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CASE REPORT

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Kidney transplant recipient with history of HIV, HBV, and past HCV infection

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Abstract

Chronic viral infections caused by the human immunodeficiency virus (HIV), hepatitis C (HCV), and hepatitis B (HBV) are common among patients with end-stage renal disease (ESKD). These infections were once considered contraindications to kidney transplantation due to potential risks associated with long-term immunosuppression. Improved management and antiviral therapies have changed the prognosis and survival of this group of patients, along with an increased experience in transplanting people with these viral infections. We report the first successful kidney transplant in an ESKD patient on hemodialysis with a history of concomitant HIV, HCV and HBV infection in Mexico.

Introduction

Chronic viral infections caused by the human immunodeficiency virus (HIV), hepatitis C (HCV), and hepatitis B (HBV) are common among patients with end-stage renal disease (ESKD). These infections were once considered contraindications to kidney transplantation due to potential risks associated with long-term immunosuppression.

HIV is currently the third leading cause of ESRD in the United States of America (USA), only behind diabetes and hypertension [2]. The prevalence of HCV infection in dialysis is higher than in the rest of the population and those coinfected with HIV have higher mortality and worse overall prognosis [1]. In contrast, the incidence of HBV infection has decreased due to widespread vaccination programs and a reduced need for blood transfusions with the use of erythropoietin-stimulating agents [1]. Before the era of effective antiviral agents, 80% of hepatitis B surface antigen-positive kidney transplant recipients developed chronic liver disease, and 57% of deaths in these transplant patients were attributed to liver-related complications [3].

Improved management and antiviral therapies have changed the prognosis and survival of this group, along with an increased experience in transplanting people with these viral infections. We report the first successful kidney transplant in an ESKD patient on hemodialysis with a history of concomitant HIV, HCV and HBV infection in Mexico.

Clinical case

A 51-year-old man, resident in Guadalajara, Mexico. He had a maternal history of focal segmental glomerulosclerosis. He had no personal non-pathological history of relevance to the case.

The individual was diagnosed with chronic kidney disease in 1994, secondary to focal segmental glomerulosclerosis. He began renal replacement therapy in 2018 with hemodialysis. Systemic arterial hypertension was diagnosed in 2018. The treatment was telmisartan 80 mg OD and verapamil 80 mg OD. He was diagnosed

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as well with a chronic ischemic heart disease since 2014, with stent placement in the anterior descending artery due to unstable angina. The current treatment for this was acetylsalicylic acid 150 mg OD, atorvastatin 40 mg OD. Other medications for ESKD were erythropoietin 4000 IU every 72 h and calcitriol 0.25mcg OD.

The HIV infection was diagnosed in 1994, on current treatment with ritonavir 100 mg OD, tenofovir 300 mg every 48 h, entecavir 0.5 mg OD, lamivudine 150 mg OD, darunavir 600 mg BD, etravirine 200 mg BD, raltegravir 400 mg BD. Viral load and CD4 count prior to renal transplant in undetectable ranges and 230 cells/mm^3, respectively.

- Hepatitis B virus infection was diagnosed in 2009, with no response to treatment with pegylated interferon alpha 2 or entecavir and lamivudina, confirmed with genotype. He was responsive to tenofovir. Prior to the kidney transplant he was in remission for 2 years, having viral load undetectable. The last surface antigen was 5521 IU/L.

A hepatitis C genotype 1b virus infection was diagnosed in 2019. The patient had a treatment during 84 days with Sofosbuvir/Velpatasvir with a sustained viral response free of infection since April 2020, and an undetectable viral load prior to the transplant.

The patient received the renal transplant from an unrelated living donor (friend) on May 18, 2021. It was decided to induce with thymoglobulin and a total accumulated dose of 4 mg/kg. Immunosuppressive therapy started with tacrolimus 0.12 mg/kg/day, mycophenolic acid 1 g BD, and glucocorticoid in decreasing doses. Due to pharmacological interactions with calcineurin inhibitors, the treatment scheme was consulted with a group of experts on resistance to antiretrovirals (GERA) which, since 2009, was founded by the Mexican Institute of Social Security to analyze the cases of prior treatment failures and to issue treatment recommendations. This strategy has resulted in a percentage of more than 90% of multi-treated patients with undetectable viral load, an outcome comparable to other results from the best hospital centers around the world. GERA requested CCR5 tropism, resulting positive, so a new treatment was started with maraviroc 600 mg BD, entecavir 0.5 mg OD, tenofovir 300 mg OD, etravirine 200 mg BD, dolutegravir 50 mg OD.

After 5 days of the kidney transplant surgery the creatinine was 1.6 mg/dl discharged home without complications.

A protocolized biopsy was performed 6 months after the transplant, finding compensatory glomerulopathy, moderate arteriopathy (Supplementary Material, Figure S1, S2, S3), with serum levels of tacrolimus 7.9. The usual creatinine was 1.5 mg/dl.

