Editorial Comment: Bloodless Orthotopic Heart Transplantation in a Jehovah's Witness

I read with interest the case report by Dallas et al.[1] They used a fibrinogen concentrate (RiaSTAP) and other time-honored approaches as part of a protocol that allowed them to perform a "bloodless" heart transplant in a patient of the Jehovah's Witness faith. At the Texas Heart Institute, we have extensive experience in performing cardiac surgery on Jehovah's Witnesses. In May 1962, Dr. Denton Cooley[2] performed the world's first open heart operation on a Jehovah's Witness. In 1977, Ott and Cooley[3] described a series of 542 Jehovah's Witness patients who had undergone cardiac surgery with an early mortality rate of 9%. In 1986, Corno et al.[4] reported the first successful cardiac transplant operation involving a Jehovah's Witness.

Our first successful heart transplant in a Jehovah's Witness was reported in 1988.[5,6] As of July 2014, we had performed heart transplants in 16 Jehovah's Witnesses (unpublished data). Two of these patients died early, but only 1 of those deaths was related to bleeding complications. Only 1 of the 16 patients required treatment for acute cellular rejection, and none of the patients was diagnosed with humoral rejection. Thus, our results have been good, although we excluded most patients who had previous median sternotomies. Also, only 1 of our patients was having a redo operation, and only 1 was being supported by an intraaortic balloon pump, so ours is a select group. The mean postoperative survival time of our 15 long-term survivors is 8 years (range, 73 days to 25.7 years). Six of these patients have survived for >20 years.

The Jehovah's Witness faith now allows some leeway for patients to receive procoagulant factors, but this was not the case when most of our heart transplants in Jehovah's Witnesses were performed. As noted by Dallas et al.,[1] the use of concentrated fibrinogen may be of significant benefit in selected patients. Like these surgeons,[1] we have also given procoagulant factors, but we have not used concentrated fibrinogen, because it was not approved for Jehovah's Witnesses when most of our cases occurred. For postoperative bleeding, we generally use cryoprecipitate rather than concentrated fibrinogen, not only because cryoprecipitate contains a similar quantity of fibrinogen in addition to other procoagulant factors but primarily because it is more cost-effective than fibrinogen.

With regard to the overall current state of organ transplantation in Jehovah's Witnesses, these patients have undergone transplantation not only of hearts and kidneys but also (more rarely) of livers and lungs. In fact, Partovi et al.[7] have performed both single- and double-lung transplants in Jehovah's Witnesses. Unfortunately, however, many transplant centers will not consider treating members of this faith. The number of transplants performed in these patients varies from country to country, being greatest in the United States and other developed countries. The United Network for Organ Sharing does not have a particular policy regarding Jehovah's Witnesses. The Jehovah's Witness headquarters, based in Brooklyn, New York, keeps excellent records, and its office of Hospital Information Services has the most reliable and up-to-date information about organ transplantation in members of this faith (www.jw.org).

In summary, Dallas et al.[1] are to be commended for performing this life-saving, successful procedure on a high-risk Jehovah's Witness patient who was undergoing intraaortic balloon pump support. This operation required courage in addition to skill. We have noted that our Jehovah's Witnesses appear to do as well as, or even better than, the typical transplant patient, although they are a selected subgroup. The minimal rejection seen in our patients may be a reflection of their not having had blood products both pre- and postoperatively. We have also found Jehovah's Witnesses, who have a strong social network, to be entirely compliant in following preoperative and postoperative orders, including drug regimens. Despite these and others good results, constant oversight from medical organizations, United Network for Organ Sharing, insurance companies, the Centers for Medicare and Medicaid Services, hospital administrators, and others remains an impediment for surgeons treating many patients deemed high risk, such as Jehovah's Witnesses.

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DOI: 10.1213/XAA.0000000000000111

Bloodless Orthotopic Heart Transplantation in a Jehovah's Witness

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We present the case of a 53-year-old female Jehovah's Witness with nonischemic cardiomyopathy who successfully underwent a bloodless heart transplantation using fibrinogen concentrate (RiaSTAP™; CSL Behring, King of Prussia, PA) and other blood-conservation methods. With a multidisciplinary team and the use of preoperative erythropoietin-stimulating drugs, normovolemic hemodilution, cell salvage, and pharmacotherapy to prevent and treat coagulopathy, we were able to maintain hemoglobin levels greater than 11 g/dL without the need for blood transfusion. We conclude that orthotopic heart transplants may be performed successfully in select Jehovah's Witness patients using standard and novel blood conservation methods. (A&A Case Reports. 2015;4:140–2.)

