Enhanced inducible nitric oxide synthase expression and nitrotyrosine accumulation in experimental granulomatous hepatitis caused by Toxocara canis

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Abstract

The involvement of inducible nitric oxide synthase (iNOS) and nitrotyrosine (NT) in pathogenesis of toxocaral granulomatous hepatitis (TGH) in a murine host was quantitatively determined by biochemical, parasitological, pathological, and immunohistochemical assessments in a 42-week investigation. Mice were sacrificed for serum collection and histological processing as well as acid-pepsin digestion of the liver in a larval recovery study. Significantly increased levels of total serum NO were found in the trial, indirectly suggesting iNOS activation in the liver. iNOS reactivity was predominantly observed in infiltrating leucocytes in lesions and normal and apocrine-like cholangiocytes; in contrast, hepatocytes and multinucleated giant cells showed negative cytoplasmic staining in TGH. Strong iNOS-like reactivity was also detected on the body wall of larvae. The locations of NT reactivity were nearly identical to those of iNOS expression; infiltrating leucocytes or cholangiocytes stained for iNOS were also stained for NT in TGH. Enhanced iNOS expression, but not invading larvae ($r = 0.256$, $P = 0.211$), seemed to play a certain role in pathological damage in TGH due to a significant correlation between iNOS expression and serum alanine aminotransferase (ALT) levels ($r = 0.593$, $P = 0.021$) in the trial. Our present results indicate a potential therapeutic strategy for treatment of GH caused by other nematodes through manipulation of iNOS expression.