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Case Reports

Pediatric Orthotopic Heart Transplant Requiring Perioperative Exchange Transfusion: A Case Report

Brian McNeer, BS; Brent Dickason, BS, RRT; Scott Niles, BA, CCP; Jay Ploessl, CCP

The University of Iowa Hospitals and Clinics, Iowa City, Iowa

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Abstract: An 11-month-old patient with idiopathic cardiomyopathy was scheduled for orthotopic heart transplantation. A perioperative exchange transfusion was performed because of elevated panel reactive antibody levels. This process was accomplished in the operating room prior to instituting cardiopulmonary bypass using a modified cardiopulmonary bypass circuit. In preparation for the procedure, the cardiopulmonary bypass circuit was primed with washed leukocyte-filtered banked packed red blood cells, fresh-frozen plasma, albumin, and heparin. Pump prime laboratory values were normalized prior to beginning the exchange transfusion. The patient's blood was downloaded from the venous line just proximal to the venous reservoir while simultaneously transfusing the normalized prime at normothermia. Approximately 125% of the patients calculated blood volume was exchanged. This technique greatly reduces the likelihood of hyperacute rejection. The exchange transfusion process, in addition to the patient immature immune system, provides additional options in orthotopic heart transplantation for patients that may otherwise not be considered suitable candidates. **Keywords:** exchange transfusion, heart transplant, pediatric, panel reactive antibodies. *JECT. 2004;36:361–363*

Despite continuing advances in the management of end-stage cardiac failure, cardiac transplantation remains the definitive treatment modality. Unfortunately, demand for these organs continues to outpace availability across all populations of potential recipients. This fact is particularly problematic when the prospective recipient is an infant. Transplantation evaluations in infants must not only address issues such as ABO compatibility but also contend with a narrow range of suitable donor size matches in an extremely small donor pool. Statistics shared by the United Network for Organ Sharing (UNOS), interestingly, reveal that a large number of donor organs in infants and children that are suitable for transplantation go unused as a result of a myriad of donor/recipient incompatibilities (1). Among the most commonly cited obstacles of matching donor organs are ABO incompatibilities and the presence of preformed antibodies to human leukocyte antigen (HLA) (2). Evidence of these humoral markers most commonly becomes apparent in infants and children after exposure to homologous blood products. Evaluation of humoral sensitization is determined by the presence of a positive panel reactive antibody (PRA) screen. Screening is accomplished by mixing the prospective recipients serum in a panel of cells containing lymphocytes with known HLA antigens, to derive a PRA titer. The PRA level is then established by looking at the total percentage of lymphocytes destroyed by the patients' antibodies (i.e., the number of wells with positive reactivity over the total number of wells tested × 100). Extensive alloimmunization is determined by a high PRA level (>10% positive wells). A high titer may pose difficulties in locating a donor, or even worse, lead to a hyperacute graft rejection, and ultimately decreased graft survival as the result of a strong immune response (2). The complement-dependent cytotoxicity assay is the method most commonly used for PRA determination, but other techniques, including flow cytometry and enzyme-linked immunosorbent assay, also are used (3).

The most common clinical approaches to treat high-titer PRA patients, in preparation for cardiac transplantation,

are plasmapheresis and administration of immunoglobulin (4). However, when faced with organ availability time constraints, and patient instability often seen with heart transplant candidates, plasmapheresis might not be a viable option immediately prior to surgery. Likewise, resources and equipment may not be available to perform plasmapheresis while on cardiopulmonary bypass (CPB). In these circumstances an exchange transfusion may offer an alternative technique for the heart transplant to proceed. In substituting the recipient's high titer PRA load with leukocyte depleted blood products, the HLA antibodies that provoke an immune system response, are decreased. Combined with an aggressive B cell immunosuppressive regimen, this treatment is successful in preventing a hyperacute immune host/graft rejection. We believe this novel use of an established technique provides an opportunity for patients that are unsuitable transplantation matches, the potential to receive the life saving heart transplant they so desperately need.

DESCRIPTION

The patient was an 11-month-old female with severely dilated cardiomyopathy, dysrhythmias, renal failure, and cholestasis. Despite optimal medical management, the patient continued to decline physiologically because of poor organ perfusion, necessitating assessment and listing for orthotopic heart transplantation. Routine patient screening evaluation consisted of ABO, Rh, CMV IgG/IgM, and PRAs. It was determined at this time that HLA alloimmunization had occurred in this patient because of previous exposure to homologous blood products, resulting in elevated PRAs. The presence of elevated PRA levels complicated the matching of this infant to acceptable donor. After consultation with hematology and immunology team members, it was decided that immediately prior to transplantation a reduction in PRA levels would be undertaken.

