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Overview of Histomorphology of Thymus, Spleen and Lymph Nodes in Animals

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INTRODUCTION

The appearance of normal lymphoid tissues, particularly peripheral lymph nodes, can vary significantly and sometimes look similar to tissues that have undergone pathological changes. Different parts of each lymphoid organ serves specific immune function and should be assessed separately for any alterations. It's crucial to understand that lymphoid tissues, especially lymph nodes and the spleen, are not static in their composition and structures. They contain both permanent and temporary cell populations, including cells that have migrated from other locations due to tissue damage or exposure to antigens.

Thymus

The thymus has macroscopic and microscopic similarities across various species. In most big mammals, such as humans, dogs, and nonhuman primates, the thymus is bilobed and situated in the cranial part of the thoracic cavity, in front of the heart and its associated vessels. However, in smaller mammals, there are some differences. For instance, in rats, one or both thymus lobes can extend into the neck region, while guinea pigs have a more cranial location in the neck, and mice have thymus lobes situated in both cervical and thoracic regions.

Thymus is enclosed by a delicate connective tissue capsule that encapsulates the organ and penetrates into its lobes, dividing it into numerous lobules. These lobules are more easily distinguishable in larger species like dogs and monkeys. On a histological level, the thymus consists of an outer cortex containing densely-packed, small lymphocytes with a dark staining appearance. This cortex surrounds a distinct inner medulla, which typically appears continuous between adjacent lobules. Within the medulla, concentric whorls made up of flattened, eosinophilic reticular cells derived from epithelial tissue, known as Hassall's corpuscles are present.

Thymic aging is noticeable in dogs, monkeys, and humans and is characterized by involution or atrophy. Functional tissue is gradually replaced by adipose tissue, interlobular stroma, and prominent epithelial structures, especially within the medulla. Thymic lymphocytes are eliminated through apoptosis, and their debris is phagocytosed by macrophages within the cortex, resulting in a "starry-sky" appearance.

Spleen

The spleen is typically an elongated and expandable organ that contains white blood cells, red blood cells, and parenchyma. It is surrounded by an outer capsule made of fibro-muscular connective tissue, which extends in irregular trabeculae into the core of the organ. The differences in the density, thickness, and relative abundance of the capsule and trabeculae contribute to species-specific characteristics.

Red Pulp: In all species, a three-dimensional network of splenic cords and venous sinuses is present within the red pulp. These splenic cords consist of reticular cells with associated fibres and macrophages, which collectively filter blood and capture aged red blood cells, bloodborne particles, iron pigment (hemosiderin), ceroid, and lipofuscin in both red pulp and marginal zone. The complex vascular system of the spleen plays a central role in the efficient filtration of blood and in recycling of RBCs.

White Pulp - PALS and Lymphoid Follicles: The white pulp of the spleen encompasses various lymphoid compartments, including the periarteriolar lymphoid sheaths (PALS), primary and secondary follicles, marginal zone, and mantle, all of which exhibit variations among species.

PALS consists of densely packed, darkly stained lymphocytes that encircle and extend along the central arteries within the spleen. These are further divided into an inner zone, which is T-cell dependent and primarily contains CD4+ T-cells, along with a smaller number of CD8+ T-cells and interdigitating dendritic cells. The outer PALS zone, which appears darker, comprises small CD3+ T-cells, macrophages, B-cells, and occasional plasma cells.

Lymphoid follicles are typically found at the branching points of central arterioles and blend with the PALS. The marginal zone (MZ) serves as a well-organized and functionally distinct region that separates the red pulp from the white pulp. It mainly contains B-cells, MZ macrophages (located on the outer side of the MZ), and marginal metallophilic macrophages (found on the inner side of the MZ). These cells originate from bone marrow cells forming the B cell lineage, migrates to the spleen, and transform into transitional B cells, which subsequently mature into either follicular B cells or, while still in the red pulp venules, into MZ B precursor (MZP) cells. MZ B cells do not re-circulate like B cells from lymph nodes but migrate into the white pulp. MZ B cells play a significant role in natural immune response and primarily support T-cell independent humoral immune responses during initial antibody responses.

Lymph Nodes

The histomorphology of normal lymph nodes can vary widely, ranging from small, uncomplicated, bean-shaped structures to nodes with diverse structures seen both within individuals and across different species. It is important to take into account the factors such as the age, species, and strain of animals, as well as the likelihood of antigen exposure to the specific lymph node being examined.

Typically, lymph nodes are bean-shaped and possess a continuous cortex that surrounds the medulla, which is located towards the center of the node. Within the cortex of the lymph node, there are lymphoid follicles categorized as primary and secondary follicles. Primary follicles are easily recognizable as distinct, rounded clusters of small, densely staining resting lymphocytes. They do not show the development of germinal centers, indicating a lack of exposure to antigens. On the other hand, the presence of secondary follicles containing germinal

centers, which are composed of lymphoblasts (larger, lightly staining, activated B lymphocytes), suggests that an antigen has been presented, often by antigen-presenting cells like dendritic cells or T lymphocytes. Subsequent cell divisions occur, leading to the differentiation into plasma cells or small memory B lymphocytes. These memory B lymphocytes eventually gather in the mantle zone of secondary follicles and have a long lifespan. T lymphocytes, on the other hand, migrate to and settle in the paracortical zone of the node, where they play roles in both cell-mediated and humoral-mediated immune responses. The remaining cells in the cortex are predominantly B lymphocytes. The medullary cords are comprised of densely packed lymphocytes and numerous plasma cells. Surrounding these cords are medullary sinuses that connects to efferent lymphatic vessels, which transport lymph away from the node. Pigs, however, have a different anatomical arrangement of lymph node compartments from the classical pattern, as well as an unusual placement of afferent and efferent lymphatics. In pigs, lymph enters the node centrally and exits through efferent vessels located on the outer surface of the capsule. Similarly, the medullary sinusoids and cords are situated peripherally, while the T cell-dependent areas and lymphoid follicles are centrally located within the node. In some cases, large, irregular medullary sinusoids may extend into the center of the node or occupy a significant portion of one end of the node.

CONCLUSION

In lymphoid tissues, regardless of the species, there are only a few potential reactions when exposed to tissue damage or stimuli. These responses encompass hyperplasia, hypertrophy, atrophy, necrosis, inflammation, and neoplasia. Nonetheless, certain histomorphological alterations might actually represent the typical functioning of that specific lymphoid tissue, such as its role in filtering lymph or producing antibodies, and may not indicate pathology in itself. It is important to identify which group of cells within the particular compartment of the lymphoid tissue is affected and this acts as a key to understand the significance of the observed histomorphological changes.

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