A 53-year-old woman with nonischemic cardiomyopathy and an ejection fraction (EF) <15% presented to Duke University Medical Center to be evaluated for heart transplantation. As a Jehovah's Witness, she was seen in our Center for Blood Conservation 4 months before surgery. The relative contraindication to surgery was that the patient would not accept whole blood, red blood cells, white blood cells, plasma, or platelets. She would accept interventions involving her own blood kept in a continuous circuit, including acute normovolemic hemodilution, cardiopulmonary bypass (CPB), and intraoperative cell salvage, along with minor fractions of blood, including albumin, immunoglobulins, and fibrinogen concentrate. The patient was informed about the risk of death with surgery and the refusal of potential life-saving blood products, but overall she was a suitable candidate. Recently published data suggest that patients presenting for cardiac surgery who refuse blood products, such as Jehovah's Witnesses, do not have a greater risk of surgical complications or mortality and may have improved outcomes.[1]

She was listed as an extended criteria recipient and was willing to accept a marginal donor organ. Because of donor organ scarcity, some transplant institutions are accepting marginal organs.[2] Her refusal of blood transfusion made her a poor candidate for ventricular assist device surgery with its associated anemia; therefore, listing her as an extended criteria recipient would increase her chance of receiving an organ faster. To reduce ischemic transit time, the transplant team decided to accept only local hearts, which also would reduce the total ischemic time and the risk of primary graft dysfunction. The patient provided verbal and written consent for publication of our case report.

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Accepted for publication April 14, 2014.

The authors declare no conflicts of interest.

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DOI: 10.1213/XAA.0000000000000067

CASE DESCRIPTION

Preoperative

The patient was admitted to our institution 3 months before transplantation with acute on chronic systolic heart failure with orthopnea, abdominal distention, and vomiting. She initially was managed with a milrinone infusion and later required dobutamine and diuresis with a furosemide infusion. Twelve days before transplantation, an intra-aortic balloon pump was placed because of the patient's increased inotropic requirements. Preoperatively, the patient's hemoglobin (Hgb) level was optimized by limiting blood draws, using pediatric phlebotomy tubes, weekly subcutaneous injections of epoetin alfa (600 U/kg) and oral ferrous sulfate to maintain the Hgb level greater than 14 g/dL. Adequate iron stores were confirmed: her iron saturation was >20% (normal range, 15%–55%), and her ferritin level was >90 ng/mL (normal range, 12–300 ng/mL).

Intraoperative

After a donor organ became available, the United Network for Organ Sharing identification number and ABO compatibility were confirmed. The organ was considered marginal because of moderate left ventricular hypertrophy. A preinduction radial arterial catheter was placed, and general anesthesia was induced with fentanyl, midazolam, and propofol. Isoflurane was used to maintain anesthesia, and vecuronium was administered for neuromuscular blockade. After a 9.0F right internal jugular central venous catheter was placed, autologous harvest was performed by removing four 400-mL bags of whole blood (Blood-Pack; Fenwal, Inc., Lake Zurich, IL). The whole blood was collected in labeled citrate-phosphate-dextrose–coated bags and remained in a closed- circuit, continuous system connected to the patient while being oscillated at room temperature. The volume from the first whole-blood bag was replaced with the crystalloid given on induction; a 1:1 volume of 5% albumin was given after each subsequent whole-blood bag was withdrawn, to maintain euvolemia. The patient remained hemodynamically stable during the harvest without any changes from the preoperative inotropic support regimen.

The patient was prepared for a routine median sternotomy. A tranexamic acid bolus of 10 mg/kg was administered,

followed by an infusion at 1 mg/kg/h to decrease fibrinolysis. The patient's blood was anticoagulated with heparin (400 U/kg); the target was an activated clotting time >480 seconds. Retrograde autologous prime was used to minimize hemodilution with CPB initiation, and the patient was cooled to 32°C.

The total ischemic time was short (80 minutes), and the total CPB time was 126 minutes. Before separation from CPB, the platelet count was 191,000 and the fibrinogen concentration was 209 mg/dL. The patient was separated from CPB with support from an epinephrine infusion (0.06 µg/kg/min) and an intra-aortic balloon pump (ratio 1:1). Protamine sulfate was used to reverse heparin anticoagulation: 1 mg protamine/100 U of the total heparin dose was administered to return the activated clotting time to normal. A 20-µg dose of desmopressin acetate was administered to increase the plasma levels of both von Willebrand factor and factor VIII.[3] The autologous harvested blood was returned to the patient in reverse order of collection and increased her Hgb by 4 g/dL (Fig. 1). A transesophageal echocardiogram revealed a left ventricular EF of 25% to 35%, septal and inferior wall hypokinesis, moderate right ventricular dysfunction, mild tricuspid valve regurgitation, and trace aortic valve insufficiency.

