LARGE JOINT ARTHRITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS IS CHARACTERISED BY T CELL RATHER THAN B CELL ACCUMULATION

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Background: Musculoskeletal involvement is a common clinical feature of systemic lupus erythematosus (SLE), that can be present either at the onset or in later disease course. SLE related arthritis is usually non-erosive and non-deforming as opposed to rheumatoid arthritis (RA). While RA synovial pathology has been extensively studied, little is known about the pathophysiology of arthritis in SLE. Objectives: to explore the cellular compartments in synovial fluid of SLE patients with arthritis manifestations.

Methods: paired synovial fluid (SF) samples from large joint aspiration and peripheral blood samples (PBMC) obtained at the same time point from five SLE patients were analyzed by multicolor flow cytometry. The patients fulfilled the ACR 1982 classification criteria for SLE [1]. Clinical records were reviewed in order to exclude the presence of comorbidities such osteoarthritis or overlap with RA.

Results: The overall frequency of CD4+ and CD8+ T cells was similar across the SF and PBMC samples. Among the CD4+ T cells, those co-expressing CCR4, showed a much higher frequency in the SF compared to the peripheral blood in 4 out of 5 patients (mean percentage 8.9±7.0% vs 2.1±1.6%, p=ns). In addition, in 4 out of 5 patients we could identify an increased frequency of CD4+ expressing CXCR3+ , a marker for Th17 cells in SF as compared to PBMC (mean percentage 35±16.6% vs 12.7±8.9%, respectively, p=ns). In all patients, a higher frequency of EOMES+ Granzyme A + CD4+ T cells was observed in SF when compared to PBMC (9.2±2.5% vs 4.5±2.5%, p=0.03). Moreover, in all patients, we could observe a higher proportion of regulatory T cells (FOXP3+/CD25+) in the SF (21.5±15.4% vs 8.4±2.7%, p=ns). No relevant differences were observed in the Th1 compartment (CXCR3+). CD19+ cells (B-lymphocytes) were scarcely present in the SF of SLE patients as opposed to the peripheral blood.

Conclusion: Although SLE is usually considered to be a B cell driven disease, its pathogenesis is increasingly being recognized to be RATHER THAN B CELL ACCUMULATION

ARE RHEUMATOID FACTORS AND ANTINUCLEAR ANTIBODIES ASSOCIATED WITH FRAILTY IN ELDERLY TUNISIAN POPULATION?

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Background: An emerging concept is the ‘frailty syndrome’, which may explain diversity in clinical outcomes in the elderly population.

Objectives: The aim of the study was to investigate the possible association between antinuclear autoantibodies, different isotopes of Rheumatoid Factor and frailty in aged individuals.

Methods: Using a validated set of frailty criteria (the SEGA tool), we conducted a cross sectional observational study to evaluate the prevalence of antinuclear antibodies (ANA) (assessed by IIF) and different isotopes of Rheumatoid Factor (RF) (determined by ELISA) in 89 Tunisian individuals aged at least 65 years living in the community. The study population were categorized into three groups: severely frail (n=29), frail (n=31), and non frail (n=29) according to the validated and widely utilized frailty criteria (SEGA tool).

Results: ANA were detected in 36 of the participants. No Significant difference was observed between the three groups. Immunofluorescence patterns observed were speckled in 34%, homogenous in 3.3%, and nucleolar in 3.3% of individuals. Nineteen of the severely frail patients had positive IgA RF compared to 11 from the Frail group and 6 only from the non-frail group (p<0.02). RF isotypes showed low correlations with other features. Indeed, the IgA RF was correlated with the age (r=-0.22, p=0.03), the C-Reactive Protein level (r=-0.45, p<0.01), and the nutritional state of the patients assessed by the MNA score (r=0.27, p=0.009). The IgG RF was correlated with hemoglobin (r=-0.22, p<0.03) and creatinin (r=-0.36, p<0.01) levels.

Conclusion: Our study showed no significant difference in the frequency of ANA amongst nonfrail, prefrail, and frail aged individuals, whereas RF isotypes were found to be slightly correlated with several biological parameters and other features.

REFERENCES

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SELECTIVE DEPLETION OF PLASMA CELLS IN VIVO BASED ON SPECIFICITY OF SECRETED ANTIBODIES

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Background: Antibody-mediated diseases like allergies and chronic-inflammatory autoimmune diseases affect more than 10% of the human population, and for most, no cure is available. This is particularly true when pathogenic antibodies are secreted by long-lived plasma cells generated early in pathogenesis, which are refractory to conventional therapies. Therapeutic concepts for the general ablation of plasma cells are currently being tested in clinical trials. These concepts target both plasma cells secreting pathogenic antibodies and those providing protective antibodies, i.e., humoral immunity. Efficient ablation of pathogenic plasma cells is inevitably accompanied by immunodeficiency and increased susceptibility to infection.

Objectives: We studied the use of an antigen-antibody conjugate to label plasma cell in vivo with the antigen and selectively ablate those that secrete antibodies specific for the antigen.

Methods: B albic mice were immunized with ovalbumin (OVA) and chicken gamma globulin (CGG), which resulted in the generation of OVA and CGG-specific long-lived plasma cells in the bone marrow. These mice were treated by a single intraperitoneal injection of a conjugate consisting of OVA and a monoclonal anti-CD138 antibody. The effect of this treatment on the long-lived plasma cells and antibody levels was analyzed by flow cytometry and ELISA, respectively.

Results: The single injection of an OVA-anti-CD138 conjugate resulted in a significant depletion of OVA-specific plasma cells while CGG-specific plasma cells were not affected. The selective depletion of OVA-specific plasma cells also led to stable reduction of serum anti-OVA antibody levels; circulating anti-CGG antibody levels remained unchanged.

Conclusion: The cellular antigen-affinity matrix strategy described here for the ablation of plasma cells in vivo according to the specificity of their antibodies enables a unique causative therapeutic approach in established antibody-mediated diseases without impairment of humoral immunity.

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