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Domestic cat hepadnavirus detection in blood and tissue samples of cats with lymphoma

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Introduction

Domestic cat hepadnavirus (DCH), a relative hepatitis B virus (HBV) in human, has been recently identified in cats. The HBV infection has been reported to be associated with non-Hodgkin lymphoma (NHL); however, association of DCH infection with lymphoma in cats is not investigated. In this study, we investigated the presence of DCH DNA in the blood obtained from cats with and without lymphoma. We also extended our investigation by postulating that DCH infection might exhibit extrahepatic behavior similar to what has been described in HBV infection. To elaborate on this speculation, we performed the quantitative polymerase chain reaction (qPCR) and in situ hybridization (ISH) to detect DCH infection in tumor tissues of different lymphoma subtypes, which were differentiated by immunohistochemistry (IHC). Tissues from benign lymphatic diseases were included in this investigation. Coinfection of feline immunodeficiency virus (FIV) and feline leukemia virus (FeLV) was also investigated.

Methods

EDTA-anticoagulated bloods and formalin-fixed paraffin-embedded (FFPE) tissues of 131 (68 bloods and 63 tumors) samples obtained from cats with lymphoma, and 586 (526 bloods and 60 lymph nodes) samples obtained from cats without lymphoma, but presented histological benign lymphatic diseases, were included.

EDTA blood samples (n=594) and FFPE samples (n=123) were viral nucleic acid extracted and further performed the detection of DCH by qPCR. Later, the samples from lymphoma group were further tested for FIV and FeLV by qPCR.

Lymphoma subtype classification was done on FFPE samples (n=63) by immunophenotyping using CD3, CD79, and Pax5 according to the Revised European American Lymphoma/World Health Organization (REAL/WHO) guidelines. The localization of DCH in lymphoma was investigated using dual labeling with ISH and immunohistochemistry (IHC) targeting CD79 that is specific to the B-cell lineage.

Results

DCH was detected in 16.18% (P = 0.002; odds ratio [OR], 5.15) of blood and 9.52% (P = 0.028; OR, 13.68) of FFPE samples obtained from lymphoma cats, whereas 3.61% of blood obtained from non-lymphoma cats was also detected. Within the 17 DCH-positive lymphoma cats, FeLV was co-detected in 8 cats (2 DCH-blood, 6 DCH-FFPE); and in 6/6 were CD79-positive B-cell lymphoma (P > 0.9; OR, 1.93) and were multicentric form (P = 0.008; OR, 1.33). Based on histologically prognostic grading, in 4/6 were low-grade and other 2 cases were characterized as high-grade lymphomas. DCH localization was found in the CD79-positive pleomorphic cells.

Conclusion

Cats with lymphoma, exclusively present in B-cell lymphoma, were more likely to be positive for DCH than cats without lymphoma. This finding was in accordance with the finding of HBV with NHL. However, there was no statistically significant difference in DCH infection between lymphoma subtypes due to the lower numbers in the T-cell-derived group in the studied period. Although the definitive role of DCH in development of lymphoma could not be determined, this finding indicates future avenues for further study regarding association DCH infection in development of feline lymphoma which is in the same alignment with current knowledge on HBV in association with lymphomas in humans.