Postoperative

The patient was transferred to the intensive care unit in stable condition but with chest tube drainage of 430 mL over the first 4 hours. Because of concerns of coagulopathy, a 35 mg/kg dose of fibrinogen factor concentrate was administered. The chest tube output subsequently decreased, and the tube was removed on postoperative day (POD) 6 (Fig. 2). The patient did not require re-exploration, and the lowest Hgb level recorded was 11.3 g/dL. Right heart catheterization and endomyocardial biopsies were performed on POD 7, which were significant for a cardiac index of 2.62 L/min/m^2 and no rejection. The patient was discharged on POD 10 in stable condition. At her 2-month follow-up, the patient reported that she was doing well and was exercising without any symptoms of heart failure. The most recent echocardiogram showed an EF of 40%, mild global hypocontractility, moderate left ventricular hypertrophy, and trivial aortic valve, mitral valve, and tricuspid valve insufficiency.

DISCUSSION

We describe a successful heart transplantation performed in a Jehovah's Witness patient being treated for cardiogenic shock, in which standard and novel blood conservation methods were applied. In the 1870s, Mr. Charles Taze established the Jehovah's Witness religion, which was incorporated in 1931. The Jehovah's Witness doctrine that prohibits blood transfusions, donation, and storage of blood was first introduced in 1945 and is based on various biblical passages.[4] In 2000, the Watch Tower Society made clarifications to the doctrine, which has allowed individuals to make a personal decision to accept minor blood fractions. The first cardiac transplantation in a Jehovah's Witness patient was performed at the University of California Los Angeles in 1986, but the literature includes only 7 cases of heart transplantations performed in Jehovah's Witnesses without re-exploration, blood transfusions, or mortality.[5]

At our institution, patients refusing blood transfusions are evaluated at least 1 month before surgery and treated with erythropoietin, iron, and B12/folate supplementation as appropriate to correct preoperative anemia. Intraoperatively, blood-conservation techniques including normovolemic hemodilution, cell salvage, retrograde autologous priming of the CPB circuit, and pharmacotherapy (including antifibrinolytics) are used to decrease blood loss. In the postoperative period, phlebotomy is minimized, the threshold is low to reoperate for suspected surgical bleeding, and anemia is tolerated. Reinfusion devices for chest tube drainage are useful but currently are not available at our institution. An experienced multidisciplinary team must communicate and work together in the perioperative management of the patient.

The United States Food and Drug Administration licensed fibrinogen concentrate, RiaSTAP™ (CSL Behring, King of

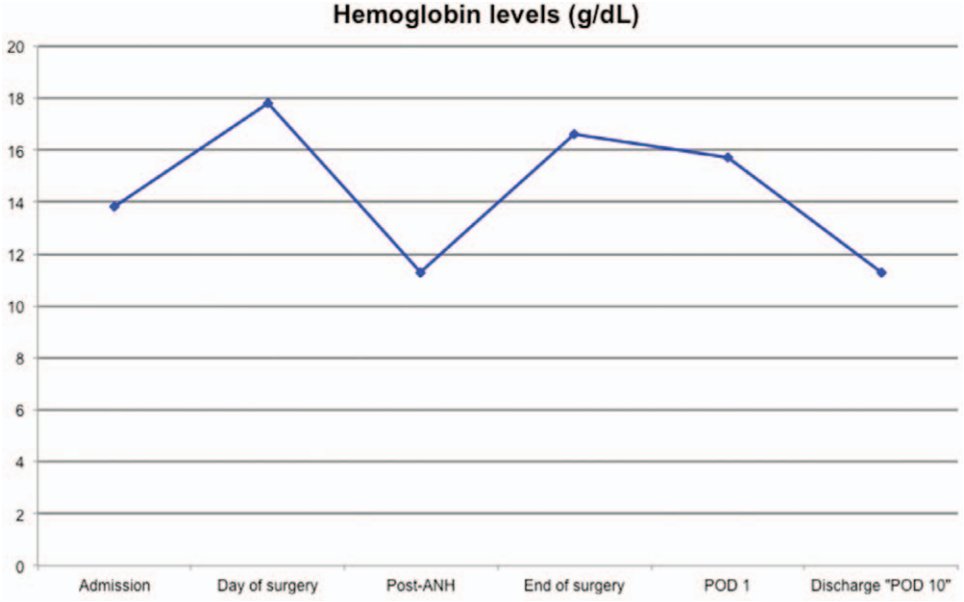

Figure 1. Patient's hemoglobin levels throughout the perioperative period. ANH = acute normovolemic hemodilution; POD = postoperative day.

