Multidisciplinary management of a Jehovah's Witness patient for the removal of a renal cell carcinoma extending into the right atrium

[La prise en charge multidisciplinaire d'un patient Témoin de Jéhovah pour le retrait d'un hypernéphrome s'étendant dans l'oreillette droite]

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Purpose: To highlight the management of a Jehovah's witness surgical patient presenting for cardiopulmonary bypass (CPB) and deep hypothermic circulatory arrest.

Clinical features: A 47-yr-old male, Jehovah's Witness, with renal cell carcinoma was admitted for left radical nephrectomy and excision of tumour thrombus extending into the junction of the inferior vena cava (IVC) and right atrium (RA). The preoperative goals were to maximize red blood cell mass, delineate the extent of tumour extension and develop a surgical plan incorporating blood conservation strategies to minimize blood loss. A midline abdominal incision was made to optimize removal of the non-caval portion of the tumour from the intra-abdominal region. CPB and deep hypothermic circulatory arrest were instituted to aid in removing the tumour from the IVC and RA. Intraoperative blood conservation strategies included the use of acute normovolemic hemodilution, antifibrinolytics, cell salvage, point-of-care monitoring of heparin and protamine blood concentrations, leukocyte-depleting filter, and meticulous surgical techniques. The patient was successfully weaned from CPB and was transported to the cardiothoracic intensive care unit without complication. The patient was discharged home one week after the operation with a hemoglobin of 10.2 $g \cdot dL^{-1}$ and a hematocrit of 31.2%.

Conclusion: Multiple blood conservation techniques were employed to manage this Jehovah's Witness patient through complex cardiac surgery, which was previously denied to him at other institutions. The successful outcome of this patient, while respecting the right to refuse allogeneic blood products, is a result of a multidisciplinary collaboration as well as the application of established blood conservation techniques.

Objectif : *Présenter la prise en charge d'un opéré Témoin de Jéhovah pendant la circulation extracorporelle (CEC) et l'arrêt circulatoire hypothermique profond.*

Éléments cliniques : *Un homme de 47 ans, Témoin de Jéhovah, atteint d'un hypernéphrome, devait subir une néphrectomie radicale gauche et l'excision d'un thrombus tumoral qui s'étendait à la jonction de la veine cave inférieure (VCI) et de l'oreillette droite (OD). Les objectifs préopératoires étaient d'augmenter la masse des globules rouges, de préciser l'extension de la tumeur et d'élaborer un plan chirurgical comprenant des stratégies de conservation du sang afin d'en réduire les pertes. Une incision abdominale médiane a été faite pour optimaliser le retrait, de la région intra-abdominale, de la portion de la tumeur hors de la veine cave. La CEC et l'arrêt circulatoire hypothermique profond ont été établis pour faciliter le dégagement de la tumeur de la VCI et de l'OD. Les stratégies peropératoires de conservation du sang ont comporté l'usage d'hémodilution normovolémique aiguë, d'antifibrinolytiques, de récupération des cellules, de monitorage de chevet pour les concentrations sanguines d'héparine et de protamine, de filtre pour la déplétion leucocytaire et de techniques chirurgicales méticuleuses. Le sevrage de la CEC a été réussi et le patient a été transporté à l'unité des soins intensifs cardiothoraciques, sans complication. Il a reçu son congé une semaine après l'opération. Son hémoglobine était alors de 10,2 $g \cdot dL^{-1}$ et l'hématocrite à 31,2 %.*

Conclusion : *Diverses techniques de conservation du sang ont été employées pour la prise en charge d'un patient Témoin de Jéhovah au cours d'une intervention cardiaque complexe, laquelle avait été refusée précédemment dans d'autres hôpitaux. Tout en respectant le droit au refus de produits sanguins allogéniques, l'intervention a été bien réussie chez ce patient grâce à une collaboration multidisciplinaire et à une application des techniques de conservation du sang.*

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Clinical features

The patient, a 47-yr-old male Jehovah's Witness with history of renal cell carcinoma (RCC) admitted for left radical nephrectomy and excision of tumour extending into the inferior vena cava (IVC) and right atrium (RA), was referred to The New Jersey Institute for the Advancement of Bloodless Medicine and Surgery at Englewood Hospital and Medical Center for additional consultation. Initially, the patient presented with symptoms of back pain unresponsive to analgesics. Subsequently, the patient developed hematuria. Further evaluation revealed a left RCC that extended into the IVC and RA. Past medical history was significant only for hypertension. The patient denied any past surgical history. Medications included bisoprolol/hydrochlorothiazide, amlodipine, famotidine, acetaminophen. Following surgical scheduling, recombinant human erythropoietin (rHuEPO), folic acid, vitamin B12, and iron were added to his current medical regiment. There was no history of smoking and only occasional alcohol intake. The physical examination was unremarkable except for left sided tenderness along the flank. Laboratory examinations (including renal function test), electrocardiogram and chest radiograph did not reveal any abnormalities except for hematuria.

