Kidney Transplant Is No Longer Contraindicated for Patients With Well-Controlled HIV

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HUMAN IMMUNODEFICIENCY VIRUS (HIV) infection has historically been considered a contraindication to transplantation. Over the last three decades, the survival of patients with HIV has improved dramatically and approaches that of non-HIV infected patients. As survival has improved, long-term management of chronic diseases associated with HIV, as well as non-HIV related comorbidities, has become increasingly important. HIV-associated nephropathy can affect up to 10% of HIV patients, even with excellent viral control. African-American patients with HIV are particularly predisposed to HIV-associated nephropathy. Approximately 1% of end-stage renal disease (ESRD) patients in the US have HIV.

While the exact mechanism remains unclear, there is direct infection of the renal epithelial cells by the HIV virus. In addition, there may be additional nephrotoxicity from the antiretroviral medications and from other required medications, such as bactrim utilized for PCP prophylaxis. In addition, HIV patients suffer from the same maladies as the rest of the US population, such as obesity, hypertension, hyperlipidemia, and diabetes — all of which occur with increasing frequency in modern society and are associated with increased risk of chronic renal failure.

Over the last decade, there has been an increased appreciation that patients with well-controlled HIV can be safely transplanted. A multicenter trial funded by the National Institutes of Health was initiated in 2003, and completed enrollment in 2009 (Stock, et al. *New Engl J Med* 2010; 363: 2004-2014). In the process, there were a number of surprising findings. One and three year patient survival were found to be similar to other kidney transplant patients. While graft survival was somewhat lower than the overall average for non-HIV infected patients, it was still superior to the survival of kidney transplant patients older than 65 years of age. The fear that immunosuppression would result in increased progression from HIV to AIDS did not materialize, and HIV-related infections were found to be well controlled. In contrast, there was an increased risk of rejection for patients with HIV. In addition, patients receiving anti-thymocyte globulin — a potent induction immunosuppressive agent — had a higher risk of graft loss. These findings emphasize that HIV should be thought of as an immunological dysregulatory disease, rather than an immunological anergic disease, as it suggests that certain T lymphocyte subsets are actually more active in HIV-infected patients when compared to non-HIV infected patients. Of note, HIV-infected patients who were co-infected with hepatitis C virus (HCV) were found to have worse patient and graft survival outcomes, as well as more infectious complications, when compared to HIV-infected patients without HCV co-infection.

At centers with kidney transplant programs open to HIV patients, there are common themes to selection criteria and program management. HIV must be well controlled, with a low HIV viral load (typically < 200 copies/ml) and a higher CD4 T cell count (typically > 200 cells/mm3). The patient should not have significant cachexia. A history of opportunistic infections or Kaposi's sarcoma in remission does not exclude the patient from transplant, although treatment needs to be completed and the patient cannot have active opportunistic infections or Kaposi's sarcoma. Progressive Multifocal Leukoencephalopathy (PML), lymphoma, and pulmonary aspergillosis usually preclude transplantation.

Peri- and post-transplant management is somewhat different for patients with HIV. As mentioned earlier, lymphocyte depleting agents such as antithymocyte globulin are usually avoided. Induction therapy is frequently accomplished with basiliximab, a monoclonal interleukin-2 receptor chimeric antibody that is nondepleting. There are a number of interactions between the antiretroviral drugs and the immunosuppressive drugs (in particular, the calcineurin inhibitors tacrolimus and cyclosporine), as many are potent inducers of the various p450 isoenzymes. In addition, mycophenolate mofetil (MMF) is a reversible inhibitor of inosine monophosphate dehydrogenase, and may increase the activity and toxicity of didanosine (ddI), tenofovir (TDF), and abacavir (ABC). Careful monitoring of both the immunosuppressive drugs and the antiretroviral drugs are required to prevent harmful dysregulation of the immune system that could result in under-immunosuppression, with the resulting risk of rejection, over-immunosuppression, with the resulting risk of opportunistic infections, or loss of HIV viral suppression, with the risk of progression of disease. Most transplant centers have a specific subset of infectious disease physicians who manage patients post-transplant, and are intimately involved in the evaluation and post-transplant processes.

As HIV therapy has improved, kidney transplantation has become a feasible option for many patients who have historically been denied access to transplant. As kidney transplant results in improved survival and improved quality-of-life when compared to dialysis, the option of kidney transplant has become an important addition to patients with HIV-associated nephropathy.

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