The Success of Liver Transplantation in Patients with Pre-transplant Positive Crossmatch Depends on the Liver's Ability to Clear Donor-Specific Antibodies: A Case Study

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Introduction

- **Purpose of Liver Transplantation:** Liver transplantation serves as the definitive therapeutic option for patients with end-stage liver disease (ESLD), offering a potential for prolonged survival and improved quality of life (1).
- **Challenges with Donor-Specific Antibodies (DSAs):** The presence of DSAs and a positive crossmatch (XM) test before transplantation significantly complicates the process (2). These antibodies can attack the transplanted organ, leading to graft rejection and failure (2).
- **Importance of Crossmatch Test:** The XM test is crucial for identifying harmful antibodies that may predispose the recipient to transplant rejection. A positive XM can persist even after the transplant, influencing post-operative care and outcomes.
- **Clinical Implications:** Managing patients with positive XM and pre-existing DSAs requires advanced immunological assessments and highly individualized medical strategies to increase the likelihood of successful transplantation outcomes.
- **Research Objectives:** We highlight two contrasting cases to demonstrate the potential impacts of DSAs and the importance of tailored immunosuppression in liver transplantation.

Case Reports

Case 1: 55-Year-Old Female with Non-Alcoholic Steatohepatitis (NASH) Cirrhosis

- **Background:** Positive hepatitis C antibody; sensitized to human leukocyte antigens (HLA); pre-existing DSAs.
- **Pre-transplant DSAs:** A1, A11, B8, Cw7
- **Post-transplant DSAs:** B8
- **Transplant Process:** Underwent liver transplantation despite a positive XM against the donor.
- **Post-Transplant Complications:** Persistently positive XM after plasmapheresis; worsening liver function; histology confirmed antibody-mediated rejection (ABMR).

Case 2: 58-Year-Old Male with Metabolic Dysfunction-Associated Steatohepatitis (MASH) and Autoimmune Hepatitis

- **Background:** ESLD from cirrhosis; urgent clinical need for transplantation.
- **Pre-transplant DSAs:** A2, A68, DR53
- **Post-transplant DSAs:** DR53
- **Transplant Process:** Received a liver transplant despite a positive pre-transplant XM.
- **Post-Transplant Outcome:** Negative XM after tailored immunosuppressive treatment; satisfactory early graft function and stable liver function thereafter.

Materials & Methods

- **Patient Selection and Ethics:** Two ESLD patients were selected based on positive DSAs and XMs. **Immunological Testing:** Pre- and post-transplant DSA and XM assessments using Luminex and flow cytometry.
- **Transplant Procedure:** Liver transplants were performed using standard surgical techniques, focusing on minimizing cold ischemia time and optimal graft preservation.
- **Immunosuppressive Management:** Customized immunosuppressive regimens post-transplant include induction with basiliximab and methylprednisolone, followed by maintenance therapy with tacrolimus and prednisone.
- **Monitoring and Outcomes:** Regular liver function tests, biopsies, and plasmapheresis as needed. Outcomes measured by liver function, graft survival, and ABMR detection.

Results

Figure 1: Pre-transplant (A) and post-transplant (B) T & B cell crossmatch histogram for 55-year-old female.

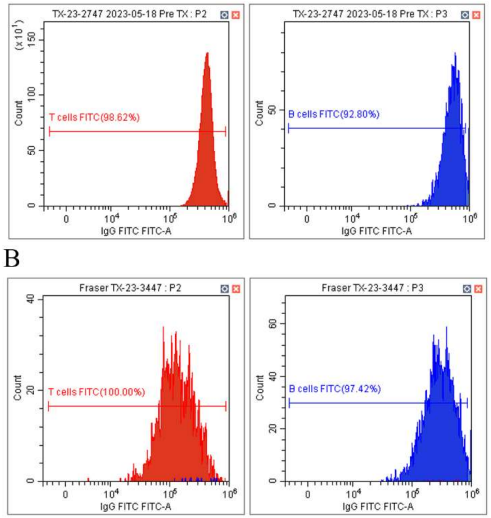


Figure 2: Pre-transplant (A) and post-transplant (B) T & B cell crossmatch histogram for 58-year-old male.

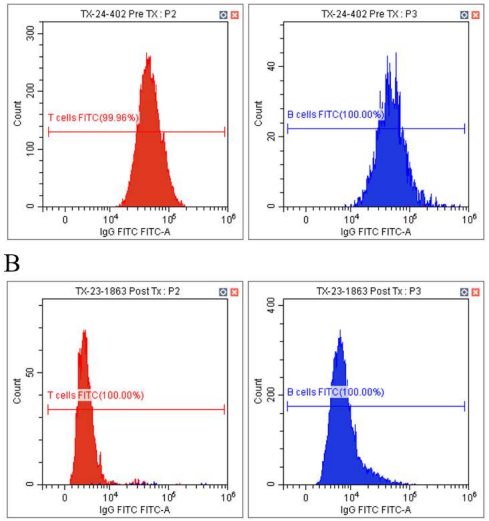
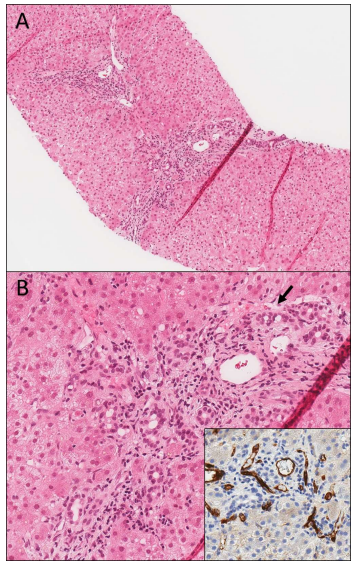


Figure 3: Liver biopsy from Case 1 showing histologic features of ABMR at low power (A) and high power (B). There is dilatation of the portal microvasculature with endothelial cell hypertrophy (arrow). Other features include prominent bile ductular reaction and occasional bile duct epithelial injury. Immunohistochemistry for C4d (inset) demonstrates diffuse staining involving >50% of the circumference of portal microvasculature. There is extension into periportal sinusoids and inlet venules.



Conclusion

- **Critical Role of the Liver in DSA Clearance:** The liver's unique immunological and circulatory properties contribute significantly to its ability to clear DSAs. Unlike other solid organs, the liver has a higher threshold for tolerance induction due to its dual blood supply, which allows for constant high-volume blood flow and exposure to antigens (3). This extensive blood exposure facilitates the clearance of circulating antibodies, including DSAs.
  - From our case studies, we conclude that the liver demonstrates a more effective clearance of Class 1 DSAs compared to Class 2. Additionally, it exhibits a higher efficiency in processing antigens associated with the A locus or C locus over those linked to the B locus.
- **Impact on Transplant Outcomes:** Successful post-transplant DSA clearance is closely linked with positive outcomes. The liver's ability to clear these antibodies can prevent the development of antibody-mediated rejection (ABMR), thus enhancing graft survival and function.
- **Case Study Insights:** The contrasting outcomes in the presented cases underscore the importance of the liver's capacity to clear DSAs. In the first case, persistent DSAs post-transplantation led to ABMR and graft failure. Conversely, the second case demonstrated successful clearance of DSAs with tailored immunosuppression, resulting in stable liver function and satisfactory graft performance.
- **Need for Personalized Strategies:** The cases highlight the importance of personalized immunosuppressive strategies and multidisciplinary care to manage DSAs effectively.
- **Research Imperatives:** Ongoing research to enhance understanding and optimization of the liver's immunological functions is vital for improving long-term outcomes for transplant recipients.

References

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