Computed tomography of the abdomen revealed a 9-cm by 8-cm heterogeneously enhancing mass arising from the upper pole of the left kidney (Figure 1). There appeared to be extension of the mass into the renal vein, IVC and a left gonadal vein. Additionally, there was evidence of perirenal lymphadenopathy without evidence of distant metastatic disease. Transthoracic echocardiography revealed a mass in the intrahepatic portion of the IVC with probable extension into the RA. Left and right-sided systolic function was within normal limits with no evidence of valvular disease.

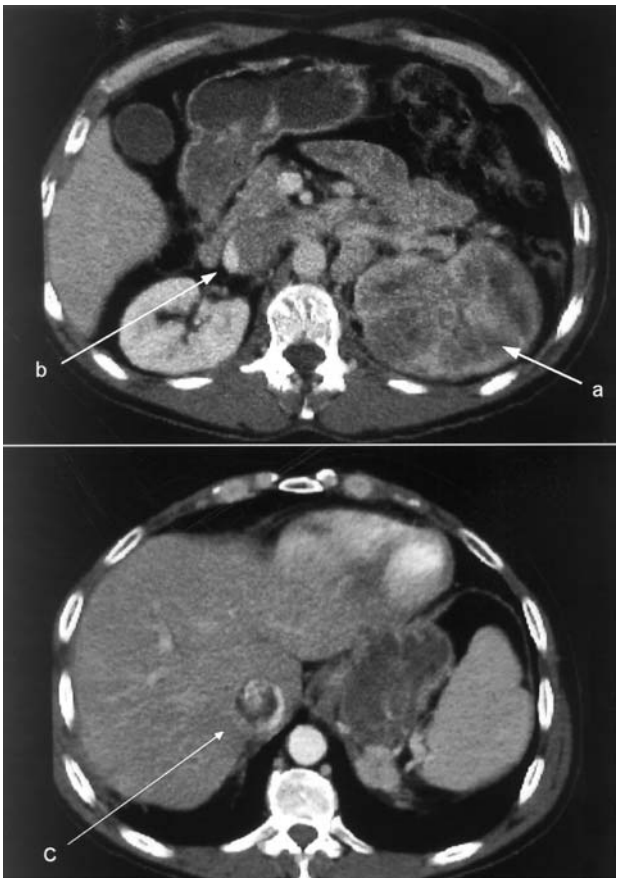

FIGURE 1a Computed tomography of the abdomen revealing a renal cell carcinoma of the left kidney (a) with tumour thrombus invading the inferior vena cava (IVC; b).
1b Computed tomography of the abdomen demonstrating tumour thrombus invading the intrahepatic portion of the inferior vena cava (IVC) near its junction with the right atrium (RA; c).

Urology, cardiac surgery, hematology and anesthesiology consultations were obtained to address the risks of surgery. After discussion the options and risks of transfusion avoidance for this type of medical condition, surgical intervention was planned with adjuvant chemotherapy/immunotherapy postoperatively. Daily subcutaneous injections of rHuEPO (20,000 units) and 100 mg of parental iron were immediately initiated to boost endogenous hemoglobin levels in preparation for surgery. Within two weeks, an adequate response was achieved (hematocrit increased from 32.4% to 46.5%), and the patient was scheduled for elective surgery.

