DYNAMICS OF COMPLEMENT SPLIT-PRODUCTS IN GRAFT REJECTION AFTER KIDNEY TRANSPLANTION

An observational explorative study

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Aim

- To explore the dynamics of complement split-products in allograft rejection after kidney transplantation
- To explore the potential of complement split-products as biomarker of ongoing immunological activity and rejection
- We hypothesized that P-C3d, P-C3a, P-C4a, P-C5a, U-C3dg, and U-sC5b-9 increase in rejecting kidney transplant recipients

Introduction

- Complement activation is thought to contribute to allograft injury in kidney transplantation and inhibition of complement could be a therapeutic strategy
- Dynamics of complement proteins reflect complement activation
- Extensive efforts are invested into identifying non-invasive markers of allograft injury to improve diagnostics and treatment of allograft rejection in the clinical setting

Results: Plasma Study

- We saw no difference ***in between*** the groups
- P-C3d and P-C3a increased significantly at time of rejection compared to stable phase ***within*** the groups
- Delayed graft function, pre-transplant P-C3d, and use of steroids had a significant effect on P-C3d, and when adjusting results accordingly, P-C3d increased significantly at time of rejection ***in between*** groups (p-0,04)

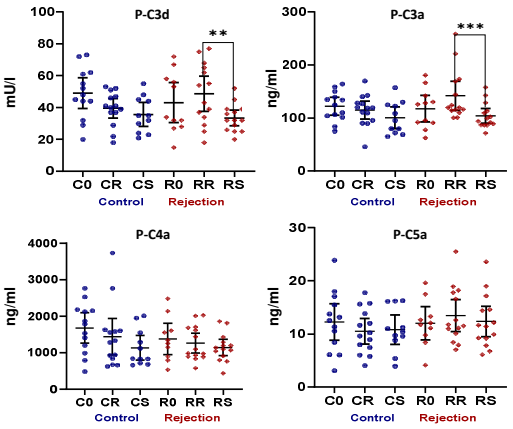


Fig. 1 Mean concentration (95 % CI) of P-C3d, P-C3a, P-C4a, and P-C5a pre-transplant, time of rejection and in stable phase in the **Control** and the **Rejection** group

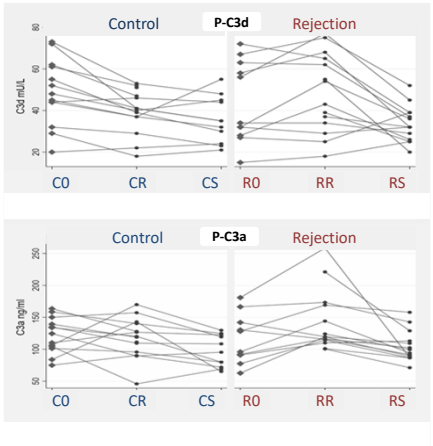


Fig. 2 Dynamics of P-C3d and P-C3a in each patient in the **Control** and the **Rejection** group

Results: Urine Study

- We saw no difference ***in between*** the groups
- U-C3dg/crea and U-sC5b-9/crea increased significantly at time of rejection compared to stable phase ***within*** both groups; as did U-C3dg/crea in the control group
- U-albumine was positively correlated with U-C3dg/crea and U-sC5b-9/crea while we saw a negative correlation with time from transplantation

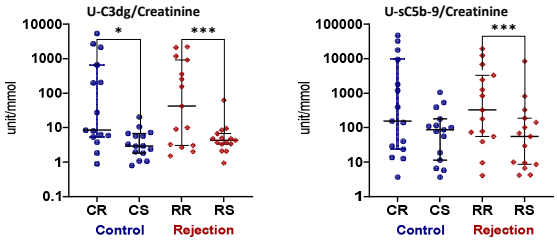
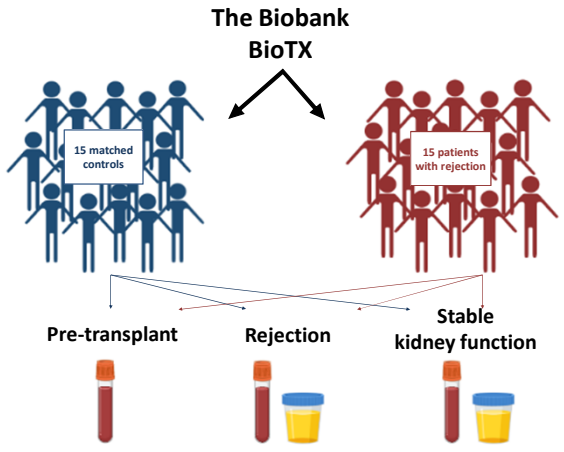


Fig. 3 Median excretion (IQR) of U-C3dg/crea and U-sC5b-9/crea at time of rejection and in stable phase in the **Control** and the **Rejection** group

Methods



C0 Control Group - time of transplantation
CR Control Group - time of rejection
CS Control Group - stable phase
R0 Rejection Group - time of transplantation
RR Rejection Group - time of rejection
RS Rejection Group - stable phase

- The biobank, BioTX provided the studies with data and plasma/urine samples
- 15 patients with graft rejection were matched with 15 controls for the Plasma Study
- 15 patients with graft rejection were matched with 15 controls for the Urine Study
- Samples taken pre-transplant (only plasma), at time of rejection, and at time of stable kidney function (stable phase) in the Rejection Group, and at matching time in the Control Group
- P-C3d analyzed with double-decker rocket immune electrophoresis, P-C3a, P-C4a and P-C5a analyzed with BD Cytometric Bead Array Human Anaphylatoxin kit, and U-C3dg and U-sC5b-9 analyzed with ELISA

Conclusion

P-C3d and P-C3a increase at time of rejection in kidney transplant patients and surveillance of the intra-individual dynamics of P-C3d and P-C3a might be applicable as biomarker of ongoing immunological activity and imminent rejection

A larger prospective study of P-C3d and P-C3a in kidney transplantation would be needed to further clarify the potential of P-C3d and P-C3a as biomarkers of rejection and could broaden our knowledge of complement activation in kidney transplantation in the era of new complement inhibitors

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