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Rheumatoid arthritis - prognosis, predictors and outcome

SAT0037 THE EFFECTS OF B CELL DIRECTED THERAPY ON DISEASE RELEVANT BIOMARKERS IN SUBJECTS AT RISK OF RHEUMATOID ARTHRITIS

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Background: Exploration of the mechanism underlying the delay of development of clinical signs of seropositive rheumatoid arthritis (RA) observed after B cell directed therapy in individuals at risk of developing autoantibody positive RA may offer insights into the mechanism of disease and may assist the development of preventive strategies.
Objectives: To explore the effects of a single infusion of rituximab (anti-CD20 antibody) on the observed delay of the onset of clinically manifest arthritis in individuals at risk of developing autoantibody positive RA.
Methods: In a study of 81 subjects positive for both anti-citrullinated protein antibodies (ACPA) and rheumatoid factor (RF) with arthralgia who never had clinically manifest arthritis and never used disease-modifying antirheumatic drugs, a 55% reduction of the risk of developing arthritis was observed 12 months after receiving a single iv infusion of 1000 mg rituximab when compared to placebo. In this group there was a delay in the development of arthritis of 12.0 months (12 months placebo vs 24 rituximab group) at the 25% quartile (75% free of arthritis) of the cumulative arthritis-free survival. Explorative analysis of disease-related biomarkers was performed in subgroups to better understand the mechanisms of the observed delay of clinical disease onset.
Results: Baseline levels of ESR (mm/h; HR 1.03; p=0.016), the total number of B cells in peripheral blood (HR 1.48; p=0.047), the presence of anti-alpha-enolase 1 (anti-CEP1) antibodies (HR 3.71; p=0.004) and the percentage of regulatory B cells (HR 1.04; p=0.002) were related to arthritis development over time. Importantly, genetic analysis of 100 RA associated SNPs showed that the top SNP associated with arthritis development in the rituximab-treated group (OR=7, MAF in cases 60% compared to 17% in unaffected) was in the PLCL2 gene, described to play a role in B cell signaling[1]. In individuals treated with rituximab, B cell numbers and subtypes mainly of the memory and regulatory compartment as well as serum levels of IgM-RF ($p<0.0001$), IgA-RF (p=0.003), total IgM (p=0.001), and anti-CCP (p=0.035) showed statistically significant changes over time compared to individuals who received placebo. Exploratory analysis showed trends for multiple biomarkers in the B cell compartment that appeared predictive of the development of arthritis.
Conclusions: A single infusion of 1000 mg rituximab significantly affects B cell numbers and subsets of memory and regulatory B cells as well as a reduction of disease-related antibodies and immunoglobulin levels in individuals at risk of RA. The changes coincide with a decrease in risk and a delay in development of arthritis in this population. PLCL2 gene polymorphism was associated with arthritis development in rituximab-treated individuals.
References:
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SAT0038 SERUM B LYMPHOCYTE CHEMOATTRACTANT PROTEIN 13 (CXCL 13) AND MUSCULOSKELETAL ULTRASONOGRAPHIC FINDINGS IN EARLY RHEUMATOID ARTHRITIS

