

P290 Absence of placental growth factor aggravates DSS-induced acute colonic injury

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Background: Angiogenesis has recently been described as a component in inflammatory bowel disease (IBD) pathogenesis. The vascular endothelial growth factor (VEGF) homologue placental growth factor (PlGF) establishes its angiogenic capacity during pathophysiological conditions. The role of PlGF in experimental colitis has never been investigated.

Aim: To investigate the role of PlGF in murine dextran sulphate sodium (DSS) colitis.

Methods: Acute DSS colitis was induced in PlGF knock-out (-/-) and wild-type (WT) mice. Disease activity was calculated during the course of the experiment. Colonic inflammation was evaluated by decrease in colon length, histological score and myeloperoxidase activity. Epithelial apoptosis was detected by a TUNEL assay. PlGF and VEGF were measured in distal colonic lysates by ELISA. Mucosal vascularization was quantified by computerized morphometric analysis of CD31 stained distal colonic sections.

Results: During DSS colitis, PlGF -/- mice showed significantly increased weight loss ($P = 0.001$), rectal bleeding ($P = 0.045$), colonic epithelial apoptosis ($P = 0.025$) and colonic shortening ($P = 0.049$) compared to WT mice. Moreover, there was a trend to higher MPO activity and more epithelial ulcerations in PlGF -/- mice. DSS colitis was associated with a significant increase of PlGF (in WT mice) and VEGF (both in WT and PlGF -/- mice) in distal colonic tissue. Despite comparable VEGF levels were reached in WT and PlGF -/- mice, the latter showed significantly less mucosal angiogenesis after DSS administration (WT vs PlGF -/-: mean vascular density: $P = 0.025$, mean vessel diameter: $P = 0.001$).

Conclusion: Knock-out of placental growth factor strongly blocks angiogenesis during DSS colitis, which worsens the disease course in this acute injury model.