Prior to arriving in the operating room, a 14-gauge catheter was placed intravenously, and a 20-gauge catheter was inserted in the right radial artery for invasive arterial pressure monitoring. ASA standard monitors (electrocardiogram, non-invasive blood pressure, pulse oximeter, and temperature monitoring) were placed and anesthesia induction and endotracheal intubation were accomplished using etomidate, fentanyl, midazolam and pancuronium. Anesthesia was maintained with oxygen, isoflurane, fentanyl and pancuronium. Gastric contents were evacuated with an orogastric tube prior to placement of a multiplane transesophageal echocardiography probe (TEE; Acuson™, Mountain View, CA, USA) along with an esophageal temperature probe. The right internal jugular vein was cannulated with a 9 French introducer (Arrow International Inc., Reading, PA, USA) and an 8 French pulmonary artery catheter (Abbot Critical

Care Systems, North Chicago, IL, USA) was placed through the introducer port. To avoid tumour manipulation, advancement of the pulmonary artery catheter through the RA into the right ventricle was performed under TEE guidance. A 20-gauge 12-cm jugular bulb catheter (Arrow International Inc., Reading, PA, USA) was also placed cephalad to the introducer for measurement of jugular mixed venous saturations in preparation for circulatory arrest. Urinary output and bladder temperature were measured using a urinary drainage catheter with a temperature probe.

Before skin incision, acute normovolemic hemodilution (ANH) was initiated using the side port of the 9 French introducer in the right internal jugular vein for blood withdrawal. The whole blood was collected in standard CPD-A blood storage bags (Fenwal®, Baxter Healthcare Corporation, Deerfield, IL, USA), which were continuously agitated using a blood agitator (Sebra®, Tuscon, AZ, USA). 2000 mL of whole blood was removed based on a previously derived formula using the patient's initial hematocrit, the target hematocrit prior to bypass, the CPB pump's prime volume, and the patients estimated blood volume to reach a target hematocrit on bypass of 18%.[1] Euvolemia was maintained using a combination of 2 L of Hextend® (Abbott Laboratories, North Chicago, IL, USA) and 1.3 L of Plasma-Lyte® (Baxter Healthcare Corporation, Deerfield, IL, USA). The patient's mean arterial blood pressure was maintained within 20% to 30% of baseline values. Blood pressure, heart rate, pulmonary artery measurements, cardiac output, urine output and TEE measurements were used to assess adequacy of euvolemia. Intraoperative salvage of red blood cells was accomplished using a cell saver (CS; Fresenius Medical Care, Bad Homburg, Germany). CS blood returned to the patient was filtered using a leukocyte-depleting filter (LDF; Pall Biomedical Products, Co., East Hills, NY, USA). A continuous blood circuit was maintained at all times with the ANH, CS, CPB circuit and the patient, to comply with the religious beliefs of the patient.

A midline abdominal incision was made and the left colon was reflected medially to help expose the renal tumour. The patient was found to have a large left renal tumour confined by the renal capsule. There was a conglomerate of periaortic nodes present. The lumen of the left renal vein was replaced by tumour thrombus, which extended all the way to the intrahepatic portion of the IVC. TEE revealed that the tumour extended to the junction of the RA and IVC (Figure 2). Once a decision was made that it was feasible to resect the renal tumour, a chest incision was made as an extension of the midline abdominal incision in order to gain access to the superior extension of the intracaval portion on the tumour thrombus. Due to venous congestion secondary to IVC tumour thrombus, only partial mobilization of the kidney and isolation of the vascular pedicle were possible prior to initiation of CPB.

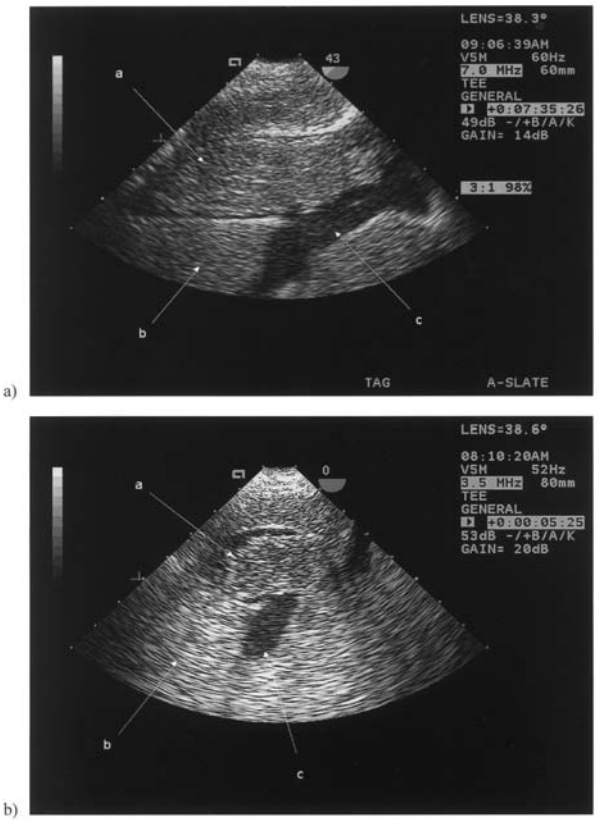

FIGURE 2a Longitudinal transesophageal echocardiography (TEE) view revealing tumour thrombus (a) in the inferior vena cava (IVC) extending up through the liver (b). The tumour extends proximally beyond where the portal vein (c) enters the IVC.
2b Transverse transesophageal echocardiography (TEE) view revealing same structures identified in figure 2a.

