SP0122 **AUTOIMMUNE PHENOMENA ASSOCIATED WITH BIOLOGICAL AGENTS**

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Biologic agents are being increasingly used in pediatric rheumatology, particularly TNF antagonists but also abatacept, tocilizumab, interleukin (IL)-1 antagonists and some other drugs. In Juvenile Idiopathic Arthritis (JIA) and some autoinflammatory diseases, data from phase 3 and extension trials or from cohorts such as Pharmachild allow to prospectively collect information on adverse events "of special interest", including autoimmune complications. A few patients develop autoimmune/dysimmune features while on biologics, as seen in adults, including central nervous system lesions, inflammatory bowel disease or psoriasis. In addition, in patients with systemic-onset JIA, anti- IL-1 treatment is usually associated with the appearance of a type 1 interferon signature (gene expression analyses) which might in some cases favour lupus-like autoimmune features.
On the other hand, among patients with early-onset arthritis, vasculitis, recurrent fever or other inflammatory manifestations, an increased number of children are diagnosed with complex monogenic diseases resulting in auto-inflammation, immune deficiency and autoimmunity. In such cases, biologics might not be responsible for the occurrence of autoimmune features that may sometimes be diagnosed on treatment. This distinction is important as biologics are useful treatments also in some of these patients, as was shown in patients with a diagnosis of Systemic-onset JIA and ANCA-associated glomerulonephritis in whom anti-IL-1 treatment was beneficial. It was also more recently shown in patients with *lipopolysaccharide-responsive beige-like anchor* (*LRBA)* mutations associated with autoimmunity and inflammation, including polyarthritis: as LRBA is a partner of cytotoxic-T lymphocyte antigen-4 (CTLA4),. abatacept has been used as a targeted treatment and shown efficacy.
We hence aim to discuss the way to explore patients who develop autoimmune features while on biologics in order to take the right decisions regarding treatment maintenance, withdrawal or modification and regarding patients follow-up.
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FRIDAY, 16 JUNE 2017

Health equity and economy - a vital relationship

SP0123 **UNCOVERING THE EQUITY GAP IN RHEUMATIC AND MUSCULOSKELETAL DISEASES**

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The aim of this lecture is to discuss the current evidence on the socio-economic inequities in disease outcomes in RMDs. Socio-economic determinants at the individual and country level will be considered, as well as the interplay between these factors. In particular, attention will be given to the role of different socio-economic factors in the access to biologic DMARDs in rheumatoid arthritis.
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SP0124 **HEALTH ECONOMICS AND HEALTH EQUITY: TWO COMPLEMENTARY DISCIPLINES**

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Health equity in the one hand refers to the absence of systematic disparities in health between different social groups in a given Society, a province, a country or a group of country. Health inequity thus corresponds to a situation in which health services are not similarly available to all people with the same health conditions and health needs, due to individual personal or socioeconomic characteristics.
Health economics in the other hand focuses on how to allocate health budgets in order to maximize the general health of the population as a whole. With regards to this, no specific attention is dedicated to socially disadvantaged subgroups. In addition, the most visible action in the field of health economics was the valorization of therapeutic innovation, i.e., the determination of its price not on production costs but on the value associated with this innovation.
Economic evaluation – i.e., determination of incremental cost-effectiveness ration – has lead during the last 20 years to substantial financial pressure on health care systems with dramatic increase in health expenditures mainly due to the costs of therapeutic innovation. Several studies have shown that such a process may increase health inequities within a country or a group of countries if specific actions are not taken to maintain or improve treatment availability and access to care to all the population members whatever their social, educational and economic characteristics.
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Biomarkers in cardiovascular rheumatology - state-of-the-art 2017

