Primary Immunodeficiencies Presenting with Inflammatory Bowel Disease

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A balance between immune responses to harmful microorganisms and tolerance to nonpathogenic antigens is essential for immune homeostasis in the gastrointestinal tract. This generally favors the development of tolerance. Multiple immune factors including barrier function, neutrophils, cytokines, IgA and regulatory T cells are essential to the process.

Inflammatory conditions affecting the bowel are common complications of primary immunodeficiency, occurring at any age. The onset of inflammatory bowel disease at an early is most commonly the manifestation of a monogenic disorder. Over 50 genes are known to cause early onset IBD but not all appear to primarily affect immune function, although the majority impact in some way. Four genes are listed in the 2015 version of IUIS tables under heading of immune dysregulation with colitis (IL-10 deficiency, IL-10Ra deficiency, IL-10Rb deficiency, NFAT5 haploinsufficiency), but 'IBD', 'diarrhoea', 'enteropathy' and 'colitis' appear frequently amongst the typical presenting features of many recognised immunodeficiencies including chronic granulomatous disease, Wiskott Aldrich syndrome, IPEX, XIAP, LRBA, CTLA4 and a range of auto-inflammatory conditions. Differences in the prognosis and management argue that a genetic diagnosis should not be missed. As a group, these diseases are rare but have high morbidity and subgroups have high mortality if untreated. Understanding the pathophysiology of a disorder can identify unconventional biological treatment options that interfere with specific pathogenic pathways. So early diagnosis, preferably genetic, is important.

This talk will highlight some of the pathogenic mechanisms leading to early onset inflammatory bowel disease in the setting of primary immunodeficiency, investigation and implications to management.