The patient was anticoagulated with bovine heparin, 300 IU·kg^{-1}, which was administered through the RA. Aprotinin (Trasylol®, Bayer Corp., West Haven, CT, USA) was started after a test dose was administered without complications. The full dose Hammersmith protocol was followed (2 million KIU loading dose followed by a continuous infusion at 0.5 million KIU·hr^{-1} and two million KIU into the pump prime volume).

Kaolin ACT tubes were used to measure adequacy of anticoagulation in the presence of aprotinin. The target ACT level was > 550 sec.[2] Heparin concentrations were also measured to assist in the management of anticoagulation using the Hepcon® HMS Plus (Medtronic, Inc., Minneapolis, MN, USA).

The CPB circuit was set up using a hollow fibre, trillium coated membrane oxygenator (Medtronic, Inc., Minneapolis, MN, USA), non-heparin coated circuit (Medtronic, Inc., Minneapolis, MN, USA), and incorporation of a LDF (Pall Biomedical Products, Co., East Hills, NY, USA) in addition to a regular arterial line filter (Medtronic, Inc., Minneapolis, MN, USA). The CPB circuit was primed with 600 mL of normal saline, 600 mL of D5W, 250 mL of 5% albumin, 3000 units heparin, 50 mEq sodium bicarbonate, and 12.5 gm of mannitol. Once an adequate ACT was achieved, CPB was initiated using a roller pump heart lung machine (3M™, Sarns™, Ann Arbor, MI, USA). Cooling was immediately begun in preparation for deep hypothermic circulatory arrest (DHCA). Two grams of methylprednisolone were administered during the initial cooling phase to aid in cerebral protection. Mean arterial pressure was maintained between 50 and 60 mmHg, with a blood flow of 2–2.4 $L \cdot min^{-1} \cdot m^2$. As needed, phenylephrine and sodium nitroprusside were used to maintain this pressure and flow rates. During the initiation of CPB, and in addition to the 2 L of ANH blood already set aside, an additional 1 L of autologous whole blood was diverted to a storage bag, connected to the venous line, to counteract the effects of hypothermia on blood viscosity.

A two-stage single lumen right atrial cannula (3M™, Sarns™, Ann Arbor, MI, USA) was inserted and was cut short so as not to contact the tumour and cause embolization. During the cooling phase but prior to circulatory arrest, complete mobilization of the left kidney was accomplished and the periaortic nodes were resected. The renal artery was ligated and divided leaving the kidney attached to the IVC by only the renal vein.

DHCA was employed to remove the intracaval and right atrial portion of the tumour. The patient's head was packed in ice. A jugular bulb saturation of > 95% was achieved (actual saturation was 97%). Core tissue cooling took approximately 45 min. When esophageal and bladder temperatures were less than 15°C and 18°C, respectively, DHCA was initiated.

The left renal vein was opened into the IVC and a plane was developed between the tumour thrombus and the normal caval intima. The two-stage single lumen venous cannula was removed from the RA and the atrium was further incised to assist in extraction of the tumour thrombus en bloc with the left kidney. The IVC was inspected for any residual tumour, of which there was none present. An additional manoeuver to remove any residual tumour thrombus was performed by placing a sponge at the IVC/RA junction and passing it caudally through the IVC. Subsequently, the cavotomy was repaired, the right atriotomy was closed, the two-stage single lumen venous cannula was reinserted into the RA and CPB was restarted. The period of DHCA lasted 27 min. Hemostatic control was achieved during the re-warming phase.

The patient was weaned from CPB on 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of dopamine for renal protection. TEE revealed that the IVC and RA were free of tumour thrombus and the left and right ventricular functions were without change from baseline. Based on the results of the heparin-protamine titration test, 330 mg of protamine were given. The postCPB hematocrit was 20%. The 2 L of ANH and 1 L of autologous whole blood removed just prior to initiating CPB were returned to the patient after separation from the CPB machine and decannulation. These units were reinfused in the reverse order of removal as per standard ANH protocol. CS totalled 713 mL and was returned using a LDF. No additional fluids were required besides a crystalloid maintenance infusion.

