PTH-049

ACTIVE ULCERATIVE COLITIS IS ASSOCIATED WITH DOWNREGULATION OF THE TH1, TH2 AND TH17 CYTOKINE RESPONSE AND ELEVATED IL-8 LEVELS IN MUCOSAL BIOPSIES

doi:10.1136/gut.2011.239301.450

D S Pearl,[1,*] K Shah,[2] J Brown,[2] J K Shute,[2] T M Trebble[1] *[1]Department of Gastroenterology, Portsmouth Hospitals NHS Trust, Portsmouth, UK; [2]Institute of Biomedicine and Biomolecular Sciences, University of Portsmouth, Portsmouth, UK*

Introduction Ulcerative colitis (UC) is a chronic inflammatory condition of unconfirmed aetiology. Microscopic examination of inflamed biopsies is characterised by an acute and chronic inflammatory cell infiltrate. There is conflicting evidence from experimental studies on the relative roles of TNFα, IL-8 and cytokines released by Th1, Th2 and Th17 lymphocytes in UC. This may be further complicated by interindividual variation in cytokine release due to genetic polymorphism. However, current therapy in inflammatory bowel disease includes cytokine targeted interventions. The authors compared cytokine profiles of inflamed and non-inflamed mucosa in UC and age-sex matched controls.

Methods Ethical approval was obtained. Patients were prospectively recruited from outpatients' clinics. Mucosal biopsies at flexible sigmoidoscopy (FS) were taken from active UC patients within inflamed (active) and endoscopically normal proximal mucosa (internal control), and age-sex matched (external) controls undergoing FS. Quantitative cytokine analysis for IL-4, TNFα, IL-17A, IL-8 and IFNγ were carried out using commercially available assays on tissue homogenates prepared with protease inhibitors, corrected for total protein. Statistical comparison was by Wilcoxon signed rank pair analysis for non-parametric data.

Results 69 active UC patients (54 paired normal/inflamed mucosa) and 69 controls were compared. No biologically significant differences were noted between normal tissue from colitis patients and external control mucosa. Cytokine measurements in inflamed mucosa compared with uninflamed mucosa from the same patients demonstrated significant reductions in IL-4 ($p<0.005$), IFNγ ($p<0.002$) and IL-17A. ($p<0.002$), whereas IL-8 ($p<0.0005$) was significantly increased. Similarly, IFNγ was decreased ($p<0.02$) and IL-8 increased ($p<0.0001$) in inflamed mucosa compared with external control tissue; TNFα was not significantly different in inflamed compared with control mucosa.

Conclusion This findings suggest that cytokine release within normal mucosa in UC patients is not significantly different from matched controls; however, in inflamed mucosa, cytokines released by Th1, Th2 and Th17 lymphocytes are reduced and TNFα is unchanged. In contrast, IL-8 (a potent neutrophil chemoattractant) is elevated. These findings suggest that the immunopathogenesis underlying the inflammatory response in UC may be reflective of an alternative to a Th1, Th2 and Th17 driven chronic inflammatory system and may involve an IL-8 mediated leukocytic infiltrate.

Competing interests None.

Keywords cytokine, IFNγ, IL-17A, IL-4, IL-8, TNFα, ulcerative colitis.