Methods

Influenced by IL-15.

CD4+ T cells of AAV patients express the same molecules as the unique sub-population of effector CD4+ T cells (CD56 (+) CD4+ T-cells) serving. It is hypothesized that IL-15 is able to up regulate the expression of NK cell receptors, e.g. NKG2D and CD56. These serve. It is rare for histological findings of MPO-ANCA positive GPA to show typical granuloma with multinucleated giant cells. We thought that the patient is an important case to consider the pathogenesis of MPO-ANCA positive GPA.

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Interleukin 15, CD56+ T-cells and ANCA-associated vasculitis (AAV)

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Introduction.– Interleukin-15 (IL-15) is a proinflammatory cytokine that is overexpressed in AAV and is linked to the expansion of CD4+ effector memory T-cells (TEM). In AAV in remission a persistent expansion of these CD4+ effector memory T-cells has been observed. It is hypothesized that IL-15 is able to up regulate the expression of NK cell receptors, e.g. NKG2D and CD56. These molecules seem to be involved in tissue injury as they activate cells via interaction with MHC class I related molecule A (MICA) or CD56 ligand respectively. NKG2D and CD56 are also expressed on a unique sub-population of effector CD4+ cells (CD56 (+) CD4+ T-cells) capable of mediating TCR-independent immune activation. In the present study we assessed the expression of NKG2D and CD56 on CD4+ T-cells of AAV and if expression of these molecules was influenced by IL-15.

Methods.– The distribution of CD4+ TEM and the proportion of CD56+ CD4+ T-cells and NKG2D+ CD4+ T-cells were analysed in 45 AAV-patients and 30 HCs by FACS. In vitro effects of IL-15 on the expansion of CD4+ TEM and up regulation of surface cytotoxic markers were assessed in the same way.

Results.– We observed an increased proportion of circulating CD4+ CD56+ T-cells in AAV as well as NKG2D+ CD4+ T-cells in patients in remission compared to HC (13.6 vs. 0.6 P < 0.0001 and 14 vs. 0.7 P < 0.0001). 80% to 90% of these cells were CD4+ effector memory T-cells. The percentages of the CD56+ CD4+ T-cells and NKG2D+ CD4+ T-cells was constant over time. We found a significant positive correlation between the percentages of CD56+ CD4+ T-cells and age in GPA patients in remission (r = 0.6 P = 0.004). Stimulation of PBMCs with IL-15 increased not only the proportion of CD4+ memory cells (CD45RO+) but also the expression of CD56 and NKG2D on these cells.

Conclusion.– Increased IL-15 expression is likely the driving force behind the persistent expansion of cytotoxic CD4+ effector memory T-cells in AAV.

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Resolution of proteinuria and hematuria in ANCA-associated nephritis

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Introduction.– Proteinuria and hematuria are hallmarks of renal involvement in ANCA-associated vasculitis (AAV). Their disappearance is considered an indication of response to therapy, however, little is known of about when this could be expected and the clinical significance if they remain positive.

Patients.– Follow-up data from 28 patients with AAV and nephritis treated with cyclophosphamide, were collected retrospectively. Proteinuria and hematuria was defined as > +1 on dipstick testing. Duration was calculated using Kaplan-Meier plots and patients were censored at death or start of dialysis.

Results.– Median age at diagnosis was 68.3 years (IQR 53.4–73.1) and median p-creatinine 240 microm/L (IQR 113–406). MPO-ANCA was detected in 17 patients and PR3-ANCA in 12. At diagnosis 1 patient did not have hematuria and seven did not have proteinuria. The median time to resolution of hematuria was 104 days (IQR 76–364) and for proteinuria 238 days (76–1213).

Duration of proteinuria and hematuria was not correlated to each other (r = −0.07), to age or to initial p-creatinine, but duration of proteinuria was related to initial U-albumine (r = 0.60). Resolution was faster in PR3-ANCA positive patients compared to MPO-ANCA (hematuria: 76 vs. 127 days, P = 0.01; proteinuria 92 vs. 843 days, P = 0.036).

At 3 months nine patients had no hematuria, none of these developed end-stage renal disease during follow-up, while five out of 18 patients with persistent hematuria experienced such event (P = 0.13).

Conclusion.– There are huge variations in the time it takes for proteinuria and hematuria to disappear in AAV-nephritis after start of treatment, but duration of hematuria is usually shorter than duration of proteinuria. Duration of both signs is shorter in PR3-ANCA associated disease.

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