Postbypass, the Thromboelastograph® (TEG; Hemoscope Corp, Skokie, IL, USA) demonstrated a mild fibrin formation abnormality, a moderate fibrin polymerization abnormality and a moderate to severe qualitative and/or quantitative defect in the platelet-platelet or platelet-fibrin interaction during clot formation r = 16.5 mm (normal = 10–14 mm); k = 11.5 mm (normal = 3–6 mm); α = 37.5 mm (normal = 53–67 mm), MA = 39.0 mm (normal = 59–68 mm) without any evidence of fibrinolysis. Deamino-8-D-arginine vasopressin (DDAVP; 3 $\mu g \cdot kg^{-1}$) was given to improve platelet function. Additionally, there were 3 L of sequestered autologous whole blood returned to the patient that was not exposed to the negative effects of the CPB circuitry.

Discussion

RCC is accompanied by tumour thrombus extending into the IVC in 4–10% of cases. Recent reports indicate that reasonable long-term survival can be obtained by surgery, unless there is evidence of distant metastases.[3–8] Tumour thrombus migration, air embolism, surgical and nonsurgical bleeding are major complications associated with tumour removal.[9–11]

A large amount of perioperative blood loss requiring transfusion of allogeneic blood products is often associated with these cases.[12] This patient was referred

to The New Jersey Institute for the Advancement of Bloodless Medicine and Surgery at Englewood Hospital and Medical Center because of the ability to perform surgery without allogeneic blood product use in cases that are associated with extensive blood loss. The decision to proceed was based on the finding that although the tumour was large and there appeared to be nodal invasion, it was possible to remove the tumour for palliation, with a lesser chance to cure. The patient consented to surgery, with the understanding that palliative surgery would improve quality of life and the remainder of time with family.

Multiple different techniques have been reported for performing removal of renal cell tumours with tumour thrombus extension into the IVC.[13] Use of CPB with DHCA appears to be the safest way to facilitate complete resection of the kidney and tumour thrombus, and repair the IVC in a bloodless environment, to minimize blood loss.[12,14–16] Less invasive methods to avoid DHCA and aortic cross clamping include removing the tumour fragments with either a fibrillating or beating heart.[17,18] Although longer CPB times are associated with DHCA, it allows for a bloodless surgical field during tumour thrombus extraction and repair of the IVC. The majority of the dissection occurred on CPB prior to DHCA. This was done to take advantage of the lower flows during the cooling phase of CPB, which minimized blood loss by decreasing venous engorgement.

The preoperative goal was to increase the patient's red cell mass, primarily through the use of rHuEPO. Studies have shown that the use of rHuEPO preoperatively can effectively increase the patient's hematocrit, thus decreasing the incidence of perioperative transfusions.[19,20] Five to seven days are required before a 1–3 $g \cdot dL^{-1}$ increase in hemoglobin level is seen. Supplemental iron is given for maximum erythropoeisis. Postoperatively, rHuEPO was continued until the hemoglobin level reached an adequate and steady state (hemoglobin 10.2 $g \cdot dL^{-1}$ and hematocrit 31.2%). The patient's personal religious conviction allowed him to accept rHuEPO, despite containing albumin as a carrier.

Intraoperative blood conservation techniques included ANH, CS, autologous blood collection prior to bypass, LDF, meticulous surgical technique, antifibrinolytics, autotransfusion, and measurement of actual heparin concentrations. ANH has been shown to be a safe and effective way to reduce the incidence of allogeneic blood transfusions during cardiac and non-cardiac surgery especially if performed with other blood conservation techniques.[21–24] Hemodilution lowers the red cell mass shed during surgery and preserves the clotting factors which are usually lost with surgery and/or CS. Hemodilution is usually performed in its entirety prior to surgical blood loss or the onset of CPB. After ANH, the hemoglobin was sufficiently high (hemoglobin = 11.3 $g \cdot dL^{-1}$, and hematocrit = 33.8%) to allow for an additional 1 L of autologous blood to be collected by the perfusionist prior to the onset of CPB. This was done to achieve the desired hematocrit for profound hypothermia and to prevent exposure of the patient's blood to the adverse effects of CPB and hypothermia.

