Small surgery-big impact: Development of HLA antibodies following sclearal patch graft in a kidney-pancreas transplant candidate

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Case description

A 39-year-old male patient with diabetic nephropathy on the waitlist for combined kidney and pancreas transplantation was being routinely monitored for anti-Human Leukocyte Antigen (HLA) antibodies. From 2019 until 2023, pre-transplant screening by Luminex Single Antigen Bead (SAB) testing demonstrated low HLA sensitization, with a calculated Panel Reactive Antibody (cPRA) of 4% using the Canadian cPRA calculator. Early 2014, a routine monitoring sample detected significant HLA antibody reactivity to class I and class II antigens and his cPRA increased to 79%, although no sensitizing events had been reported to the laboratory.

Careful review of the patient's medical history revealed that he had undergone ocular surgery for glaucoma in late 2022, which included the use of scleral patch allograft in his right eye. Since the HLA antibodies emerged following the exposure to the scleral patch allograft. Although no sample from the tissue donor was available for retrospective HLA typing, epitope analysis using HLA Matchmaker Software indicated potential reactivity to epitopes epitopes 166DG and 56R for class I and 96HK for class II.
A surrogate crossmatch with a DR12 donor showed B cell strong positive result, indicating the presence of antibody reactivity against DR12 antigen.

Patient HLA typing

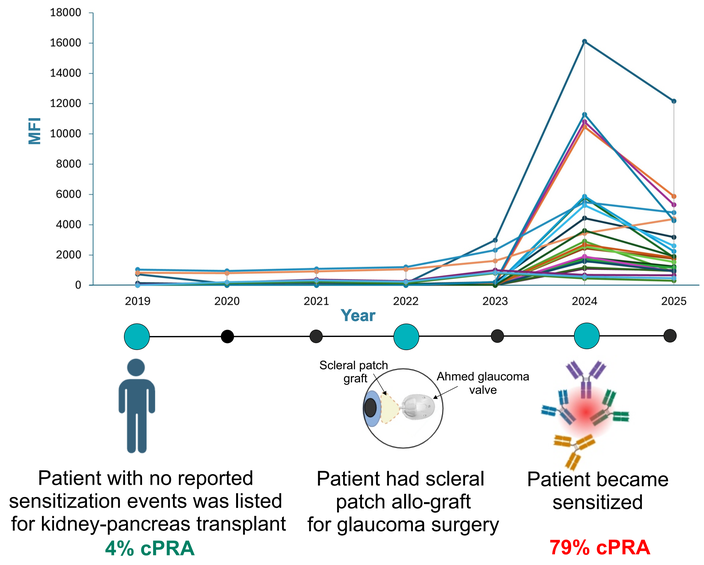
A	B	Bw	Cw	DR	DRB 3/4/5	DQA1	DQB1	DPA1	DPB1
2	27	4	9	4	53	03	7	01	03:01P
3	60	6	10	4	53	03	8	01	04:01P

Serological equivalents were used for HLA-A, B, Cw, DRB1, DR345 and DQB1, and molecular typing were used for HLA-DQA1, DPA1 and DPB1.

Methods

- HLA typing was performed using rSSO from One Lambda Thermo Fisher Scientific.
- HLA antibody screening was performed using LIFECODES ® LifeScreen Deluxe (LMX) from Werfen-Immucor GTI Diagnostics, Inc.
- Serum samples were pre-treated with EDTA and tested for antibody specificity by Single antigen bead testing (LSA) from One Lambda Thermo Fisher Scientific.
- Pre-ocular surgery samples were ran on Luminex 200, while the post-ocular surgery samples were ran via Luminex Flexmap 3D with no divider.
- Eplet analysis was performed using MatchMaker software from One Lambda Thermo Fisher Scientific.
- Canadian cPRA calculator of the Canadian Transplant Registry.

Results



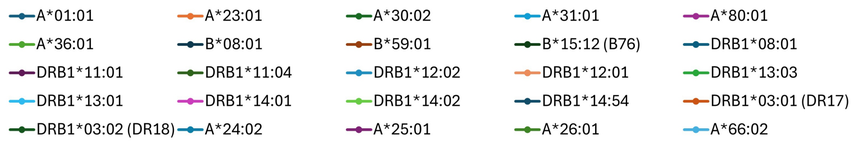


Figure 1. Development of HLA antibody reactivity following scleral patch allograft surgery in a kidney-pancreas transplant candidate.

A line graph illustrates the Mean Fluorescence Intensity (MFI) of class I and class II anti-HLA antibodies in a kidney-pancreas transplant candidate on the waiting list. The timeline below the graph correlates a key clinical event with our patient's immunological status. The patient has developed a significant sensitization and his cPRA increased from 4% to 79% following a scleral patch allograft for glaucoma surgery.

