

REVIEWS

ZI. Kolarov. BIOLOGIC AGENTS INFLUENCING B-LYMPHOCYTES IN RHEUMATOID ARTHRITIS

Summary. The aim of rheumatoid arthritis treatment is outlined pointing out the lack of effect on the long-term disease prognosis of the classic antirheumatic agents – disease activity modifying drugs, corticosteroids and non-steroidal anti-inflammatory drugs. This is the reason for introduction of biologic agents into everyday clinical practice. Presented are the main groups and the respective biologic agents based on the internationally accepted guidelines and consensuses for their use in rheumatoid arthritis, the greatest part of them being the agents against TNF-alpha. Described is the pathogenetic role of B-lymphocytes in the light of the recent immunology achievements – antigen presentation followed by activation of T-lymphocytes, synthesis of autoantibodies and cytokines. Viewed are the main properties of Rituximab – monoclonal antibody against the cell membrane receptor CD20, the first biologic agent directed against B-lymphocytes, as well as the indications for its use in rheumatoid arthritis therapy. Listed are the new biologic agents against-B lymphocytes, some of them being still in a process of study like Belimumab – fully humanised MAB against B-lymphocyte stimulator BLyS; Atacicept (TACI-Fc Ig) which binds to B-lymphocyte activating factor (BAFF known also as BLyS) and proliferation-inducing ligand (APRIL); Orelizumab – humanised MAB against CD20, variant of Rituximab; Ofatumumab (HuMax-CD20) – humanised MAB against epitope of CD20; TRU-15 – MAB against CD20; Epratuzumab – anti-CD22 MAB with expected effect in LES and Sjogren syndrome, not studied till now in RA.

Key words: rheumatoid arthritis, B-lymphocytes, biologic agents, new representatives

R. Stoilov, M. Ivanova and I. Manolova. ANTIPHOSPHOLIPID SYNDROME AND ATHEROSCLEROSIS

Summary. In this article, we briefly discuss the contribution of autoimmune elements, such as autoreactive lymphocytes and autoantibodies to atherosclerosis, and the nature of enhanced atherosclerosis progression in autoimmune rheumatic diseases. We review an update of the classification criteria for definite antiphospholipid syndrome (2006) and the international consensus statement on this problem for clinical practice necessity. We summarize therapeutical dilemmas in the treatment of APS and atherosclerosis, which are not answered yet.

Key words: atherosclerosis, autoimmunity, APS, rheumatoid arthritis, systemic lupus erythematosus

K. Yablanski, ZI. Kolarov and S. Vladeva. MECHANISMS OF FIBROSIS IN SYSTEMIC PROGRESSIVE SCLEROSIS

Summary. Systemic sclerosis is an autoimmune disease in which diffuse fibrosis of vasculature, skin and major organs may lead to severe disability and death. The accumulation of increased extracellular matrix proteins is a result of increased fibroblast biosynthetic activity regulated at gene level. Fibroblast interactions with activated immune cells and their products – cytokines (TNF, TGF- β , IL-1, IL-6) contribute to the altered fibroblast phenotype. Scleroderma fibroblasts display a variety of phenotypic defects. Both immune inflammation and repair involve the recruitment, activation, apoptosis of effector cells. The activated immune cells may damage vascular endothelium, cause proliferation of fibroblasts, or stimulate fibroblasts to produce collagen. Endothelial cell damage can also activate the immune system or induce fibroblast proliferation. Collagen production and organ damage can induce immune activation thus perpetuating the cycle.

Key words: systemic progressive sclerosis, fibrosis, pathogenesis

D. Dimov. ACTUAL ASPECTS OF GOUT DIAGNOSTICS

Summary. 10 key recommendations for diagnosis of gout, developed by a task force of EULAR on the basis of the literary evidence material collected over the period from 1945 to 2005 as well as the expert consensus are presented. The recommendations strongly suggest that definitive diagnosis should be based on urate crystal observation in either acutely symptomatic or previously symptomatic but presently asymptomatic joints: that clinical, laboratory, and radiological findings are significant but not necessarily diagnostic; and that the risk factors and co-morbidities and, especially those associates with the metabolic syndrome should be taken into consideration, too. The survey also shows data available so far concerning the potential of the ultrasound investigation (ultrasonography) for diagnosis of gout and monitoring of its evolution spontaneously or under urate-lowering therapy.

Key words: gout, diagnostics, monitoring, ultrasonography

K. Nikolov and M. Baleva. ANCA IN THE DIAGNOSIS OF CHURG-STRAUSS' SYNDROME

Summary. The authors discuss clinical symptoms, main clinical stages and diagnostic criteria of the Churg-Strauss' syndrome (CSS). The major classification criteria for the diagnosis of the CSS are: asthma, involvement of the paranasal sinuses, eosinophilia (>10%), mono- or polyneuropathy, migrating lung infiltrates, biopsy verification showing extravascular eosinophilic infiltrate. Three major phases in the clinical course of CSS have been defined: early – "prevasculitis", vasculitis and postvasculitis phase. The investigation of ANCA in patients with severe asthma, rhinitis, nasal polyposis, eosinophilia and other CSS-associated symptoms and signs could help the differentiation from other chronic lung diseases (i.e., asthma, bronchopulmonary aspergillosis, chronic eosinophilic pneumonia, etc.), in patients with X-ray data for lung infiltrates and peripheral eosinophilia without concomitant asthma (i.e., in strongiloidosis, ascariidosis, toxocarosis, ankylostomatosis, allergic reaction to medications, hypereosinophilic syndrome, mycoses, tuberculosis), and in other systemic vasculitides (mainly Wegener's granulomatosis).

Key words: Churg-Strauss syndrome, ANCA

DRUG THERAPY

ZI. Kolarov. RITUXIMAB (MABTHERA): A BIOLOGIC AGENT WITH UNIQUE MECHANISM OF ACTION

Summary. In the light of the last achievements of immunology, the pathogenetic role of B-lymphocytes in rheumatoid arthritis is shown – antigen presentation followed by activation of T-lymphocytes, synthesis of autoantibodies, cytokine synthesis, and the conception of use of biologic agents for discontinuance of the enhanced B-cell activity. Presented are the main properties of Rituximab (MabThera) – monoclonal antibody against the cell membrane receptor CD20, the first biologic agent directed against B-lymphocytes, as well as the indications for its use in rheumatologic practice. Scrutinized are the mechanism of action of the drug, its pharmacokinetics, positive and negative effects, warning for the risk of anaphylactic reactions, use schema and measures against adverse allergic reactions. Listed are rheumatologic, oncologic and other diseases, potential candidates for treatment with rituximab.

Key words: Rituximab, mechanism of action, indications and contraindications

ZI. Kolarov. USE OF RITUXIMAB (MABTHERA) IN RHEUMATOLOGY PRACTICE

Summary. Viewed are the basic properties of rituximab (MabThera) – a monoclonal antibody against the cell membrane receptor CD20, first biologic agent directed against B-lymphocytes, and the indications for its use in rheumatologic practice. Scrutinized are the mechanism of action of the preparation, its pharmacokinetics, positive and negative effects. There are cited the results of the first investigations of rituximab (MabThera) and of two large scale randomized, double-blind, placebo-controlled studies – REFLEX and DANCER, in patients with rheumatoid arthritis. Several rheumatologic, oncologic and other diseases, potential candidates for treatment with rituximab (Mabthera), are pointed out. Unsolved problems, connected with the use of the preparation in everyday clinical practice are shown.

Key words: Rituximab, indications, pharmacokinetics, unsolved problems

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