IDCases 6 (2016) 74–76

Contents lists available at ScienceDirect

IDCases

journal homepage: www.elsevier.com/locate/idcr

Case report

HIV infection with viro-immunological dissociation in a patient with polycystic kidney disease: Candidate for transplantation?

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ARTICLE INFO

Article history:
Received 6 September 2016
Received in revised form 27 September 2016
Accepted 27 September 2016

Keywords:
HIV
Polycystic kidney disease
Viro-immunological dissociation
Lymphopenia
Transplantation

ABSTRACT

Here we describe the case of a HIV-infected patient with polycystic kidney disease and end stage renal diseases not transplantable due to the persistence of a CD4 count <200 notwithstanding a good virological response to highly active antiretroviral therapy and suggest that such limitation to kidney transplantation in such as cases might be bypassed.

Autosomal dominant polycystic kidney disease (ADPKD) is the most common of the inherited cystic kidney diseases. It is characterized by the development of renal cysts and various extrarenal manifestations: cysts in the liver, seminal vesicles, pancreas and arachnoid membrane. Other abnormalities, such as intracranial aneurysms, mitral valve prolapse and abdominal wall hernias can occur. Over 50% of patients with ADPKD eventually develop end-stage renal disease (ESRD) and require dialysis or kidney transplantation [1].

Human immunodeficiency virus (HIV) infected subjects, at the same risk to develop ADPKD as the general population, are at increased risk of developing acute kidney injury and chronic kidney disease (CKD) [2–4]. Factors associated with an increased risk of CKD in HIV infected individuals include older age, female sex, diabetes, hypertension, injection drug use, low CD4+ cell count, specific antiretroviral drugs and higher HIV RNA levels [5,6]. Additionally, HIV-HCV coinfection has been identified as a risk factor for kidney disease in a number of studies and in a recent meta-analysis [7]. Some reports have linked improvements in kidney function or proteinuria to use of antiretroviral therapy and suppressed HIV RNA levels [8]. Pathologic changes reported in HIV kidney biopsies include thrombotic thrombocytopenic purpura, membranous nephropathy or membranoproliferative glomerulonephritis (associated with hepatitis B or C coinfection and syphilis), diabetic nephropathy, hypertensive glomerulosclerosis, acute tubular necrosis, interstitial nephritis, postinfectious glomerulonephritis, chronic pyelonephritis, and amyloid [9–11].

Here we describe the case of a HIV infected in a patient with ADPKD and with dissociative viro-immunological responses to highly active antiretroviral therapy (HAART) and suggest the consideration of kidney transplantation for this category of patients, regardless of CD4+ cell count.

Case

A 40-year-old homosexual man with history of ADPKD was admitted to Palermo University Hospital in July 2012 complaining of high fever, headache, and general malaise. Physical examination showed oral candidiasis, seborrheic dermatitis, skin lesions on the trunk compatible with Kaposi's sarcoma and hepatosplenomegaly. Blood tests on admission showed severe renal failure with a creatinine clearance of 18 ml/min.

The abdomen CT scan showed bilateral multiple renal cysts that were replacing the parenchyma (Fig.1).

HIV infection was diagnosed by enzyme-linked immunosorbent assay (ELISA) and confirmed with Western Blot assay. CD4+ lymphocyte T-count was 13 cells/mm^3 (1.6%), with CD4/CD8 ratio

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http://dx.doi.org/10.1016/j.idcr.2016.09.017

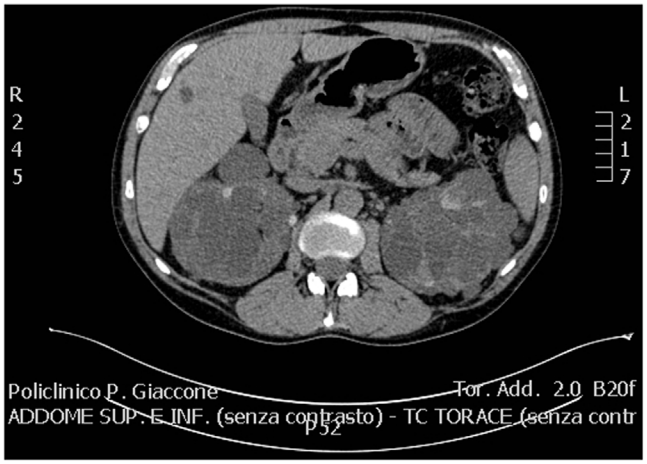

Fig. 1. Computerized tomography of abdomen showing multiple bilateral renal cysts.

of 0.02; HIV-RNA viral load was 936.000 copies per ml. Serology for syphilis, toxoplasmosis, hepatitis B and C were negative.

