Transplant Immunology

Stanley C. Jordan, M.D.

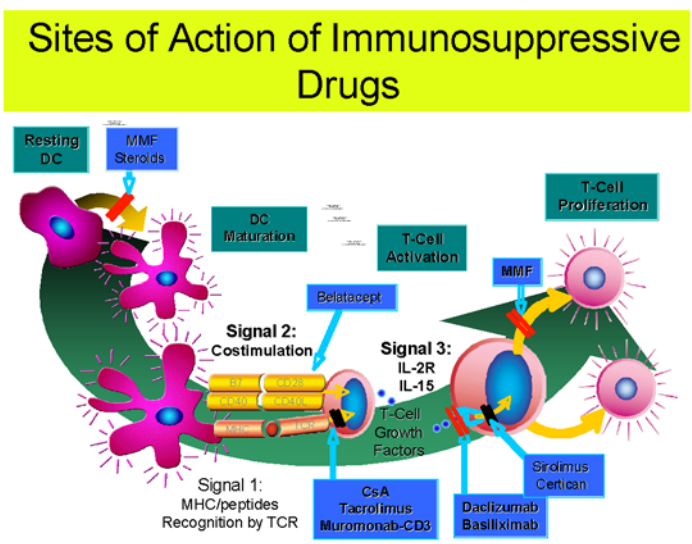
Comprehensive Transplant Center, Cedars-Sinai Medical Center, Los Angeles, CA

Case Presentation

HP is a 49 y.o. AA female with end-stage heart/lung disease secondary to sarcoidosis and pulmonary hypertension. The patient is a candidate for combined heart-lung transplantation, but was noted to have an elevated panel reactive antibody (PRA) test of 85%. This test indicates the patient has been exposed to human leukocyte antigens (HLA) of other individuals. This usually occurs as a result of blood transfusions, previous pregnancies or previous transplants. In this case, HP had 4 previous pregnancies and a history of blood transfusions. Although listed for H-L transplant, the patient could not receive a transplant due to a persistently positive cross-match with prospective donors. She was deteriorating on the wait list and was referred to our center for consideration of desensitization therapy with intravenous gammaglobulin (IVIG) and rituximab (anti-CD20, anti-B-cell). The patient received two doses of IVIG (2 g/kg day#0, day#30) and rituximab (1 g day #7 & day #21). Repeat PRAs were checked. Approximately 2 months later, the PRA was 35% and the patient received a CMX (-) H-L transplant. She has subsequently done well without evidence of rejection or infection.

Summary

The evolution of our understanding of basic immunology has contributed greatly to the advancements in human transplantation. Currently, there is a sophisticated understanding of T-cell activation and regulation that has led to a more rational approach to development of immunosuppressive/immunoregulatory agents. Advancements in basic



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immunology continues to hold the promise for advancements in the care and outcomes for transplant patients.

Figure : Immunosuppressive drugs can be categorized by their site(s) of action in the immune activation cascade. Drugs that interfere with Signal 1 include calcineurin inhibitors such as CsA and tacrolimus. Signal 2 inhibitors are not currently available but one drug (Belatacept) is in phase III trials for kidney transplantation and allows calcineurin-free transplantation. Signal 3 inhibitors include the antiproliferative agents such as Rapamycin, mycophenolate mofetil and the IL-2 receptor blockers Daclizumab and Basiliximab. Understanding the sites of action of particular drugs results in more rational approaches to combination therapy (i.e., combining a Signal 1 blocker with a Signal 3 blocker).