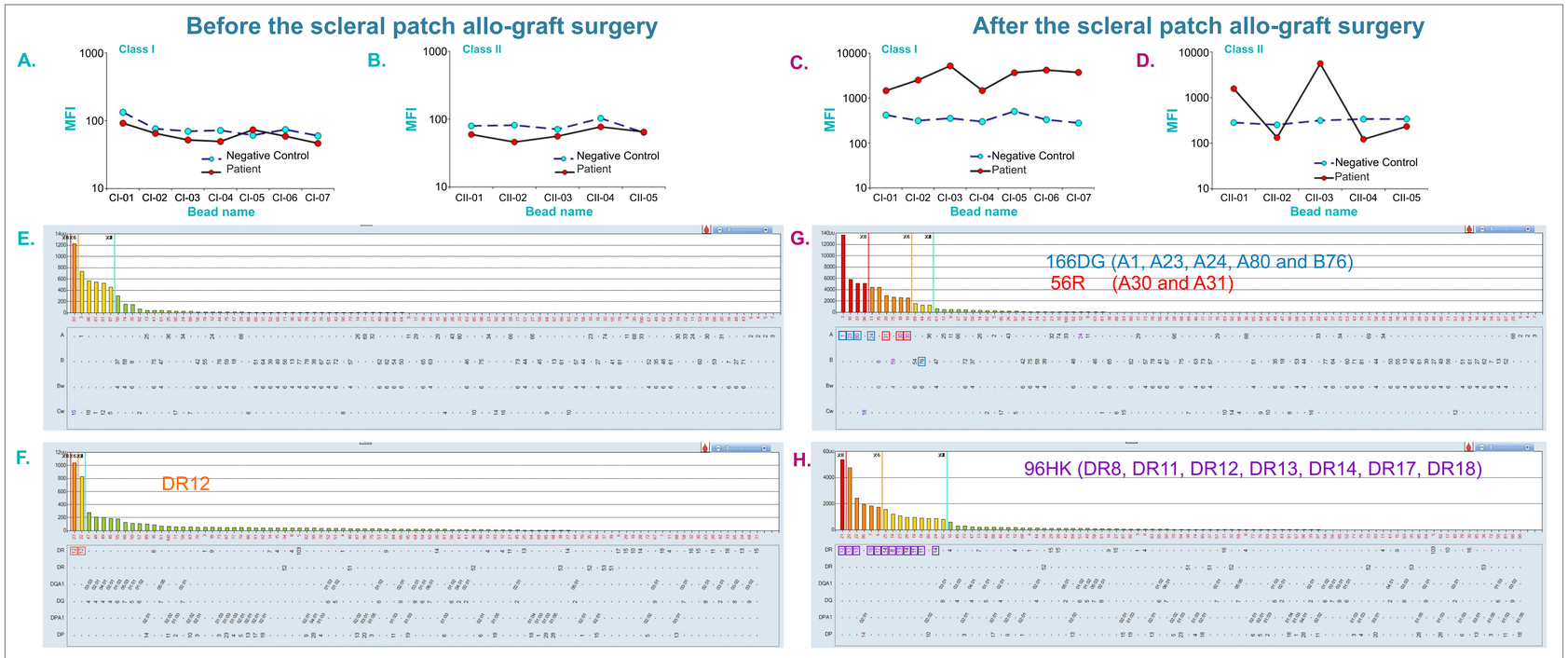


Figure 2. Identification of HLA eplets reactivity in patient sera samples after receiving scleral patch allograft. HLA antibody reactivity screening via LIFECODES® LifeScreen Deluxe (LMX) shows low level of HLA antibody reactivity before the optical surgery (**A** and **B**), and the detection of antibody reactivity after the scleral patch allograft surgery (**C** and **D**). Epitope analysis using HLA MatchMaker software from One Lambda single antigen bead testing of the patient's serum showed low sensitization in both class I (**E**) and class II (**F**) HLA- antibodies before the scleral allograft, with only moderate DR12 antibody reactivity. However, after receiving the scleral graft, a peak serum sample revealed development of distinctive eplet reactivity including 166DG (A1, A23, A24, A80 and B76) and 56R (A30 and A31) for class I (**G**), and 96HK (DR8, DR11, DR12, DR13, DR14, DR17, DR18) for class II (**H**).

Conclusion

This case underscores the importance of considering all tissue allografts used in surgical procedures as potential HLA sensitization events. There are other surgeries that routinely use donor tissue and each of these may carry a similar risk. This case suggests the need for improved education and informed consent for patients who are potential transplant candidates that may require surgical procedures employing these donor tissues. It also emphasizes the value for comprehensive HLA typing of tissue donors. Enhanced communication between the transplant coordinator, HLA laboratory, and the clinical team can improve the immunological risk assessment for solid organ transplant candidates on the waiting list. Knowledge of these risks may lead to consideration of intervention that may reduce the likelihood of sensitizing transplant candidates.