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 arthritic 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 as osteoarthritis or overlap with RA. Three different lineage-specific panels for B cells, T cells (cytotoxic and helper) were developed.

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 CCR6+, 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 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 SF of SLE patients as opposed to the peripheral blood.

Conclusion: Although SLE is usually considered to be a B cell driven disease, its common clinical features like arthritis could be driven in situ by T cells, namely subsets of CD4+ (helper) cells such as TH17 cells and CD4+ T cells with cytotoxic profile. Further confirmation of the present findings is needed.

REFERENCES

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SELECTIVE DEPLETION OF PLASMA CELLS IN VIVOBASED 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 genetic 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: Balb/c 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.

REFERENCES

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