

REVIEWS

Y. Sheytanov and I. Sheytanov. RANK/RANK LIGAND/OSTEOPROTEGERIN SYSTEM – PROGRESS IN BONE BIOLOGY RESEARCH. DENOSUMAB – A NEW POSSIBILITY FOR TREATMENT OF OSTEOPOROSIS

Summary. In the last 15 years, a considerable progress in the research of bone biology has been made. There was identified and clarified the RANK/RANK Ligand/OPG pathogenetic pathway. The balance RANK Ligand/OPG turned to be decisive for osteoclast differentiation, activation and survival. It plays a crucial role in the pathogenesis of osteoporosis and some other bone diseases characterized by increased bone resorption. The inhibition of RANK-Ligand is a new therapeutic strategy in this kind of bone pathology. It can be accomplished with antibodies against RANK-Ligand, blockade with synthetic OPG or blockade of post-receptor signals. Lately, there was elaborated a fully-human monoclonal antibody targeting the RAN- Ligand – denosumab with trade name Prolia. In experimental models and in some clinical studies, Prolia inhibits bone resorption and considerably increases bone mineral density. Impressive results were achieved in the 3-year study FREEDOM in postmenopausal women: reduction of the risk of new vertebral fractures by 68%, of hip fractures – by 40%, and of other extravertebral fractures – by 20%. Denosumab presents a new therapeutic alternative for osteoporosis and for prevention of associated fractures as well.

Key words: RANK, RANK-Ligand, osteoprotegerin, denosumab

ORIGINAL ARTICLES

L. Miteva, I. Manolova, M. Ivanova, R. Stoilov, R. Rashkov and S. Stanilova. LACK OF ASSOCIATION BETWEEN PROMOTER POLYMORPHISM –1082A/G IN INTERLEUKIN-10 GENE AND GENETIC PREDISPOSITION TO SYSTEMIC LUPUS ERYTHEMATOSUS

Summary. The aim of this study was to establish the association between –1082A/G polymorphism of IL10 gene and susceptibility to SLE in individuals from Bulgaria. A total of 157 patients who fulfilled the 1982 revised criteria of the American Rheumatism Association for the diagnosis of SLE were studied. Patients were compared with 126 healthy controls. Genotyping for –1082A/G polymorphism in IL10 gene was performed by amplification refractory mutation system (ARMS) – PCR assay. The distribution and the frequencies of the –1082A/G genotypes among the SLE patients were the following: 56 (0.36) AA, 74 (0.47) AG and 27 (0.27) GG. In the control group, 44 (0.35) were homozygous for the wild A-allele, 65 (0.52) were heterozygous, and the rest of 17 (0.13) were homozygous for the variant G-allele. The genotype GG was more frequent in SLE patients (27% vs 13%), although the difference did not reach statistical significance ($p = 0.393$). In addition, no association was found between the investigated polymorphism and the clinical manifestations of SLE. In conclusion, our current results suggest that promoter polymorphism –1082A/G in IL10 gene could not play an important role in the susceptibility to SLE in the Bulgarian patients.

Key words: interleukin-10, –1082A/G polymorphism, SLE

I. Gruev and A. Toncheva. CHRONIC RHEUMATIC INFLAMMATION AND SUBCLINICAL ATHEROSCLEROSIS – THE DIFFERENT FACE OF THE PATIENT AT RISK

Summary. The patients with inflammatory rheumatic diseases (IRD) have chronic autoimmune inflammation and high cardiovascular morbidity and mortality, due to accelerated atherosclerosis. The measurement of IMT is a non-invasive method for detection of subclinical atherosclerosis. Several clinical studies have shown that the patients with IRD have significantly higher values of IMT, compared with healthy controls. The aim of our study was to investigate the role of the chronic inflammation for the development of subclinical atherosclerosis (assessed by carotid sonography) in patients with IRD (rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis), in order to demonstrate the increased cardiovascular risk in this specific group of patients. 105 IRD patients and 72 hypertensive patients with one or more additional risk factor were investigated. Assessment of the traditional risk factors for atherosclerosis and markers of inflammation (SR, CRP) and bilateral carotid sonography were done to all patients. For the IRD group, additionally an X-ray and assessment of the number of the affected joints were performed. The IRD patients had better traditional risk profile and higher markers of inflammation, compared to the hypertensive group. They also had thicker intima-media (0.98 mm vs 0.84 mm) and more plaques (27,6% vs 22,2%) compared to sex- and age-matched hypertensive controls. Age and presence of IRD appeared to be independent predictors of subclinical atherosclerosis. In the IRD group, the subclinical atherosclerosis correlated with the duration of

the disease, number of affected joints, age and serum uric acid. Despite of their better traditional risk profile, and on the background of the higher markers of inflammation, the IRD-patients have more apparent signs of subclinical atherosclerosis. The traditional risk calculators should be adapted for this specific group of patients.

Key words: inflammatory rheumatic diseases, atherosclerosis, intima-media thickness

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