SP0125 **INFLAMMATION AND CARDIOVASCULAR DISEASE – RELEVANT METABOLIC BIOMARKERS**

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Patients with RA have increased mortality compared with the general population mostly due to higher cardiovascular disease (CVD), which is up to 50% more frequent [1]. Even after adjusting for traditional cardiovascular risk factors such as smoking, diabetes and hypertension, the risk for CVD is increased by up to twofold compared with the normal population [2]. Whilst traditional cardiovascular risk factors, contribute to the increased risk of mortality in RA patients, they do not fully explain increase in cardiovascular risk [3,4]. European League Against Rheumatism (EULAR) recommend regular assessment of cardiovascular risk in patients with RA [5]. Since traditional cardiovascular risk factor assessment equations, such as Framingham and the Systematic Coronary Risk Evaluation Score (SCORE) models, underestimate cardiovascular risk in RA, EULAR recommends multiplying such traditional cardiovascular risk scores by 1.5 for patients with RA. Such adjustment operates at the population level. Ideally, cardiovascular biomarkers that can predict future cardiovascular event in the individual patient will improve screening and management.
Biomarkers of cardiovascular disease can be divided into five major categories: lipids, inflammation, endocrine, vascular and prothrombotic [7]. HDL and LDL are used in routine clinical practice. However, they do not predict future cardiovascular events in patients with RA as the levels of HDL and LDL are suppressed during inflammation [8]. The ratio of HDL/LDL or total cholesterol/HDL is less affected by inflammation. Other lipid biomarkers include apolipoprotein A-1, apolipoprotein B, cholesterol ester transfer protein lipoprotein-associated phospholipase A2, small-dense LDL and paraxonase-1. They have been measured in patients with RA but their precise value in predicting cardiovascular risk in RA has not been determined.
High level of inflammation as measured by ESR and CRP is associated with increased cardiovascular risk in patients with RA. EULAR recommended adequate suppression of inflammation as a key strategy to reduce cardiovascular events [5]. Disease flares increased cumulative cardiovascular risk [9]. Many inflammatory mediators are elevated in RA, whether they can add to traditional cardiovascular risk score to improve individual risk prediction should be evaluated.
The vascular biomarker of cardiovascular disease, VCAM-1, has also been shown to elevated in patients with RA. High level of VCAM-1 was associated with high cardiovascular risk score[ix].
Metabolic syndrome is common in patients with inflammatory arthritis. Insulin resistance is a feature of metabolic syndrome. Fibrinogen and other prothrombotic molecules are part of the acute phase response, their levels are elevated in RA. Neither endocrine nor prothrombotic factors have been studied systematically in RA.
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SP0126 **THE VESSEL WALL IN IMIDS – NEW EMERGING VASCULAR MARKERS**

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Cardiovascular disease dependent on inflammatory accelerated atherosclerosis

leads to increased mortality in rheumatoid arthritis (RA). In addition to traditional, Framingham risk factors, several immuno-inflammatory cells, mediators and molecules may link atherosclerosis to arthritis. Among immune cells, primarily TH1 cells, as well as endothelial cells play a crucial role in synovial and vascular inflammation. Various cell surface molecules, such as adhesion receptors, CD40-CD40 ligand or members of the RANK-RANK ligand-osteoprotegerin system, as well as soluble pro-inflammatory cytokines, chemokines, autoantibodies and proteases have been implicated in RA and vascular damage. The early assessment of atherosclerosis and early intervention would decrease cardiovascular risk in RA.

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SP0127 TAPERING BIOLOGICS INDUCES A PROTHROMBOTIC STATE IN RHEUMATOID ARTHRITIS?

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In addition to the "traditional" risk factors for venous trombo-embolism (VTE), like age, trauma and immobilisation, inflammation could also be regarded a risk factor for VTE. For example, patients with acute inflammatory conditions (sepsis), but also patients with chronic inflammation, like inflammatory bowel disease (IBD) and rheumatoid arthritis (RA), have an increased risk of thrombosis.

Inflammation can lead to activation of coagulation, and vice-versa, coagulation also has considerable effects on overall inflammatory activity. First, the inflammatory cytokine network induces several pro-thrombotic conditions including insulin resistance, dyslipidaemia, endothelial dysfunction and alteration of coagulation and fibrinolysis. Second, activation of the extrinsic coagulation system and impairment of the fibrinolytic pathway may contribute to amplify and perpetuate the inflammatory response. Previous studies have reported several blood parameters that reflect a prothrombotic state in RA. These include increased levels of thrombin-antithrombin complex, prothrombin fragment F1+2, von Willebrand factor, plasmin-alpha2-antiplasmin complex and D-dimer, as well as an increased platelet count. Impaired fibrinolysis combined with increased antithrombin levels have also been reported in RA. An important mediator in the inflammatory pathway is tumor necrosis factor-α (TNF-α). In the general population, TNF-α induces a disbalance between clotting and fibrinolysis, resulting in a hypercoagulable state. Since TNF-α is the key player in RA, RA is an ideal "human model" to study the interplay between inflammation and coagulation. Hence, RA can be considered as a pro-thrombotic state, which explains partly why patients with RA are at increased risk of thrombo-embolic cardiovascular events.(1)

