

Reduced diversity of immunoglobulin and T-cell receptor gene rearrangements in chronic inflammatory gastrointestinal diseases in dogs.

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Source

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Abstract

Inflammatory bowel disease has a multifactorial etiology in dogs as it does in humans. Evidence has been accumulated showing an abnormal response of the immune system, mostly represented by lymphocyte infiltration in the lamina propria of the gastrointestinal tract and in the epithelium, likely driven by chronic antigenic stimulation against luminal microorganisms. A relevant role is also ascribed to the genetic predisposition typical of some canine breeds. The role of chronic antigenic stimulation is still under debate. It may be responsible for selective pressure on the lymphoid population, favouring the emergence of some lymphocyte clones. This cross-sectional study is aimed at investigating the immunoglobulin and T-cell receptor gene rearrangements in a group of dogs affected by inflammatory bowel disease. The database of a referral Veterinary Laboratory was investigated. Based upon the histological evaluation of the bioptic samples collected during endoscopy, 54 canine cases met the WSAVA criteria for diagnosing IBD and were included in the study. The histological slides were retrieved and the gDNA was purified using protocols for formalin-fixed tissue. The gDNA was PCR amplified using fluorescent-labelled primers specific for canine immunoglobulin and T-cell receptor gene rearrangements; the PCR products were analysed with fragment analysis by means of capillary electrophoresis on an automatic sequencer (GeneScanning). In 47/54 (87.3%) cases, it was possible to amplify the gDNA. Twenty-one patients out of 47 (44.7%) showed polyclonal patterns in both the immunoglobulin and the T-cell receptors, 18/47 (38.3%) showed at least one oligoclonal pattern without monoclonal ones while 8/47 (17.0%) cases showed an Ig (7/47; 14.9%) or TCR (1/47; 2.1%) monoclonal pattern. These findings indicate that reduced diversity of the immunoglobulin and T-cell receptor repertoire occurs in canine inflammatory bowel disease. The reduced diversity correlated significantly with the severity of the histological lesions and carried a significantly increased risk of death. Beside its possible role as a reliable ancillary assay, immunoglobulin and T-cell receptor GeneScanning analysis points to the possible role of aberrant chronic antigenic stimulation, leading to clonal expansion of certain lymphocyte subsets in the pathogenesis of canine IBD.

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