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Contribution of Biology in Kidney Transplantation from a Living Donor in Morocco: A Review Article

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ABSTRACT

The kidney transplant is above all a social project, based on a gift of generosity and solidarity. The specific activity of kidney transplantation from a living donor requires close collaboration between clinicians and biologists. Living-donor renal transplants are further characterized as genetically related (living-related) or non-related (living-unrelated) transplants, depending on whether a biological relationship exists between the donor and recipient. It's the interest of this review with in the last part the path of the donor and the recipient for a possible kidney transplant with a donor living in the renal transplant department at the military hospital of Rabat.

Introduction

Kidney transplantation is the most effective, efficient and cost effective replacement therapy. Studies of these patients indicate that the quality of life [1] and functional prognosis [2, 3] is transformed by performing a kidney transplant but its development is constrained by lack of availability. Living donor transplant has many benefits for the recipient [3-7]. The stratification of the level of immunological risk is a particularly important point in the management of patients despite the current advances pushing back the immunological barriers.

History of Kidney Transplantation

The first transplant with lasting success was performed on December 23, 1954, in Boston, between two twin brothers. Living donors, then selected from the nearest possible family to meet tissue compatibility requirements, remained the only source of grafts until 1963, the date of the first cadaver donor transplant. Due to the preference given to deceased-donor, living donor renal transplants have experienced a significant eclipse in France [8, 9].

The first living donor kidney transplant was performed in Morocco in 1986 with foreign medical team, in 1990 the first kidney transplant was performed from living donor with a Moroccan team and in 2011 there were 151 transplants from living donors [10].

Kidney Transplantation in Morocco

In 2005, Morocco had the first register "MAGREDIAL" (Morocco-Graft-Dialysis) of the end stage of renal disease (ESRD). In MAGREDIAL's first annual report (2009), the prevalence of ESRD was estimated at 267.1 per million population (pmp) [10-13].

Renal replacement therapy (RRT) activity is still very low in Morocco.

In 2012, it was 36 kidney transplants for the whole country against 16 in 2007. There are less than 10 transplants per year per million population with a number of patients in dialysis estimated at 13 000 at the end of 2013[14].

Biological Screening of Living Kidney Donor

The French Health Authority recommends informing patients about the possibility of transplantation 12 to 18 months before the start of a possible replacement renal therapy [15, 16].

Firstly, a biological assessment including blood group determination, fasting blood glucose and serum creatinine, estimation of glomerular filtration rate, as well as the search for hematuria and proteinuria. Later, morphological and immunological investigations and a general assessment, cardiological and HLA compatibility tests are performed: It is the study of the expression of the immune response of the recipient with respect to a genetically non identical graft.

This response is mainly directed against the ABO erythrocyte blood group antigens (Ag) and the histocompatibility Ag carried by the graft cells. Histocompatibility Ags are encoded by the genes of the major histocompatibility complex, called HLA (Human Leucocyte Antigens) in humans: Class I genes (A, B, C locus) and class II genes (DR, DP, DQ locus).

ABO System

The ABO grouping is done according to conventional agglutination techniques, on two different samples, according to two techniques, with two batches of different reagents. The ABO compatibility rules are the same as for transfusions. The anti-A and anti-B IgM antibodies are systematically present, IgG anti-A/B alloantibodies being also present in some individuals. Some teams use a support "tube" and others, majority, a microfiltration support to reveal

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haemagglutination, the results obtained being in the two superimposable cases [17].

Some teams use flow cytometry, but the time to report results is longer and requires trained and available staff.

It is now possible to consider grafts with living donor incompatible in the ABO system, subject to prior "de-immunization" in order to reduce the rate of anti-A and / or anti-B antibodies of IgG and IgM type to an acceptable level at the time of the transplantation, to prevent their reappearance and to promote the acquisition of a state of accommodation [18]

"Desimmunisation" is obtained by injection of rituximab one month before kidney transplantation associated with plasma exchanges. This treatment may also be associated with polyvalent immunoglobulins with monitoring of Anti-A and / or B antibody at each plasma exchange and also frequently within the first 15 days after transplantation.

