Malignant catarrhal fever (MCF)

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PATHOGENESIS

Despite the severe pathological changes that occur in animals affected by MCF the pathogenesis remains to be fully elucidated. What is certain, however, is that the lesions do not arise through direct virus-induced cytopathology as there is no evidence of herpesvirus cytopathic effects and very little evidence of viral antigen or nucleic acid can be found in them. Consequently, numerous authors have suggested a variety of immunopathological mechanisms to explain the pathogenesis of the lesions, none of which is entirely satisfactory.

The pathology of MCF consists of three components:

- T-lymphocyte hyperplasia in lymphoid organs and accumulation of these cells in non-lymphoid tissues,
- Epithelial degeneration/necrosis and hyperkeratosis, and
- Vasculitis.

In an explanation of these lesions, Plowright was the first to suggest that immune mechanisms were responsible for their development which involved a hypersensitivity to viral or viral-induced antigens. Explanations from other researchers include suggestions that the different lesions resembled both an Arthus (Type III) response and a cell-mediated (Type IV) response, or that they arose through immune-complex formation. None of these suggestions is compatible with the nature of the lesions or with the lack of identifiable viral antigens in affected tissues. Another observation was that there was a strong histological resemblance of the disease to that seen in graft-versus-host reactions and it was speculated that this could result from virus infection of lymphocytes causing activation of autoaggressive T-lymphocytes, either directly through clonal stimulation or by depression of specific suppressor cell populations. This concept was further developed when the surface markers, cytokine expression, and cultural characteristics of virus infected lymphoblastoid cell lines derived from cattle naturally infected with OvHV-2 and from experimentally infected rabbits were characterized. It was concluded that the cell lines most closely resembled anergic T-cell clones. Such cell lines can regularly be derived from animals affected with MCF induced by either AlHV-1 or OvHV-2, the cells morphologically resembling large granular lymphocytes that function as indiscriminate killer cells. Such cells most closely resemble lymphokine-activated killer cells.
There is evidence that viral DNA is present in episomal form and only limited viral transcription occurs in the cells with no intact virions being detectable. It is concluded that only early transcripts of virus replication are present, probably the latency-associated virus products. In the natural host, OvHV-2 is present in B-lymphocytes, presumably as a latent infection. Thus it is tempting to propose that these same virus transcripts expressed in the T-lymphocytes of MCF susceptible animals drives an immunological response that precipitates the reaction characteristic of MCF.