Keynote Lecture

01 CYTOKINES IN SLE: TRANSLATIONAL PERSPECTIVES 2019

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Systemic lupus erythematosus (SLE) is characterised by a dysregulated immune system, which leads to an ongoing autoimmune reaction. Many different cytokines are produced during an autoimmune response causing chronic inflammation, and studies in both animal models of lupus and patients with SLE have revealed a number of cytokine pathways important in the disease process.[1]Amongst these is the B lymphocyte stimulator (BLyS), which promotes B-cell survival and autoantibody production, the interferons that activates most immune cells, tumor necrosis factor (TNF), which contributes to organ inflammation and interleukin (IL)-17, which can induce the production of additional inflammatory cytokines and chemokines. Most cytokines have pleiotropic effects and can either positively or negatively affect the expression or function of other cytokines. Thus, a cytokine can both promote organ inflammation and at the same time down regulate a central autoimmune process. Furthermore, different cytokines may be operative during early or longstanding SLE, as well as in different disease subsets. Consequently, the precise role of a single cytokine in SLE as well as other autoimmune diseases has proved difficult to determine. Despite this difficulty, targeting cytokines in several rheumatic diseases, such as rheumatoid arthritis and ankylosing spondylitis, has been a remarkably successful approach. However, in SLE it has been far more difficult to demonstrate clinical efficacy with drugs targeting a single cytokine and a large number of studies have, after early promising results, failed in Phase III trials. At the moment only belimumab, a human mAb that binds to BLyS, is the only approved specific anticytokine treatment in SLE.[2] Targeting cytokine receptors or downstream signaling molecules, such as the Janus kinase-signal transducers and activators of transcription (JAK-STAT) pathway, is at the moment intensively studied as therapeutic possibilities.[3] Another approach is administration of a regulatory cytokine, and induction of regulatory T cells by low dose IL-2 is now explored as new therapy for SLE.[4] However, In order to be successful in obtaining remission in our patients, we need to better understand the cytokine network in the disease and stratify patients not only on organ manifestations, but also on involved molecular pathways.[5]

Learning objectives

- Understand the pleiotropic effects of cytokines and their possible role in autoimmunity
- Review key cytokines involved in the SLE disease process
- Discuss different possibilities to modulate cytokine effects in SLE

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Debate: New developments in Basic Science and Clinical Research: Defining SLE

01 WE NEED BETTER CLASSIFICATION CRITERIA FOR LUPUS

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Systemic lupus erythematosus (SLE) is a complex disease characterised by a wide range of clinical manifestations and autoantibodies and virtually any manifestation is considered to be possible in patients with SLE. Classically the disease has a relapsing remitting course and is characterised by damage accrual, increased morbidity and mortality, comorbidities. Early recognition of the disease could allow early intervention, prevent damage accrual and improve long term outcomes. However, the disease onset may be insidious, with clinically evident disease developing over years, and this can delay both the diagnosis and the classification of SLE; in addition some patients presenting with signs and symptoms of systemic autoimmune diseases will never develop SLE but will remain undifferentiated over time (UCTD, undifferentiated connective tissue diseases). Finally many different conditions may mimic SLE.

Classification is required to include patients in clinical trials and these difficulties suggest the need for classification criteria able to classify early disease. The existing classification criteria (ACR and SLICC) appear to have a lower specificity in early disease, with an increase after 5 years of disease.

New classification criteria for SLE have been developed to define a threshold above which experts could classify SLE for the purpose of research.[1-4] Clinical and serological characteristics of early SLE patients compared with mimicking diseases, were identified to inform the development of these criteria with the specific aim to develop classification criteria able to capture patients in the early disease.

Learning objectives

- Describe the variability of the clinical picture of SLE and describe the characteristics of early SLE
- Highlight the difficulties for early diagnosis of SLE
- Differentiate early SLE from mimicking conditions
- Discuss the development of the new EULAR/ACR criteria and their performance in early SLE

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