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Protocol biopsies and pathologic markers of progression in HLA-incompatible kidney transplants

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Transplantation across HLA and ABO barriers is now possible with pre-transplant desensitization for highly sensitized patients, but recipients of HLA incompatible allograft are at increased risk of rejection and graft loss. 745 renal transplant biopsies, including 380 protocol biopsies at 1, 3, 6 and 12 months post-transplant, from 129 recipients of HLA-incompatible kidney allograft, with follow up of more than 1 year (median 3 years) at the Johns Hopkins Hospital were analyzed. Biopsy-proven rejection was associated with approximately 30% lower 5 year graft survival. Subclinical rejections were identified by protocol biopsies in a significant proportion of patients: 36% for cell mediated rejection (CMR) and 13% for antibody mediated rejection (AMR). Protocol biopsies detected glomerulitis, a feature of AMR and an important risk factor for development of chronic transplant glomerulopathy, in 41% of all biopsies performed in the first year post transplant. Transplant glomerulopathy within the first year post transplant is associated with worse graft survival and was observed in 22% of patients in this study. Transplant glomerulopathy at 1 year was detected by protocol biopsies in approximately 75% of cases. Arteritis was noted in the graft of approximately 30% patients. Protocol biopsies detected about half of the arteritis in the renal grafts. Preliminary analysis of the data did not show significant association of arteritis with worse graft survival. The observation support the value of protocol biopsies performed serially after transplantation in revealing early subclinical lesions amenable to treatment, and improving graft survival.

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Application of digital pathology systems for biomarker analysis in translational pathology: Challenges and caveats for the pathologist

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An important aim in translational pathology is the discovery of novel biomarkers in human tissue samples, especially those with predictive value. A traditional method for biomarker analysis is based on the immunohistochemistry (IHC) staining of formalin fixed paraffin embedded tissue sections which is then evaluated with light microscopy by a pathologist, who usually provides a semi quantitative scoring. However, this method is subjective and effort consuming, including also a variability between observers. The current development of digital pathology systems, including faster scanners and more powerful image analysis software, provide an important tool for biomarker evaluation. However, the application of image analysis technologies requires a higher quality and consistency of IHC. Furthermore, in our experience we have learned that the application of digital pathology demands a new role for the pathologist who has now to provide a more rigorous IHC quality control, including the selection of markers for image analysis depending on their expression pattern, and also and type of image analysis technique available for a particular project, in order to provide reliable and useful data with translational meaning.

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