Sarcoidosis is a Th1/Th17 multisystem disorder: wider implications

Facco et al demonstrated elevated levels of T helper 17 (Th17) cells in the peripheral blood and in the bronchoalveolar lavage of patients with active sarcoidosis; increased expression of interleukin 17 (IL-17) and IL-23R in lung and lymph node specimens was also noted. These results suggest a role for the IL-23/Th17 inflammatory axis in the pathogenesis of sarcoidosis.

Crohn’s disease (CD) is a severe inflammatory bowel disease (IBD). Many components of the IL-23 pathway (IL23R, IL12B, STAT3, JAK2, TYK2) are true IBD susceptibility genes, suggesting a crucial role for this pathway in maintaining intestinal immune homeostasis.

We recently reported the development of multisystem sarcoidosis in two CD patients who had received maintenance therapy with natalizumab, a selective adhesion molecule inhibitor that prevents lymphocyte migration to the gut. We hypothesised that natalizumab may have contributed to the development of the disease by allowing dysregulated lymphocyte trafficking to the respiratory mucosa and other extraintestinal mucosal surfaces in genetically predisposed individuals.

Complex disease genetics has been revolutionised by the advent of genome-wide association (GWA) studies. Shared susceptibility genes between IBD and other immune mediated/inflammatory disorders (ankylosing spondylitis, psoriasis, systemic lupus erythematosus, rheumatoid arthritis, asthma, atopic dermatitis, coeliac disease, multiple sclerosis, type 1 and type 2 diabetes mellitus, mycobacterial disease) have already emerged, paralleling the reported epidemiological evidence. A combined analysis of a limited (100 kb) GWA study in CD and sarcoidosis identified a common susceptibility locus on 10p12.2 (but not at GWA levels of significance). We feel that this recent publication provides further intriguing evidence of common immunopathogenic pathways between CD and sarcoidosis. Ongoing research into common pathways and susceptibility regions between these two granulomatous conditions is essential, with further exploration of the IL-23/Th17 axis looking increasingly like a good starting point.

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