HLA Typing

It specifies the degree of tissue compatibility, the HLA compatibility between donor and recipient is established at least on the comparison of HLA-A, -B, -DR, -DQ typing. HLA typing must be performed on two different samples and with two different techniques:

a) "Serological" LCT lymphocytotoxicity typing: HLA molecules expressed on the surface of lymphocytes are identified by means of cytotoxic monoclonal antibodies directed against HLA molecules of known specificity.

If the antibodies bind to the cell surface antigens, an antigen-antibody complex is formed and the complement is then specifically activated, causing lymphocyte lyses visualized by inverted fluorescence microscopy.

b) Genotyping: The most widely used molecular biology methods are PCR-SSO (Polymerase Chain Reaction-Specific Sequence Oligonucleotide) which consists of amplifying the entire HLA region with a pair of primers and hybridizing it with a panel of probes specific oligonucleotides and PCR-SSP (PCR-Specific Sequence Primer) that allows to directly amplify the HLA alleles using a panel of specific primers. Luminex technology, recently developed combining PCR-SSO and flow cytometry [19].

Immunological Monitoring of anti-HLA Antibodies

It aims to detect antibodies against the HLA molecules of the future graft, called Donor Specific Antibodies (DSA), which may be responsible for a decrease in the survival time of the graft [20, 21]. These antibodies may appear after pregnancy, blood transfusions or previous organ transplants. This analysis is based on LuminexTM technology, which uses fluorescent polystyrene microspheres coated with purified HLA molecules. This cytometer-type instrument is able of individually identifying about one hundred beads and detecting fluorescence on their surface [22, 23].

The search for anti-HLA antibodies must also be carried out by an LCT test, it makes it possible to identify any IgM isotype antibodies that are not detected by Luminex TM technology and to detect cytotoxic anti-HLA antibodies that are not revealed by Luminex TM due to a prozone effect [24].

Cross Match (CM)

It is the ultimate test that allows rapid detection of antibodies against cytotoxic donors, preformed in the serum of the recipient, responsible for a hyper-acute rejection. The CM causes the test serum of the recipient to interact with the lymphocytes of the potential donor in the presence of the complement. Several serums are tested: the serum of the day, the most recent as well as all the known historical serums positive. Since the level of Ac is fluctuating over time, an immunization may not be detected by the pre-transplant CM. However, as immune memory persists, transplantation can reactivate immunization and cause over-acute rejection. The most commonly used technique is LCT, the donor lymphocytes are separated into T and B, and then incubated with the recipient's serum at different dilutions. Furthermore, a CM in the presence of human anti-globulin (CM sensitized), made in parallel, increases the sensitivity of the test. CM can also be performed by flow cytometry. The donor lymphocytes are incubated with the serum of the recipient.

The decision to graft will depend on the specificity of the Ac detected (Ac HLA (deleterious) or an auto Ac (non-deleterious))

Experience of the Nephrology, Dialysis and Renal Transplantation Department of the Rabat Military Hospital

The transplant project concerns military patients in periodic dialysis or in pre-term renal failure. The selection of living donors is done according to legal, clinical, immunological and psychological criteria.

Moroccan law (Article 9, Law No. 16-98) authorizes family donations from: ascendants, descendants, brothers, sisters, uncles, aunts or their children and spouse if the marriage has been contracted for at least one year after initial consultation with the recipient and his / her potential donor.

At the first consultation, a clear and concise explanation of donation conditions and risks for the recipient and the donor, a card is filled in containing personal data and personal and family history, data from the initial clinical examination searching for absolute contraindication or relative to the graft.

At the end of this first consultation, a biological assessment is requested (nephrological, hematological immunological, infectious and metabolic assessment) and subsequently a morphological assessment is also required.

Immunological criteria for donor selection are: ABO compatibility, HLA compatibility, it is important to determine the immune status of the recipient.

