Introduction

We present a unique case of chronic rejection due to HLA-antibody formation during pregnancy.

Clinical Presentation of ACR & CR

Liver Biopsy Findings of Acute Cellular Rejection (ACR)	Liver Biopsy Findings of Chronic Rejection (CR)
- Subendothelial damage of hepatic portal veins and terminal hepatic venules - Bile duct inflammation - Mixed infiltrate (predominantly mononuclear lymphocytes)	- Obliterative arterial inflammation progressing to hepatic ischemia and ductopenia - Interstitial inflammation and bridging fibrosis - Atrophy of parenchyma - Cirrhosis

Case Description

A 51-year-old female with a history of autoimmune hepatitis received a live donor liver transplant (LDLT) with her husband as the donor in January 2008. HLA crossmatch testing was performed prior to transplant with a negative result. Patient was well overall for 8 years following liver transplant. Moderate elevation of liver enzymes during this period lead to liver biopsy consistent with autoimmune hepatitis but no evidence of acute rejection.

The authors have no conflicts of interest to report.

Case Description

Patient became pregnant 8 years after LDLT. She developed moderate-chronic elevation of liver enzymes during pregnancy with the most prominent peaks being 731 IU/L alkaline phosphatase (N: 40-140 IU/L), 200 IU/L aspartate aminotransferase (N: <35 IU/L), and 160 IU/L alanine aminotransferase (N: <52 IU/L). In December 2016, the patient had a liver biopsy displaying microvesicular steatosis, endotheliitis, and bile duct damage representative of acute cellular rejection. The patient was placed on quadruple immunosuppression therapy: everolimus, tacrolimus, prednisone, and mycophenolate mofetil.

HLA antibody testing was performed at that time to check for donor specific antibodies (DSA). DSA was identified against HLA DQ6, suggesting sensitization to her husband's HLA antigens that occurred during pregnancy/delivery.

Despite extensive treatment, chronic rejection of the liver transplant prevailed with bile duct damage progressing to ductopenia.

Additional treatments for her condition included intravenous immunoglobulin (IVIG) therapy every 28 days, with photopheresis and plasmapheresis to reduce leukocytes and immunoglobulins attacking the transplanted liver respectively. However, even with multi-modal therapy, the patient's condition worsens indicated by a rising MELD (model of end-stage liver disease) score and bilirubin concentration to 8 mg/dL.

Figures

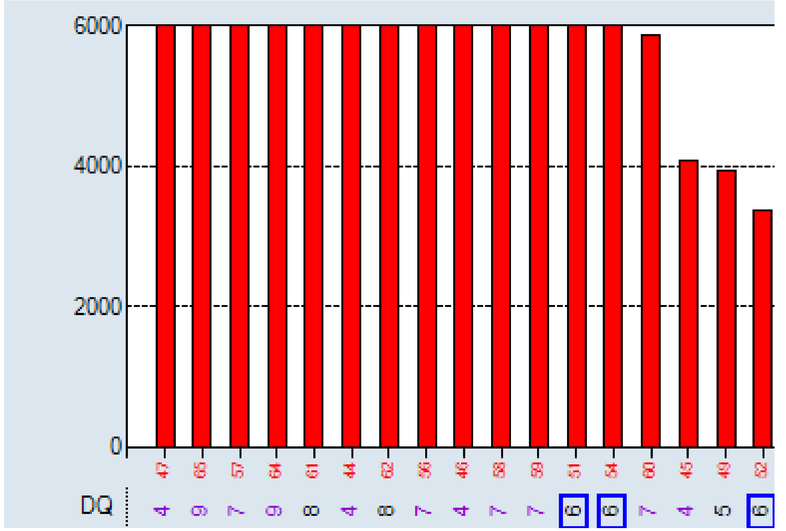

Figure 1: Numerical values on the y-axis represent mfi (mean fluorescence activity). Mfi> 2000 are positive for the respective DQ antigen shown along the x-axis. Positive results for DQ6 presence in the patient are boxed in blue.

Discussion

We present a unique case of acute (antibody-mediated) rejection progressing to chronic rejection in a LDLT patient following pregnancy due to sensitization to donor HLA DQ6. Consistent post-transplant HLA antibody testing should be a consideration for LDLT patients for early detection and treatment of DSA before memory B-cell production allows rejection to become chronic. Testing is especially important for monitoring female patients with LDLTs from spouse due to risk of blood exposure during pregnancy.

References

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