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Background: Patients in clinical remission may continue to have synovitis detected by the musculo skeletal ultrasonography (MSUS).Recently,B-lymphocyte chemoattractant chemokine (CXCL13) has reported to be upregulated and risen to be a possible new marker of disease inflammation in RA
Objectives: to detect early synovitis by grey scale and power Doppler MSUS, measure serum levels of CXCL13 and to correlate these levels with both clinical and ultrasonographic disease activity in early RA patients
Methods: RA was assessed by the modified disease activity score (DAS28).Hands and feet plain radiography were evaluated by Laresn score. A semi-quantitative score (0–3) was used to score synovial effusion (SE), synovial proliferation (SP) and power Doppler (PD) signals by MSUS in 6 synovial sites in 3 joints bilaterally: wrist (dorsal radiocarpal recess). 2nd MCPJ (dorsal and palmar side) and knee (suprapatellar recess) according to the European Leauge Against Rheumatism guidelines. A total MSUS score is the sum of scores for SE, SP and PD signals of the six joints in each patient (0–54).Quantitative detection of serum (CXCL13) levels of all subjects was done by ELISA.
Results: The mean serum CXCL13 values were highly significantly higher in fifty RA patients than in 30 age and sex matched control subjects with a mean of (388.86±283.63 pg/ml) and (62.96±32.5 pg/ml) respectively ($p<0.001$) and were significantly positively correlated with morning stiffness durations ($p<0.001$), Tender Joint Counts ($p<0.001$), Swollen Joint Counts ($p<0.001$), VASs ($p<0.001$), ESR 1st h values ($p<0.001$) and the platelets count ($p<0.05$), negatively correlated with disease durations ($p<0.05$) and HB concentrations ($p<0.05$) and showed no differences according to presence of extra-articular manifestations or CRP, RF or ACCP seropositivity.($p>0.05$). In our RA patients' group, MSUS detected either synovial effusion and /or synovial hypertrophy with or without PD signal in 132 (65%) joints out of 203 clinically silent joints and and detected erosions in 93/300 joints (31%) compared to 27/300 joints (9%) detected by x ray.the serum CXCL13 levels were highly significantly positively correlated with the total MSUS score for each patient ($p<0.001$),SP and SE gradings ($p<0.001$) and ($p<0.05$) and were significantly higher in RA patients with MSUS detected erosions but were not correlated with either PD gradings (p=0.11) or Larsen scores ($p>0.05$).
Conclusions: MSUS is more sensitive than clinical assessment and conventional radiology in detecting synovitis and erosions in RA. Serum CXCL13 levels correlated with MSUS and DAS 28 scores and can be used as a marker for activity and severity of RA.Screening early RA patients by MSUS for more precise evaluation of synovitis activity, severity and better management of the disease and follow up patients to detect if elevated CXCL13 affect RA disease progression or patient disability are recommended.
References:
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SAT0039 LARGE TENDER JOINTS HAVE THE GREATEST IMPACT ON LONGITUDINAL TRAJECTORIES OF FUNCTION IN EARLY RHEUMATOID ARTHRITIS

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Background: Physical function remains suboptimal in patients with early rheumatoid arthritis (ERA) despite adequate disease control. Hence, factors impacting function need further evaluation. Large weight bearing joints are more likely to impact overall function than small non-weight bearing joints although the magnitude of impact may be task dependent. By weighting large joints more than small joints, the Lansbury Articular Index (LAI) may have stronger associations with function than standard joint counts that give equal weight to small and large joints.
Objectives: 1) To compare the correlations of weighted and non-weighted arthritis joint measures with physical function over time; and 2) to determine the impact of large compared to small joint involvement on the trajectory of HAQ in ERA.
Methods: ERA participants had <1 year symptom duration at enrolment in a multicentre Early Arthritis Cohort and were followed prospectively. Arthritis activity measures (DAS28, tender 28 joint count (TJC28), swollen 28 joint count (SJC28), function (Health Assessment Questionnaire; HAQ) were captured at each visit. The LAI weighted 28 joint count (LT28) and swollen joint count (LS28) were calculated based on the standard 28 joint sites. Correlations of trajectories were calculated using joint modeling for each of the following: DAS28, TJC28,SJC28,LS28 LT28 with the HAQ (2 trajectories/model). Unadjusted effects of large joints (shoulders, elbows, hips knees, ankles) and hand joints (time-varying) on the HAQ trajectory were estimated with a series of generalized estimating equations (GEE). GEE models were adjusted for baseline age, sex and education.
Results: ERA subjects (n=2125, 73% female; baseline mean (SD) age 53 (15) years, DAS28 5.1 (1.4)), were followed for median (IQR) 24 (10,48) months. At their last visit 44% were in remission ($DAS28<2.6$). HAQ over time was highly correlated with the following: DAS28 (r=0.83), LT28 (r=0.83), and TJC28 (r=0.85) and moderately with the LS28 (r=0.59) and SJC28 (r=0.61) trajectories. Each increase in joint involvement was associated with increase in HAQ: large tender joint (0.110 (95% CI 0.102–0.116)); large swollen joint (0.109 (0.099–0.120)); tender hand joint (0.036 (0.032–0.039)); swollen hand joint (0.035 (0.032–0.039)).