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Lymphoma is an enigmatic and fascinating disease complex that involves almost all vertebrates and can be of B, T, or NK cell of origin. More than 70% of canine lymphomas are of B cell origin. Since the discovery of Hodgkin's lymphoma by an anatomist Thomas Hodgkin in 1832, all malignant lymphomas in humans were characterized as either Hodgkin lymphoma or non-Hodgkin lymphoma at the beginning of the twenty-first century [2]. Follicular lymphomas (FL) are the common subtype of non-Hodgkin lymphoma in humans and are associated with an indolent i.e. slowly progressive biological behavior in early stages.

Follicular lymphoma in animals is rare with incidence ranging from 0.3-4%. This wide range likely reflects changing interpretations of follicular lesions and the use of immunohistochemical assistance in detecting poorly differentiated follicular lesions [1].

Follicular lymphoma has been reported mostly in dogs which are generally over 10-year-old. It is often noticed on incidental examination and may be present in multiple external and internal lymph nodes but those in head, neck, prescapular, and popliteal region are likely to be involved. Animals are generally active and have normal appetites. Spleen, liver and bone marrow may be involved in the late stage.

Follicular lymphoma is a unique tumor because, in the early stages, cells do not die and keep on accumulating due to mutation of the anti-apoptotic (BCL-2) gene. As these cells proliferate they acquire additional mutations e.g. p53 which aid in tumor progression. In humans, FL is characterized by the chromosomal breaks at 18q21 and rearrangement of the BCL-2 gene. By this translocation, the BCL-2 gene in chromosome 18 is juxtaposed to the

immunoglobulin heavy-chain region of the chromosome 14 that results in the BCL-2/Ig-H rearrangement and since the Ig heavy chain region is in active transcription, there is up-regulation of the BCL-2 gene. As a result of this translocation, the affected cells have constitutively high levels of anti-apoptotic protein BCL-2 [1,2].

Follicular lymphomas are derived from germinal center centroblast which is of B cell origin. In early stages, FL is composed of variable mixtures of centroblasts and centrocytes. Histologically, it is a nodular lymphoma which lacks light and dark poles of reactive germinal centers and is surrounded by a thin or fading rim of non-neoplastic mantle and marginal zone cells. In contrast to the reactive germinal centers, post-capillary venules are often displaced on the periphery of the neoplastic follicles. In early stages, neoplastic follicles, like their reactive counterparts, contain dendritic reticulum cells and reactive follicle T-cells (CD3⁺, CD4⁺, CD57⁺, PD-1⁺) admixed with centroblasts and centrocytes [2]. As the disease progresses, FLs acquire more centroblasts and genetic heterogeneity and development of histological areas of diffuse architecture so that the tumor may contain follicular and diffuse or completely diffuse areas [1,2]. There are at least 10 different morphological variants of FL in humans [2].

Neoplastic cells express surface and cytoplasmic immunoglobins, in particular IgM. Neoplastic cells are CD79a⁺, CD20⁺, CD10⁺, BCL2⁺, BCL6⁺, CD5⁺, CD23⁺, and CD43⁺ [2]. Positive staining for CD45RA (MT2) may help to distinguish neoplastic from reactive follicles [2].

According to WHO grading system, FL is graded as FL grade 1 to grade 3. FL grade 1 has 0-5 centroblasts per hpf, FL grade 2 have 6-15 centroblasts per hpf, and FL grade 3 have more than 15 centroblasts per hpf. Centroblasts are morphologically round cells which have round to oval nuclei with deep clefts and measure 2-2.5 RBC diameter. Chromatin is fine and dispersed and there are 1-3 nucleoli which are characteristically impinging on nuclear membrane. Cytoplasm is minimal to mild and amphophilic. Centrocytes are small round cells with scant cytoplasm and a single, cleaved nucleus that measure 1-1.5 RBC diameter. The nuclear irregularities are relatively shallow with dense chromatin and small inapparent nuclei.

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