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ONTOGENETIC PATTERNS OF MICROARCHITECTURAL MODULATIONS IN THE SPLEEN OF THE GROWING AND AGING RATS

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Abstract:

Spleen is the largest lymphoid organ involved in cellular and humoral immune response. It becomes structurally and functionally mature in early life, undertakes dynamic age-dependent modulations and undergoes involution during aging of the body. In many current immunological research works developmental modifications in the spleen at different ages remain underestimated, while they may overlap with the changes caused by modelled immunopathology which will result in misinterpretation of data on the effectiveness of immune response, sensitivity to immunomodulatory treatments, etc. While age-related thymic involution is described in details, patterns of ontogenetic immunomodulation in spleen at different ages were hardly updated since last century. The objective of this research is to provide a comprehensive picture of splenic development at different stages of postnatal development and to assess possible mechanisms of the age-related splenic involution. Total of 80 Sprague Dawley rats were involved in the study; out of them 54 were used for digital morphometry being divided into 9 subgroups with 6 rats each: 0, 10, 20, 30, 60, 90, 180, 270 and 360 days of age. Another 26 animals were used for qualitative assessment of the splenic microstructure with 2 animals per group of every day of early life, starting from the 2nd day until the 29th day. Each animal and its spleen were weighed, relative weight of the spleen was estimated. Histological slides of the paraffin-embedded tissue were stained with haematoxylin-eosin and immunohistochemically for markers of the lymphoid and stromal cells (CD3, CD4, CD8, CD20, CD90, S100 protein, OX-62), PCNA and caspase-3. Image analysis was used to assess volume density of the immunopositive structures. Our results demonstrated that developmental changes in the spleen of the growing rats occur faster than it was described in classical papers on postnatal spleen development over fifty years ago: primitive PALS appear on the 2nd day of life, marginal zone – on the 8th day, primary lymphoid nodules – on the 18th day, secondary lymphoid nodules – on the 24th day. Lymphoid cells depletion becomes significant in aging rats, while stromal cells significantly reduce their volume density starting from the middle age. Among mechanisms of age-related lymphoid and stromal cell depletion are increased apoptotic rate, decreased proliferative rate and reduced traffic of T-cells in the T-zones of spleen. These data may be used for discrimination of the developmental and pathological changes in the compartments and zones of the spleen in experiments with modeling of the lymphoid tumors, evaluation of the efficacy of the immunomodulatory drugs, transplantation and stress-related experiments.

Key words: *spleen, age, senescence, involution, immunohistochemistry*

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