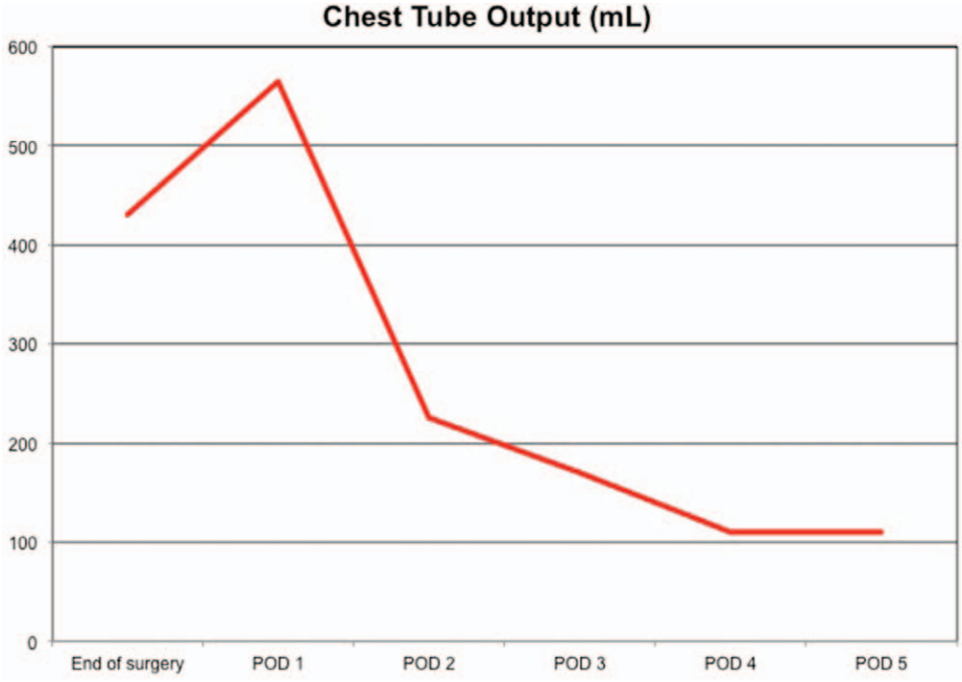

Figure 2. Chest tube output in milliliter throughout the postoperative period. POD = postoperative day.

Prussia, PA), in 2009 to treat congenital fibrinogen deficiency, afibrinogenemia, and hypofibrinogenemia. RiaSTAP is a preservative-free concentrate made from pooled human plasma. Fibrinogen assists in the stabilization of hemostatic platelet plugs. The size and frequency of RiaSTAP doses can be calculated on the basis of an expected fibrinogen level increment of 100 mg/dL after the recommended 70 mg/kg body weight dosing.[6] In this case, because previous laboratory findings showed a fibrinogen concentration of 209 mg/dL, the initial dose used was half the recommended dose, or 35 mg/kg. Although the American Society of Anesthesiologists' guidelines recommend administering fibrinogen concentrate for values <100 mg/dL, more recent European guidelines suggest supplementation for values <200 mg/dL.[7] Our patient had a borderline fibrinogen concentration intraoperatively, which was suspected to be lower (<200) in the immediate postoperative period. Given the excessive chest tube output in the intensive care unit, we administered RiaSTAP with the goal of preventing coagulopathy in this Jehovah's Witness patient.

Research studies have described the use of fibrinogen concentrate to treat dilutional coagulopathy, thrombocytopenia, and acquired hypofibrinogenemia.[8] These off-label uses of RiaSTAP have been described in trauma, orthopedic, cardiothoracic, urologic, and obstetric patients presenting for invasive procedures.[8,9] A prospective observational study reported that fibrin formation after CPB was more impaired than both the platelet count and total thrombin generation,[10] supporting the use of fibrinogen concentrate to promote fibrin formation after CPB. The fluid volume required to mix and dissolve fibrinogen concentrate is small in comparison with that of both cryoprecipitate and fresh-frozen plasma, which decrease the risk of hemodilution.

We believe that the novel use of RiaSTAP in this patient was a useful addition to minimize blood loss and maintain an adequate Hgb level without blood transfusion. Fibrinogen concentrate as a supplemental blood conservation strategy may be considered in select Jehovah's Witness patients who present for cardiac surgery.

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