

Hepatosplenic and Hepatocytotropic T-Cell Lymphoma: Two Distinct Types of T-Cell Lymphoma in Dogs

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Abstract

The clinical, clinicopathologic, and pathological findings of 9 dogs with T-cell lymphoma that involved the liver in the absence of peripheral lymphadenopathy were assessed. Seven dogs had hepatosplenic T-cell lymphoma (HS-TCL). Dogs with HS-TCL presented with hepato- and/or splenomegaly, regenerative anemia, thrombocytopenia, and hypoproteinemia. The clinical course was rapidly progressive with all dogs but 1 dead within 24 days of initial presentation. Neoplastic lymphocytes were centered on hepatic and splenic sinusoids and had a CD3+ (5/7), TCR α β+ (5/5), TCR γ δ+ (3/5), CD11d+ (6/7), granzyme B+ (5/7) immunophenotype. Bone marrow and lungs were consistently but variably involved. These findings closely resemble the human disease and support the classification of HS-TCL as a distinct World Health Organization entity in dogs. The remaining 2 dogs markedly differed in the pattern of hepatic involvement by neoplastic lymphocytes, which were not confined to hepatic sinusoids but invaded hepatic cords. In addition, neoplastic cells had a CD11d− immunophenotype, and clinicopathologic data indicated marked cholestasis and mild to absent anemia. Based on the distinct tropism of neoplastic lymphocytes for hepatocytes, the name hepatocytotropic T-cell lymphoma (HC-TCL) is proposed. Given the histomorphologic, clinicopathologic, and immunophenotypic differences, HC-TCL likely represents a separate biological entity rather than a histomorphologic variant of HS-TCL.

Keywords

emperipolesis, gamma delta T cell, hepatosplenic T cell lymphoma, hepatocytotropic T cell lymphoma, molecular clonality, WHO classification, PTCL-NOS

Considerable effort has been directed toward a generally accepted classification scheme for canine lymphomas.^{1,2} An appropriate classification scheme should adequately group tumors into clinicopathologic entities and serve as a basis for prediction of biological behavior and choice of treatment. With advances in research and diagnostic methods, classification schemes are subject to constant refinement and evolution.

The current most commonly accepted classification scheme for human lymphomas is the World Health Organization (WHO) system.¹⁸ The majority of WHO entities are defined by clinical, morphological, immunophenotypic, and genetic criteria. One such example is hepatosplenic T-cell lymphoma (HS-TCL). HS-TCL is defined as a T-cell lymphoma that is centered on the liver and spleen without significant involvement of peripheral lymph nodes.¹⁸ HS-TCL is thought to arise from splenic cytotoxic T cells and is predominantly of γ δ T-cell origin.^{1,4,19,21} Patients clinically present with splenomegaly and/or hepatomegaly, thrombocytopenia, and anemia. Histologically, neoplastic cells are predominantly found within splenic and hepatic sinusoids with concurrent bone marrow involvement in most cases.

HS-TCL has recently been adopted as a new entity in the canine WHO classification. However, so far only 2 cases have

been reported in dogs.^{18,19} Although these cases resembled the human disease, their singularity precluded identification of general characteristics of HS-TCL in dogs. Additional data are needed to more precisely characterize this tumor type and to validate its status as a distinct WHO entity in dogs.

In contrast to HS-TCL, other WHO entities are more heterogeneous and include a range of different tumor types that have not been further characterized. One such example, in humans as well as in dogs, is peripheral T-cell lymphoma—not otherwise specified (PTCL-NOS).^{18,19} In humans, this entity is



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