The key to proper hemodilution is to maintain euvolemia. Euvolemia was maintained with the judicial use of synthetic colloids (Hextend®, 2 L) and a balanced salt solution (crystalloids, 2.4 L). Multiple monitoring modalities were combined to assess the patient's volume status and maintain euvolemia. This was accomplished using a thermodilution cardiac output monitor to optimize stroke volume. End-diastolic area was intermittently evaluated with the TEE, and invasive monitoring was utilized continuously for absolute and relative changes in pressures along with inspecting the waveforms for respiratory variation and area under the curves.

Hetastarche may adversely affect the coagulation system and platelet function. However, there are no prospective blinded studies that demonstrate a higher incidence of clinical bleeding and adverse outcomes associated with the use of hetastarches, especially if the dose used is within the recommended limit of 20 $mL \cdot kg^{-1}$. Recently, the use of Hextend® was shown not to cause any adverse events in patients undergoing noncardiac surgery despite the use of massive amounts of this synthetic colloid.[25] The results of the TEG were abnormal and consistent with the coagulation defect that occurs during a prolonged CPB time and DHCA. Additionally, Hextend® can cause a decreased angle and MA by suppression of the factor VIII:C protein and by interfering with platelet function. DDAVP was given to offset this effect.[26,27] Hextend® was arbitrarily limited to approximately 25 $mL \cdot kg^{-1}$. If further volume replacement was needed ANH, cell salvaged blood, crystalloids or albumin would have been used in lieu of giving more Hextend®. Despite the known negative effect of hetastarches on platelet function and the TEG results, there was no evidence of clinical bleeding postCPB.

Alternatively, crystalloids could have been used exclusively to maintain euvolemia. However, with the extensive surgical bowel manipulation, there would have been a great deal of interstitial edema. This approach would have lead to the infusion of more than 6 L of crystalloid to maintain euvolemia. This

side effect of crystalloids can be partially offset with the use of hemofiltration and diuretics either during and/or postCPB. We chose to infuse a combination of colloids and crystalloids. There is evidence that microperfusion and tissue oxygenation are superior using hetastarches compared to crystalloids.[28] With euvolemia maintained throughout the case and 3 L of autologous blood to return postCPB, diuretics were given during the rewarming phase on CPB.

The use of the CS in cancer surgeries remains controversial. Some research indicates that cancer cells are shed in the operating field and may be reinfused intravascularly when blood is recycled. One possible solution to eliminate cancer cells is irradiation (2500 rads of gamma irradiation) of the intraoperative salvaged blood prior to its reinfusion. Irradiation would reduce the possibility of metastases. In light of the patient's religious beliefs, the processed cell salvaged blood could not be disconnected from the circuit and sent for irradiation. We used a LDF to decrease the risk of reintroducing tumour cells so that the processed blood could be reinfused.[29]

Antifibrinolytics have been shown to decrease the incidence of bleeding and mediastinal re-explorations during surgery with CPB.[30,31] Aprotinin is clearly more effective than either tranexamic acid or aminocaproic acid, but not more cost effective.[32] Aprotinin also has anti-inflammatory properties that may protect central nervous system function from the adverse effects of CPB.[33] Therefore, aprotinin was used in this case because of its greater efficacy for reduced bleeding and potential central nervous system protection.

CPB strategies included the minimization of tubing lengths, thereby decreasing the amount of priming solutions required. The LDF was used to possibly decrease the degree of the systemic inflammatory response syndrome and offset the CPB induced coagulopathy.[34] Heparin concentration measurements were also utilized using the Hepcon® HMS plus to prevent inadequate heparinization and excessive protamine administration, which can lead to bleeding postCPB.[35] Postoperative autotransfusion was connected in a continuous circuit to the patient, but was not necessary as the 24-hr chest tube drainage was only 165 mL of serosanguanous fluid.

Numerous case reports and articles have described the management of Jehovah's Witness patients undergoing cardiac surgery with CPB and other major surgical procedures. This case is unique because it describes the successful outcome of a Jehovah's Witness patient undergoing removal of a RCC requiring CPB with DHCA, that is associated with a significant amount of blood loss, using a multidisciplinary approach and numerous blood conservation techniques to avoid allogeneic transfusions. Strategies included perioperative administration of rHuEPO, ANH, antifibrinolytics, heparin/protamine guided administration, CS, autotransfusion, meticulous surgical hemostasis, and modification of surgical and CPB techniques. The patient was discharged to home one week after the operation with an uneventful postoperative course and a hemoglobin of 10.2 $g \cdot dL^{-1}$ and a hematocrit of 31.2%.

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