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Determining The Role Of Complement Pro-Inflammatory Factors And Regulatory Proteins In Antibody-Mediated Rejection (ABMR) In Paediatric Kidney Transplant Recipients

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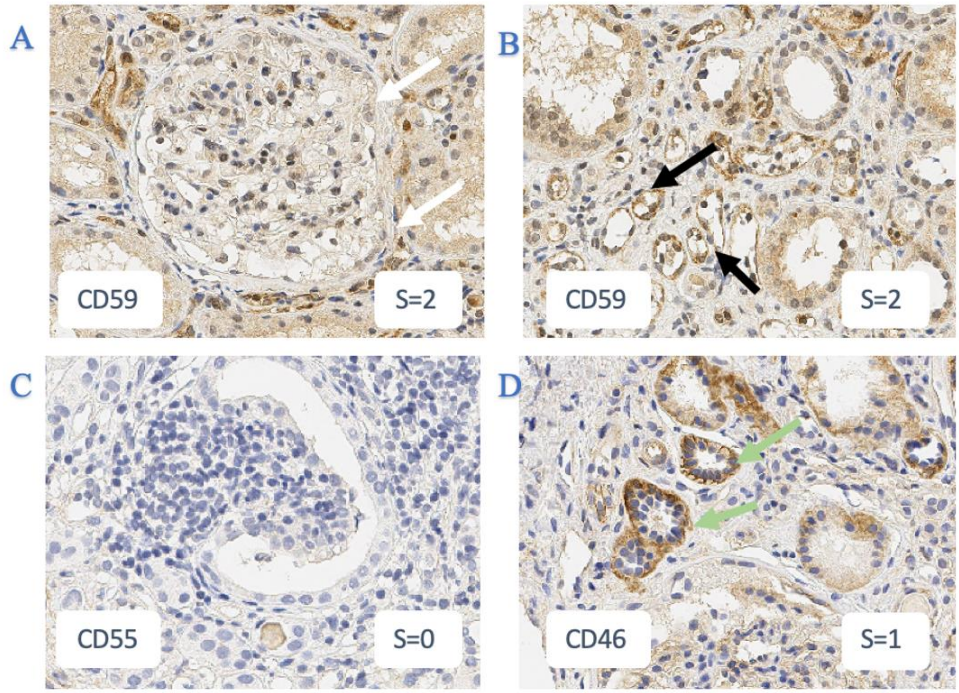
Objectives : Membrane-bound complement regulatory proteins (mCRPs), such as CD46, CD55, and CD59, are expressed throughout the body to prevent over-activation of the complement system. We looked to investigate if there are dynamic markers that could monitor the degree of complement activation, that could subsequently be used either as treatment targets or monitoring tools.
Methods : We performed a retrospective, single centre study to assess the expression of complement induced pro-inflammatory factor (SYK, C3D) and inhibitory proteins (CD55, CD46, CD59). The tissue materials of 54 pKTR who were positive for DSAs, and had a final diagnosis of allograft rejection, were retrieved for IHC staining. A semi-quantitative scoring system was used based on the strength of staining. For our controls, we stained transplant biopsies with no sign of rejection.
Results : When compared to the staining in our controls, CD55, CD59 and C3D, showed no difference in expression. However there was variability in expression of CD46 and Syk. For CD46 there was a difference between the non ABMR biopsies in which only 20% showed positive staining, and the ABMR biopsies where 58% showed positive staining. For the pro-inflammatory factor Syk, there was no positive staining in non ABMR biopsies, and this increased to 100% positive staining in ABMR biopsies.
Conclusions : Our results suggest that these mCRPs demonstrate varying degrees of expression and location in kidneys undergoing ABMR, showing the important role of complement activation in ABMR. There is possibly stronger natural protection against terminal complement by CD59 compared to proximal regulators CD46 and CD55. There is also an increase in expression in CD46 and Syk in ABMR tissue compared to non-ABMR tissue, suggesting they could be useful as treatment targets or monitoring tools in an at-risk population.

Screenshot 2024-01-25 at 19.49.26.png


A
CD59
S=2
B
CD59
S=2
C
CD55
S=0
D
CD46
S=1