Only one small study suggested that TNF-inhibitors (TNFi) is accompanied with normalization of thrombotic biomarkers: an improvement of clinical and laboratory parameters as well as a reduction in the activation of coagulation and endothelial dysfunction was found in RA patients treated with a TNFi. In addition, we previously demonstrated that combination therapy with corticosteroids improves the procoagulant state that exists in early RA. (2)

Nowadays, tapering of biological therapies is becoming more and more standard of care. However, the effects on the coagulation status in RA are unknown. In light of the growing evidence of an increased cardiovascular morbidity and mortality in RA, mostly independent of traditional risk factors, treatment strategies in RA should not only aim at relieving symptoms and inhibiting joint destruction but should have a beneficial effect on the vasculature and haemostasis to reduce cardiovascular events. Although modest, there is evidence suggesting a beneficial effect of TNFi on the haemostatic status in RA. Unfavourable changes in haemostatic markers, such as TAT, F1+2, vWF, PAP, D-dimer and thrombin generation, which indicate a pro-thrombotic state, may therefore (re)occur when RA patients stop with TNFi treatment. We first assessed arterial wall inflammation with 18F-FDG PET scans in RA patients in remission under TNFi therapy or DMARD therapy versus controls. The FDG uptake in the aorta in DMARD remission patients was similar to the controls, whereas the uptake in RA patients in remission under antiTNF was significantly higher than in controls either when looking at the overall aortic uptake or the most diseased segment. Theoretically, stopping TNF blockade in these patients might lead to increased inflammation and thus coagulation activation. Therefore, we are presently investigating it and to what extent tapering/stopping TNFi therapy induces a pro-thrombotic state in RA patients.

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MRI I & II

SP0128 MRI OF ENTHESITIS – BY CONVENTIONAL AND WHOLE-BODY MRI - INCLUDING QUIZ CASES

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Entheses are sites of attachment of tendons, ligaments, fascia, or capsule into bone, providing a mechanism for reducing stress at the bony interface. Entheses dissipate biomechanical stress and, in doing so, are thought to be subjected to repeated micro traumas.

Inflammation of the entheses, enthesitis, is a well-known hallmark of spondyloarthritis (SpA), playing a central role in disease pathogenesis. It can also be associated with degenerative, endocrinologic, metabolic and traumatic conditions. Magnetic resonance imaging (MRI) is a sensitive tool for the detection of early signs of enthesitis in patients with SpA. The MRI features of enthesitis are well described, and include thickened enthesis with altered signal intensity and perientheseal soft tissue edema. Bone marrow edema and erosions at the adjacent bone appear mainly in SpA-associated enthesitis. Contrast material administration improves the reliability, sensitivity and specificity of detecting enthesitis on an MRI.

Whole-body (WB) MRI allows assessment of all peripheral and axial joints and entheses from "head-to-toe" in one examination. The promising role of WBMRI in the evaluation of enthesitis in SpA and other rheumatic diseases was evaluated in several cross sectional and prospective studies. Indeed WB MRI was shown to be sensitive in the detection of inflammatory lesions, including enthesitis, on multiple sites, potentially serving as a one stop shop for the estimate of active disease load.

In the current presentation, the typical imaging properties of enthesitis on conventional and WB-MRI will be presented along with several challenging quiz cases.

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SP0129 CLASSIFICATION, DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS OF AXIAL SPONDYLOARTHRITIS BY MRI - INCLUDING QUIZ CASES

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Magnetic resonance imaging (MRI) is essential in the process of diagnosis of axial spondyloarthritis (axSpA) in clinical practice, as described in recent EULAR recommendations (1). However, several important differential diagnoses need to be considered. MRI is also key in the Assessment in SpondyloArthritis International Society (ASAS) classification criteria for axSpA (2), for which a consensus definition of a positive MRI was made in 2009 (3). The ASAS MRI working group has recently provided an updated definition of what is needed to fulfill the MRI-criterion in the ASAS criteria (4), based on a consensus excercise. This talk will describe the evidence behind the use of MRI for diagnosis of axSpA, describe the current ASAS consensus on how to use MRI for classification of axSpA, and examples of the most important differential diagnoses will be shown. The presentation will include patient cases for audience review.

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WIN & HOT session

SP0130 WIN SESSION: OSTEOPOROSIS

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The clinical pathway for fracture prevention consists of a 5-step approach: case finding, risk evaluation, differential diagnosis, treatment and follow up. For each of these steps new insights have emerged during the last year.