT at a dose of 12.5-20 mg/week, NSAIDs were also regularly used as an additional medication on demand in every case. IF treatment was provided by the common protocol. Measurement of TNFα was carried out using ELISA kits, its upper limit of reference interval was 6 pg/ml.

Results: All RA patients had high disease activity. After the 3^{rd} IF infusion, 88.9% of them showed marked clinical and laboratory improvement. In most patients pretreatment levels of serum TNFa did not significantly go beyond the normal range. The exception was 11.1% of patients who had elevated serum TNFa (mean level 6.96 pg/ml), all of them had more pronounced effect of therapy on the clinical and laboratory manifestations. At the same time, patients with high CRP level (more than 3 times higher than upper reference limit), higher TNFa concentrations, higher DAS28-CRP(4) scores, normal BMI (19.6-23.3 kg/m²), and extraarticular manifestations had very good of moderate response for treatment and higher extent of decrease of all these markers at the end of follow-up.

Conclusion: The groups with a good and satisfactory response after 30 weeks of MT and IF treatment were consisted of patients with a normal BMI, a higher degree of disease activity, higher concentrations of CRP and TNF α , as well as with the extraarticular manifestations.

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ANGIOPOIETIN-LIKE PROTEINS AND ANTIBODIES TO MODIFIED VIMENTIN PARTICIPATE IN VARIOUS MECHANISMS OF DEVELOPMENT OF PERIARTICULAR OSTEOPOROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Objective: To evaluate the role of immune and biochemical markers in increasing bone resorption and the development of periarticular osteoporosis (OP) in rheumatoid arthritis (RA).

Methods: Levels of angiopoietin-like protein type 4 (ANGPTL4) (RayBio Human ANGPTL4 ELISA Kit test system, RayBiotech), ANGPTL3 (Human Angiopoietin-like Protein 3 ELISA test system, Bio Vendor), ESR, C-reactive protein (CRP), IgM rheumatoid factor (RF), antibodies to cyclic citrulline peptide (anti-CCP) and antibodies to modified vimentin (anti-MCV) were determined in the blood serum of 88 patients with reliable RA. 57 patients with RA (64.8%) underwent osteodensitometry on a bone X-ray densitometer Lunar DPX (GE, USA) with an assessment of the condition of the bone tissue of the proximal femur according to the T-criterion (reduction from -1.0 to -2.4 – osteopenia; from -2.5 and below – osteoporosis).

Results: There was established a direct dependence of the level of ANGPTL3 on the presence of OP (r=0.36) as well as the level of ANGPTL4 on the presence of osteopenia (r=0.44). A negative relationship was found between the values of criterion T and anti-MCV (r=-0.673), but not anti-CCP (p>0.05). Anti-MCV has been shown to induce differentiation and activation of osteoclasts. ANGPTLs can activate the proliferation processes in the synovial membrane, and ANGPTL4 is able to regulate the activity of osteoclasts through the hypoxia/HIF (hypoxia inducible factor) system in order to enhance osteoclastic bone resorption.

A significant negative dependence of ANGPTL3 on a marker of cartilage damage - urine CartiLaps (r=-0.24) and creatinine level in urine (r=-0.28) was revealed. A negative dependence of ANGPTL4 on triglycerides (r=0.42, p=0.018), vitamin D (r=-0.417) and calcium levels in the blood (r=-0.522) and in urine (r=0.797) was found. There is no relationship between the presence of anti-MCV and the level of both ANGPTL3 (p>0.05) and ANGPTL4 (p>0.1). All these facts may indicate different mechanisms of development of periarticular OP in patients with RA positive for anti-MSV and ANGPTL proteins types 3 and 4.

Conclusion: ANGPTLs are potential markers of the destruction of major joint components in RA. The progression of periarticular OP occurs according to various development mechanisms in the groups of seropositive for ANGPTLs and anti-MCV patients with RA.