A suitable donor heart became available 43 days after transplant registry listing. Because of the severely debilitated conditions and young age of this patient, the transplant team agreed upon initiating a perioperative exchange transfusion as a means of reducing the PRA level. This planned response was to be initiated immediately before CPB in an effort to maintain hemodynamic stability and patient safety.

The patient was transported to the operating room, where standard monitoring lines were placed; she was intubated, prepped, and draped in sterile fashion. The quarter-inch infant bypass circuit (Jostra-Bentley, Irvine, CA) incorporating a Minimax Plus PRF (Medtronic, Minneapolis, MN) Carmeda-coated oxygenator, a RV-500-1 venous reservoir (Medtronic. Minneapolis, MN), an EL402 cardiotomy (Medtronic), an AF-540-D arterial filter (Jostra-Bentley), a HPH 400 hemoconcentrator (Minntech, Minneapolis, MN) and a CDI 500 in-line monitoring system (Terumo Cardiovascular Systems, Ann Arbor, MI). A Stockert Shiley CAPS™ Roller Pump (Stockert Shiley, Munich, Germany) served as the pump platform. The circuit was modified for the exchange transfusion by placing a stopcock and 600 mL Blood Transfer Pack (Baxter Healthcare Corp., Deerfield, IL) immediately proximal to the venous reservoir (Figure 1). The pump was primed with Plasma-Lyte-A® (Baxter Healthcare Corp.). The exchange goal was to replace one blood volume and achieve an on-bypass hematocrit of 28–30%. To accomplish this, three units of washed leukofiltered homologous red blood cells (600 mL); one unit of fresh frozen plasma (200 mL), and 100 mL of 25% albumin were added to the prime. Excess volume was removed with a hemoconcentrator to achieve a hematocrit of 28% in the prime solution. Heparin sodium (2000 units), sodium bicarbonate (22.5 mEq), Aprotinin® (30,000 KIU/Kg), and calcium chloride (200 mg/L) were also added to the prime. Blood gases and electrolytes of the prime were tested and normalized.

A median sternotomy was preformed; the patient was heparinized to achieve an activated clotting time of greater than 480 seconds. An arterial cannula (12 Fr., 77112; Medtronic) was placed in the ascending aorta, appropriately deaired, and connected to the circuit. Integrity was tested by fluid administration. Bicaval venous cannulas, were (16 Fr., 67316; Medtronic) placed in the superior vena cava, and a (16 Fr., 66116; Medtronic) in the inferior vena cava. Venous cannulas were deaired and connected to the circuit in preparation of the procedure. Immediately prior to commencement of CPB, a clamp was placed between the transfer pack and the venous reservoir (Figure 1). Patient blood was then allowed to fill the transfer pack via the venous line while simultaneously transfusing (at approximately 100 mL/min) a normalized blood prime, at normothermia, as needed to maintain a mean arterial blood pressure of 50 mmHg. Approximately 125% of the patient's calculated blood volume was exchanged in this fashion. Once the exchange transfusion was complete, CPB was initiated without event. While on bypass, an additional unit of washed leukofiltered homologous red blood cells was added to increase the red cell mass to greater than 30%. The orthotopic heart transplant was preformed without incident. Modified ultrafiltration was initiated after bypass, achieving the ultrafiltration goal of one blood volume (550 mL) in 17 min.

DISCUSSION

This case demonstrates the effective use of a whole body exchange transfusion to reduce PRA levels under conditions of patient instability and operative time constraints. Patients that display a presensitization prior to

transplantation pose a challenge for the transplant team, due to the increased risk for hyperacute rejection. The requirement for negative alloantibody screens in transplant candidates can pose surgical and logistical problems, ultimately preventing the transplant from occurring due to organ donation constraints (5). For these reasons, other avenues to facilitate the transplantation needed to be pursued by the transplant team.

Patients with elevated PRA levels have three options before transplantation: preoperative plasmapheresis, intraoperative plasmapheresis, or whole-body exchange transfusion (4,6). Preoperative plasmapheresis is performed preferentially in adult populations; however, many institutions lack the resources to perform plasmapheresis in infants. In this case report, patient instability and time restrictions regarding organ availability, preclude this option. Intraoperative plasmapheresis while on CPB, in this patient was considered, however, due to the relative short duration of CPB expected it was not felt that a sufficient reduction in PRA load could be achieved. Ultimately the surgical team decided on a pre-CPB exchange transfusion, which proved to be a safe and effective alternative to conventional practices.

We have successfully demonstrated that, by using this technique, it is possible to effectively perform heart transplants in patients with elevated PRA levels. This technique described may open the door of options afforded to the perfusionists and the transplant team members. This alternative may allow orthotopic heart transplants to be made feasible, for patients that may have otherwise been considered an unsuitable candidate due to presensitization.

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