The patient promptly started HAART with daily darunavir/ritonavir 800/100 mg and abacavir/lamivudine 600/300 mg, and prophylaxis for opportunistic infections with trimethoprim/sulfamethoxazole 160/800 mg daily and azithromycin 1200 mg once a week. After one month into HAART, the HIV-RNA load had markedly decreased to less than 250 cpm and CD4+ count had raised to 83 cells/mm^3 (4.9%). During the follow up, the laboratory tests showed a descending trend of creatinine clearance values and metabolic acidosis.

In June 2014 HIV RNA level was undetectable and CD4+ count was 187 cells/mm^3 (17%) and, in anticipation of hemodialysis, HAART with abacavir/lamivudine was replaced with raltegravir 400 mg twice a day due to raltegravir being removed by hemodialysis only in minimal quantities.

The patient started hemodialysis three times a week in October 2014 and it was not possible to place him on the transplant list because of a CD4+ cell count under 200 cells/mm^3 despite undetectable HIV RNA level [12]. Though virologically suppressed, the patient has not yet been transplanted because his CD4+ count remains below 200 cells/mm^3.

Discussion

ESRD is a serious complication of chronic HIV infection that carries significant morbidity and mortality. Initially, HIV infection was considered an absolute contraindication for transplantation [13]. Since 1996 when HAART became widely available and the prognosis of HIV infection dramatically improved, many transplant programs have reevaluated the policies regarding the exclusion of patients with HIV infection. Nowadays, kidney transplant has become a viable alternative for HIV infected individuals with ESRD since it is associated with better quality of life, fewer medical complications, longer survival and lower cost than chronic dialysis treatment [14–16]. Obviously, current indications and contra-indications for transplantation also apply to HIV-infected patients. In addition, a CD4+ cell count above 200 cells/mm^3 is required for all organs (with the exception of liver, that has a lower requirement of 100 cells/mm^3), as well as an undetectable HIV RNA level, and a stable potent antiretroviral regimen for at least three months [12].

HAART allows the reconstitution of immune functions in most treated HIV patients, but sometimes discrepant responses may occur, including failure to achieve a significant increase in circulating CD4+ T cells despite undetectable plasma viral loads, with a substantially increased long-term mortality for all causes of death [17]. The relevance of this case is to focus on the condition of a viro-immunological dissociation which in fact does not allow the inclusion in the transplant list. Our patient has not yet been transplanted because, although he remains virologically suppressed, his CD4+ count remain below 200 cells/mm3. Also, hemodialysis could contribute to maintain the number of CD4+ cells low. Indeed, lymphopenia frequently occurs in hemodialysis patients waiting for kidney transplantation; it could be related to an increased turnover of lymphocytes, to a disturbance in lymphocyte homeostasis due to uremia, and/or to increased peripheral lymphocyte apoptosis associated with an activation stimulus [18]. Indeed, a vicious cycle is established. In fact, ESRD is associated with premature aging of the T-cell system [19], and even if the consequence of ESRD related accelerated immunesenescence are mostly unknown [20], it is reasonable that may worsen the immunological status of the HIV infected patient.

For all these reasons we believe that lymphopenia should not contraindicate kidney transplantation in selected HIV infected patients with a CD4+ count <200 cells/mm^3 if HIV RNA level is undetectable and the patient is doing a stable potent antiretroviral regimen. Several studies have shown that with sustained suppression of viral replication, Pneumocystis jiroveci pneumonia prophylaxis may not be necessary, regardless of CD4+ T-cell count [21,22]. Furthermore it is known that HIV infection is associated with a two- to threefold increased risk of rejection following kidney transplant and that the administration of antithymocite globulin (ATG) is used to reduce the risk of rejection to that of HIV negative recipients even if it increase the risk of infective complications [18,23].

A randomized clinical trial should be designed to investigate whether patients with a CD4 count <200 cells/mm^3 and undetectable HIV RNA level might benefit from kidney transplantation and whether ATG induction should or not be administered in these cases.

Conflict of interest

Authors declare that they have no competing interest.

Authors' contributions

CC, MT, and CG developed the idea of the study, participated in its design and coordination and helped to draft the manuscript. CC, MT, CG and AM contributed to the acquisition and interpretation of data. CG and DDB performed and collected laboratory test. CC and AC were involved in critically reviewing data for important intellectual content. All authors read and approved the final manuscript.

Consent

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Acknowledgement

We have not received substantial contributions from non-authors.

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