A182 INTERLEUKIN 17-PRODUCING CELLS ARE INCREASED IN THE PERIPHERAL BLOOD OF PATIENTS WITH RHEUMATOID ARTHRITIS AND ARE ENRICHED AT THE SITE OF INFLAMMATION

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Background Th17 cells are a recently identified CD4 T cell subset characterised by production of interleukin 17α (IL17). Due to the highly proinflammatory and osteoclastogenic effects of IL17, Th17 cells are likely to have an important role in the pathogenesis of rheumatoid arthritis (RA). The aim of this study was to identify if Th17 cells are increased in peripheral blood from patients with RA, and if these cells are increased at the site of inflammation. The authors also investigated relationships between Th17 cells and disease activity/inflammatory markers.
Methods Peripheral blood mononuclear cells (PBMCs) were isolated from healthy controls or patients with RA and stimulated with phorbol 12-myristate 13-acetate and ionomycin for 3h in the presence of Golgistop. Paired synovial fluid (SF) or tissue (ST) from inflamed knee joints was analysed where available. Synovial tissue was digested with collagenase prior to stimulation. Intracellular expression of IL17, interferon (IFN)γ and tumour necrosis factor (TNF)α was determined by multicolour flow cytometry.
Results Peripheral blood (PB) samples were collected from 32 patients with established RA and 24 healthy controls. Th17 cells were present at increased levels in PBMCs from RA patients with median (IQR) of 0.56% (1.36) vs 0.32% (0.36) in healthy controls (p=0.02). A small percentage of cells positive for both IL17 and IFNγ were observed, which was higher in RA patients. Paired PB and SF samples were analysed for 16 patients (18 knees). Cytokine-producing cells were generally elevated in SF. The percentage of total IL17-producing CD4 T cells was significantly elevated within SF versus PB, particularly those with a dual Th17/Th1 phenotype rather than a specific increase in Th17 cells. IL17-producing T cells were present in ST, with three of five patients showing very high levels (>8%). Interestingly, the two patients with low levels (<1%) were clinically in remission with DAS28 <2.6. The authors also found a highly significant correlation between C-reactive protein (CRP) and the percentage of Th17 cells in SF (rs=7, p=0.07), but not between CRP and the percentage of Th1 cells.
Conclusions Th17 cells are increased in PB from patients with RA relative to healthy donors. Furthermore, the authors demonstrate an increased percentage of IL17-producing cells in RA SF, with a shift towards a Th1/Th17 phenotype. Th17 cells are not always increased in ST, and higher levels of IL17 cells may indicate more active disease.