Subject Area: Nephrology

Outcome of a case of living donor kidney transplant with high levels of pre-transplant donor specific antibodies

Ahmed Hassan Elthakaby

Aza Elmenyawi
ORIGINAL STUDY

Outcome of a case of living donor kidney transplant with high levels of pre-transplant donor specific antibodies

Ahmed H. Elthakaby a,*, Azza A. Elmenyawib

a Department of Nephrology, National Institute of Urology and Nephrology, Cairo, Egypt
b Department of Clinical Pathology, National Institute of Urology and Nephrology, Cairo, Egypt

Abstract

For patients with end stage renal disease (ESRD), kidney transplant offers significant survival and quality-of-life advantages compared with dialysis. Non-sensitized renal transplant recipients when compared to patients with pre-formed alloantibodies, the latter are at greater risk of cellular, humeral rejection and premature graft failure. In this paper we will present a successful case of young adult who has ESRD and maintained on regular hemodialysis and undergo live related renal transplant with high dose HLA class I and class II antibodies and negative cross match by CDC and flow cytometry.

Keywords: Cross match, High level panel reactive antibodies, Kidney transplantation

1. Introduction

The presence of donor specific anti-HLA antibody (HLA-DSA) has significant impact on the short-term and long-term allograft outcomes after kidney transplantation. Low dose HLA-DSA is associated with increased acute antibody mediated rejection in living donor kidney transplantation. In low dose HLA-DSA, HLA-DSA class II rather than HLA-DSA class I is considered to play an important role in increased acute antibody mediated rejection [1]. Renal transplant recipients with high panel reactive antibodies (PRA) have worse outcomes than those with lower PRA. High PRA recipients of first transplants had poorer patient survival than high PRA re-transplant [2].

2. Case report

Male patient 32 years old is known to have end stage renal disease (ESRD) and is maintained on regular hemodialysis for 1.5 yrs before renal transplant operation. The primary cause of kidneys failure is chronic glomerulonephritis (hypertension, proteinuria and bilateral atrophic kidneys in ultrasound). He is planning to undergo living related renal transplant from his mother with 3 MM 1:1:1, the main problem of this patients that he has a high level of PRA class I and class II (>60% and >90% respectively). We don't have the facility to desensitize the patient, as it is costly and its success rate may not be achieved. Our plan to reduce PRA<50% for both class I and II, search for a donor that has HLA antigens for which the recipient antibodies are not directed against them that was fitted to his mother. Initially, he receives azathioprine 3 mg/kg and prednisolone 20 mg/day. Follow up testing of PRA were done (every 6 months). Fluctuation were noticed till last PRA class I (62%), class II (17%) just before transplantation. Cross match by lymphctotoxicity, followed by flow cytometry were negative (Tables 1–3).

Our plan for transplantation was to give the patient combined induction therapy, Rituximab 1 week before renal transplant 375 mg/m², ATG 5 mg/kg together with four successive sessions of
plasmapheresis 1.5 volume exchange before transplantation. Maintenance immunosuppression in the form of Tacrolimus (to maintain the level $10^{12}$ ng/ml early post-transplant), MMF was started 1 gm/12 h D-3 pre-transplant to decrease dose day 0 with the initiation of ATG and steroid. Intraoperative there was smooth course with no complication total ischemic time reasonable around 45 min with immediate diuresis after declamping. Smooth course postoperatively with immediate graft function s creatinine day 3, 1.5 mg/dl day 5 1.2 mg/dl (Fig. 1).

3. Discussion

The major histocompatibility complex is called human leucocyte antigen (HLA) is located on the short arm of chromosome 6. HLA compatibility and lymph cytotoxic cross-matching of renal donors against prospective renal allograft recipients are the most important fundamental steps in pre-transplant evaluation to avoid renal allograft rejection and loss. The complement-dependent cytotoxicity assay has been the mainstay technique for detection, the presence of donor-specific antibodies (DSAs), since the 1970s. The introduction of more sensitive and specific techniques such as flow cytometry, and highly sensitive enzyme-linked immunosorbent assay, Luminex platforms and virtual cross-match improve the performance of cross-matching [3]. Antibody-mediated rejection presents in three forms with hyperacute rejection occurring within minutes to hours following transplantation owing to
an amnestic response to alloantigen exposure. Acute rejection occurs within weeks, whereas chronic rejection occurs several years post-transplantation. During the initial stages of transplantation, it was observed that a high number of kidney transplants performed in patients with DSAs resulted in hyper acute rejection [4,5]. The major histocompatibility complex in humans is called human leucocyte antigen (HLA) and is located on the short arm of chromosome 6. Mismatch of HLA between donor and recipient would determine the frequency and magnitude of allograft acute rejection.