Discussion

HIV infection has been a contraindication to kidney transplantation because of transplant immunosuppression, HIV-associated renal dysfunction, and nephrotoxicity associated with antiretroviral therapy. One study showed that 20% of HIV-positive patients completed a full evaluation and they were transplanted, compared to 73% of HIV-negative patients evaluated at the same institution during the same time. Factors associated with lack of progress beyond the baseline screening were a low CD4 count at baseline, black race, and a history of drug use [4]. This is not the only study showing a barrier to transplantation of patients with such characteristics. For example, Cohen et al. found that compared to uninfected candidates, HIV-positive patients were 12% less likely to receive a first offer and 18% less likely to undergo a transplant after receiving a first offer [5]. They also found that HCV-positive patients were similarly likely to receive a first offer, but this group had a higher chance of transplant (23% more likely than HIV-positive patients). The HCV-positive population also has a reduced access to kidney transplant waiting lists as shown in a retrospective cohort, with a 33% likelihood, although it has been shown that they live longer with the transplant (58% higher survival rate) [6]. This study is consistent with Cohen's data that these patients have the same kidney transplant rate once they enter the waiting list compared to HCV-negative patients.

Outcomes after kidney transplant

Since the beginning of the era of antiretroviral therapy, an NIH-funded, multicenter, prospective trial found a three-year survival rate of 88% and a graft survival of 73.7% in HIV-positive patients, which was compared with contemporary HIV-negative patients [7]. Although acute rejection rates were higher than expected (31% within the first year); this increased rate of acute rejection is thought to be due to prejudices around the choice of induction and maintenance immunosuppression, as well as a suboptimal exposure to immunosuppressive drugs or toxicity due to significant drug interactions between immunosuppressants and antiretroviral medication.

On the other hand, Sawinski and colleagues [8] compared outcomes between HIV infection or HIV/HCV co-infection versus an uninfected control group, and although they found results that were consistent among similar patients and graft survival rates when comparing HIV-infected with uninfected, HIV/HCV co-infected patients had worse outcomes.

As for HCV-infected patients, the risk of acute rejection and post-transplant glomerulonephritis is also increased (perhaps for the same reasons as HIV-positive recipients) [9]. There could be some hesitation about using standard immunosuppression for HCV-positive patients because this could worsen the extent of liver disease and infection, but the evidence so far has shown that there is likely a benefit to using induction therapy to decrease the probability of death in general (HR 0.75, CI 95% 0.61–0.90, p = 0.003) [10]. The data on the evolution of liver disease helps to dissipate the concern of a deteriorating liver function, finding that 77% have histological stability or improvement and only 23% show progression of liver injury [11]. A HCV infection has also been identified as a risk factor for new-onset diabetes after transplantation (NODAT) [12].

An HBV reactivation can occur after transplantation, but because of too many effective antiviral agents to treat HBV infection that have been recently developed, the transplant outcomes have improved significantly in recent years. Although a systematic review found that a "positive HBsAg status was significantly associated with an increased risk of mortality after kidney transplantation (OR 2.48, 95% CI 1.61–3.83) and an increased risk of graft failure", there were significant negative correlations between the risk of mortality and allograft failure and year of medical examination, representing potential improvements in patient and overall graft survival [13].

Treatment challenges

The complex drug interactions between antiretrovirals (ARVs) and calcineurin inhibitors (CNIs) are well known and quite challenging. Protease inhibitors (PIs) have been widely used in many ARV combinations. They significantly affect the CYP3A enzyme system [14], resulting in very high levels of CNI when used together. Non-nucleoside reverse transcriptase inhibitors (NNRTIs) are metabolized in the liver and primarily induce CYP3A, leading to low CNI levels, which could derive into an acute rejection. In a single-center retrospective study by Rollins et al., rejection rates of 42 kidney transplant recipients with HIV were found to be significantly higher with PI-boosted regimens at 1, 2, and 3 years (59–68%) [15] In addition, PI-based regimens have been associated with an increased risk of patient death (HR 1.91, 95% CI 1.02–3.59) and allograft loss (HR 1.84, 95% CI 1, 22–2.77). [16].

According to recent guidelines, patients with chronic HBV should receive a potent antiviral treatment at the time of transplant, which should be continued indefinitely after it. Due to the increased risk of resistance, lamivudine, the first approved HBV reverse transcriptase inhibitor, is not recommended for long-term prophylaxis. Tenofovir disoproxil fumarate (TDF), on the other hand, is very potent and has a high barrier to resistance, but unfortunately it is nephrotoxic. Tenofovir alafenamide (TAF), a prodrug of tenofovir, is more rapidly absorbed, reaches higher levels of active drug, and has less toxicity to the kidneys and bones. Many transplant centers now use TAF or entecavir, another highly potent antiviral with a high genetic barrier to resistance, as first-line therapy for kidney transplant recipients who need long-term treatment for HBV infection (17).

Conclusion

Kidney transplantation has become the standard of care for HIV-positive ESRD patients. However, the accessibility to kidney transplantation needs to be improved. Patients with HCV, HBC and HIV coinfections treated with new antivirals represent a better prognosis to this group of patients.

Supplementary Information

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Supplementary Material 1

Author contributions

1. Investigator principal, coordinator 2-4. Manuscript editing 5-10. Manuscript corrections 11. Nephropathologist.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Competing interests

The authors declare no competing interests.

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