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P420 -Changes in regulatory and Th2-like populations, but not "senescence" phenotype characterise lymphocytes in older adults with non-dialysis CKD.

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Introduction

Chronic kidney disease (CKD) is associated with a diminished immunocompetency, as evidenced by a higher infective burden and poorer vaccine responses compared to healthy individuals (1, 2). Accelerated immune ageing is a characteristic of lymphocytes in dialysis populations, with expansions of lymphocyte populations with poor replicative capacity (deemed "senescent") (3), but the picture in non-dialysis CKD is less clear. Latent cytomegalovirus (CMV) infection is common and also associated with an expansion of "senescent" lymphocytes (4) and thus could influence T cell phenotypes in this population. Therefore, we sought to systematically characterise the adaptive immune "landscape" in non-dialysis CKD and to evaluate the impact on this of latent CMV infection.

Methods

Peripheral blood mononuclear cells (PBMCs) were isolated from 33 patients with non-immune CKD (eGFR 15-60ml/min/1.73m²) and 28 age and gender matched controls. Cross-sectional analysis of multiple lymphocyte phenotypes was performed in the same individual using flow cytometry, evaluating naïve/memory and regulatory populations of T and B cells, together with T helper subtypes. The presence of latent CMV infection was defined using a clinically-verified serum CMV-specific IgG ELISA. Individuals with a history of immune-mediated disease, immunosuppression or malignancy were excluded from the study.

Results

Most patients with CKD had stage G4A2-3 disease (70%) with a median eGFR of 23ml/min/1.73m² and comorbidities typical of the wider CKD population. Total white cell count, neutrophil count and hsCRP were significantly higher in patients with CKD than controls ($p<0.001$) - in keeping with CKD-associated chronic inflammation. Prevalence of latent CMV infection was high (72% across the study), but the CMV-specific IgG titres of seropositive individuals were similar in patients with CKD and controls.

Patients with CKD had similar naïve/memory proportions of T and B cells (defined by surface expression of CCR7/CD45RA or CD27/IgD, respectively) and similar proportions of "senescent" T cells (defined by loss of surface CD27/28 and/or gain of CD57/KLRG1). Latent CMV infection was a significant predictor of "senescent" T cell expansions in both study groups, independent of age and comorbidity ($p<0.001$).

CKD status was associated with greater proportions of "Th2-like" (CCR4+CCR6-CXCR3-) and regulatory T cells (CD4+CD25+/highFoxP3+) and lower proportions of regulatory B cells (CD19+CD24highCD38high), independent of CMV serostatus.

Conclusion

Previously reported expansions of "senescence"-associated lymphocyte populations in CKD may be confounded by memory inflation resulting from chronic viral exposure e.g. latent CMV infection. However, Th2 polarisation of CD4+ T cells and expansion of Treg populations, as shown in patients with CKD in this study, are associated with chronological ageing (5, 6), and may represent a CMV-independent CKD-

associated accelerated immune ageing phenotype. An altered balance of regulatory lymphocyte populations in CKD may result in poorer immune responses through excessive suppression of T cell effector function.

References

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