The use of calculated panel reactive antibodies (cPRA) is a standardized method of estimating the possibility of the recipient having DSA through measuring the difference between antibody specificities and the prevalence of HLA alleles in a target population [6]. The basis of cPRA values is the list of HLA antigens considered as unacceptable for a prospective kidney transplant patient against a panel of 10,000 newly assigned deceased donors, and thereby giving an estimation of being allocated a suitable donor from a pool [7]. Luminex is a solid-phase immunoassay that is more sensitive than other forms of cross-matching and uses recombinant HLA antigens instead of lymphocytes [8]. The platform consists of a dedicated instrument and a fluorescent-bead-based array. The fluorescent beads act as a solid substrate for an immunocaptive assay similar to polystyrene plates in a traditional ELISA. The bead types are of different colors and intensity. Each unique bead type is labeled by a particular antibody for detecting specific proteins of interest. For screening purposes, beads may be multi-HLA antigen coated, and for specific, precise antibody definition, single HLA antigen coated beads can be used. The result is determined by using a dual beam laser that measures the fluorescent intensity of the complement detection antibody reporter dye on the beads. Different beads can be combined together in a single well. When beads pass through the two lasers, the reporter laser reports occurrence of antigen–antibody reaction, whereas the classification laser recognizes the beads as per color coding [9]. Hanaway et al. defined high-risk patients by repeated transplant, a peak or current value of PRA >20%, or black race [10]. Brennan et al. enrolled patients considering donor, recipient, and transplant procedure factors, which put the recipient at high risk for acute rejection (PRA >20%, multiple transplantsations, at least one donor HLA mismatch, and black race) or delayed graft function such as cold ischemia time >4 h, donor aged >50 years or who had acute tubular necrosis, high inotropic support, or donors after cardiac death [11]. A registry study defined high-immunologic risk recipients as those with peak PRA >20%, prior kidney transplantation, or black race [12]. Our patient considered high risk as he has high PRA >50% class I and class II, indeed received kidney transplant from his mother her age >50 years and male patient. Our patient received 4 session of plasma exchange within a week and one dose of rituximab in a dose of 375 mg/m², one week before transplantation together with an ATG 5 mg/kg as total dose in divided doses was given starting from day 0 of renal transplantation, maintenance immunosuppression tacrolimus, MMF and prednisolone. Therapeutic plasma exchange (TPE) treatments required for the management of the sensitized patient, although it appears that benefit plateaus after 3 to 4 sessions and high-titer antibodies do not reduce to a clinically useful level [13,14]. Multiple sessions are typically necessary to achieve low levels of circulating antibodies. Reported protocols range from 1 to 5 sessions per week for 1–4 weeks [15]. Rituximab is believed to deplete B lymphocytes through a combination of antibody-dependent cytotoxicity,
complement-mediated cell lysis, and induction of apoptosis [16]. It is commonly administered at a dose of 375 mg/m² intravenously weekly for 1–4 weeks [17]. Rituximab in combination with either IVIG or TPE, has been shown to decrease circulating antibodies for 1–4 months [18]. It is effective at lowering DSAs at the time of transplantation, preventing rebound DSAs compared with IVIG alone, and preventing AMR [19]. Laftavi & his colleagues revealed that, in high risk recipients with high PRA, addition of rituximab to rATG provided superior outcomes to rATG alone. They recommended combination induction therapy should be considered for a high-risk population [20]. In a conclusion the use of combined ATG & rituximab as an induction therapy together with plasma exchange are effective treatment for patient with high PRA before renal transplant.

Conflicts of interest

There is no conflict of interest between us and the patient.

References