The last criteria are based on the CM results, as follows:

- A negative CM in a recipient with a regular immunological follow-up authorizes the transplantation.
- A positive CM with anti-HLA antibodies class I reject the graft.

In addition, the isotype of the antibody is also important :IgG are dangerous whereas IgM are often directed against non-HLA molecules and are not deleterious.

When ABO and HLA compatibilities are established between the donor and the recipient, the CM is performed with all available serum. Finally, a few days before the planned date of transplantation, a last CM is performed with the most recent serum.

A regular biological and immunological follow-up is also assured after renal transplantation searching for the appearance of impaired renal function or the appearance of antibodies indicating a renal biopsy, in search of humoral rejection (C4d deposits).

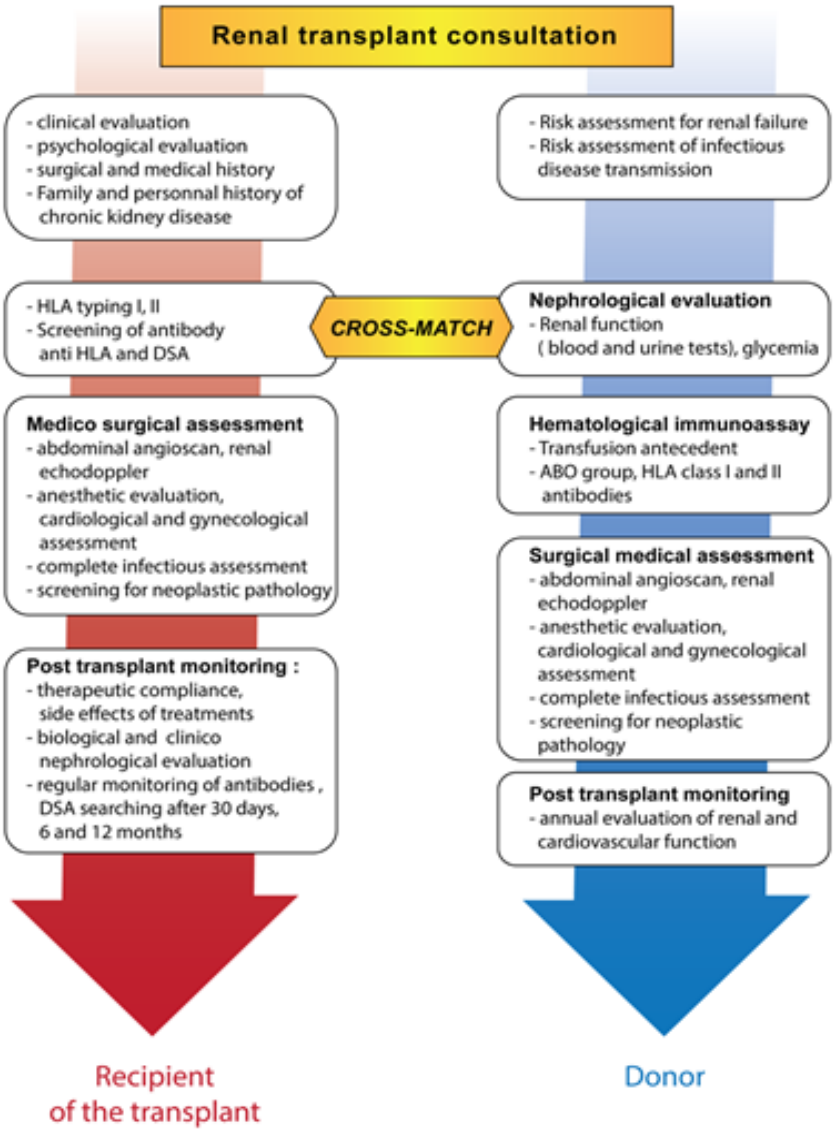

Figure 1. Donor and transplant recipient Pathway for a Renal Transplantation of a Living Donor.

Conclusion

Kidney donation is an human experience and a remarkable altruistic act whose success requires an indispensable multidisciplinary collaboration between nephrologists, biologists, radiologists and surgeons.

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