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Cardiopulmonary Bypass in the Setting of Waldenström's Macroglobulinemia

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Abstract: Waldenström's Macroglobulinemia (WM) is a rare lymphoma caused by the overproduction of immunoglobulin M (IgM). The elevated level of IgM causes serum hyperviscosity, cold agglutinins, and cryoglobulinemia. Anemia is also present because of impaired production of erythrocytes. For these reasons, placing a patient with WM on cardiopulmonary bypass (CPB) requires careful preparation. In this case, the patient was a 73-year-old male with known Waldenström's disease who required coronary artery bypass graft surgery. This report details the perioperative considerations used for successful CPB on a Waldenström's patient. Critical to this case was the use of plasmapheresis before surgery. Temperature management and acid/base status were carefully controlled. A successful coronary revascularization surgery was performed. Many of the Wadenstrom's disease complications expected on CPB failed to materialize.
Keywords: Waldenström's Macroglobulinemia, hyperviscosity, cardiopulmonary bypass, cold agglutinins. *J Extra Corpor Technol. 2018;50:120–3*

OVERVIEW

This is a case report documenting management of cardiopulmonary bypass (CPB) on a patient with coronary artery disease and comorbid Waldenström's Macroglobulinemia (WM). WM, or lymphoplasmacytic lymphoma, is a chronic myoproliferative disease characterized by monoclonal gammopathy of immunoglobulin M (IgM). The IgM level is elevated because of overproduction by cancerous B type lymphocytes. Other characteristics of the disease include elevated serum viscosity due to increased levels of IgM (leading to hyperviscosity syndrome [HVS]) and lymphoplasmacytic infiltrate of cancerous lymphocytes in bone marrow (1). A type of non-Hodgkin's lymphoma, WM results in anemia due to lymphocyte proliferation interfering with red blood cell (RBC) formation. Affecting 1,500 patients per year on average in the United States, the disease is rare and its indolent nature allows patients to live long and fulfilling lives (2). WM is often comorbid with cryoglobulinemia in roughly 30% of patients due to increased levels of IgM cryoglobulins. These patients often also have cold agglutinins. Both disorders can cause blood vessel occlusion at low temperatures. In addition, hyperviscosity syndrome caused by Waldenström's disease can reduce the ability to perfuse the microcapillary beds and lead to end organ ischemia. For these reasons, management of WM patients on CPB will require enhanced cooperation and preoperative preparation by perfusion, anesthesia, and surgery.

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DESCRIPTION

The patient is a 73-year-old male (Height = 170 cm, Weight = 94 kg, Mosteller Body Surface Area [BSA] = 2.1 m^2) with known WM. His medical history was unremarkable for prior cardiac disease. Ten days before

surgery, however, the patient presented to the emergency department with substernal chest pain and dyspnea. An electrocardiogram (EKG) showed nonspecific changes, and enzyme studies specific for serum troponins were negative. A transthoracic echocardiogram (TTE) indicated no evidence of valvular disease and an ejection fraction of 55%. No ischemic wall motion abnormalities were noted on TTE. Stress EKG was negative for ischemic changes. A myocardial perfusion study was consistent with reversible inferolateral wall ischemia. Cardiac catheterization revealed three-vessel coronary artery disease (LAD 90%, Ramus 100%, RCA 90%). The cardiac surgical team was consulted and coronary artery bypass graft surgery was scheduled.

The patient's baseline IgM level was 6,120 mg/dL. Safe CPB protocol recommends the level be reduced to less than 3,000 mg/dL (3). Plasmapheresis was utilized to decrease the IgM level to 2,150 mg/dL. Volume maintenance was augmented with serum albumin transfusions. Plasmapheresis was performed 3 days before surgery.

The relevant laboratory values drawn the morning of surgery were: IgM = 2,150 mg/dL, activated clotting time (ACT) = 111 seconds, hemoglobin and hematocrit (H/H) = 10.8 g/dL and 33%, and platelets = 139,000. Serum viscosity tests were not completed because of sample error. The patient's family history is significant for lymphoma. Thermal amplitude for cold agglutinins was determined to be positive at 4°C. No additional temperature thresholds were established. Titer measurements were not determined.

Anesthesia was induced following a slightly modified protocol consisting of doses of versed (2 mg preoperatively, with an additional 1 mg during induction), fentanyl (200 mcg), propofol (200 mg), and rocuronium (50 mg). Normal protocol calls for up to 5 mg of versed and 1,000 mcg of fentanyl. Anesthesia was maintained before and during CPB using an isoflurane vaporizer at 1 MAC. Intermittent fentanyl and propofol boluses were given as needed to further maintain adequate anesthesia. Blood pressure was controlled greater than 65 mmHg using ephedrine and phenylephrine. Six thousand units of heparin were given prophylactically during conduit harvesting. The remainder of the calculated loading dose for CPB of 33,000 units was subsequently administered. CPB prime consisted of 1,500 mL of crystalloid, 45 g of mannitol, and 10,000 units of heparin (normal protocol is 5,000 units). A liter of crystalloid fluid was removed by using retrograde prime technique. Boluses of amicar (10 g) and adenosine (12 mg) were administered before initiation of CPB. In addition an amicar infusion was started at 1 g/h. Prebypass ACT was measured to be 735 seconds. CPB was commenced at the surgeon's direction.

The patient was monitored intraoperatively using standard monitoring systems including nasal and Foley catheter temperature probes; EKG leads; and arterial, central venous, and pulmonary artery pressure monitoring lines. In addition, the INVOS Regional Saturation Monitor (Medtronic, Minneapolis, MN) was utilized to monitor bilateral cerebral oxygen saturations. On bypass, inline monitoring was performed using the CDI 500 (Terumo Cardiovascular Systems, Ann Arbor, MI) and temperature probes built into the bypass pump. Transesophageal echocardiography was performed before, during, and after coronary grafting as needed.

Successfully supported on CPB, the patient was cooled to an arterial inflow blood temperature of 27°C. This deviated from the normal protocol of an arterial inflow temperature of 20°C before placing the aortic cross clamp. With the clamp in place, 1,000 mL of blood cardioplegia solution was delivered containing potassium chloride (30 mEq) and magnesium sulfate (10.125 mEq). Cardioplegia was delivered 500 mL antegrade and 500 mL retrograde at 25°C (normal is <10°C) via the Quest MPS 2 Myocardial Protection System (Quest, Allen, TX). Asystole was quickly achieved. Following asystole, the blood temperature was immediately rewarmed to 34°C which resulted in the lowest bladder temperature on bypass sustained at 34.5°C.

Low circulating blood volume restricted blood flow to an average of 4 L/min or 1.9 L/min/m^2 (calculated flow at a cardiac index of 2.4 L/min/m^2 was 5 L/min). The circulating volume was augmented with Plasma-Lyte A given as needed during the case (2,000 mL total). The patient's blood pH was purposefully maintained slightly acidotic with base excess of −3 and a P_aCO_2 of 42 mmHg. The fraction of inspired oxygen was 70%, controlling P_aO_2 between 250 and 300 mmHg. Isoflurane at .5% was used to maintain anesthesia on CPB. The H/H on bypass reached as low as 5.8 g/dL and 21%. Mean arterial blood pressure was maintained at 70 ± 10 mmHg with phenylephrine at a concentration of .8 g/dL. The patient was returned to normothermia (36–37°C via the Foley catheter temperature probe) before termination of bypass. Management of CPB was otherwise uneventful and terminated after 111 minutes. The aortic clamp time was 74 minutes and the patient spontaneously converted to sinus rhythm. Total urine output for the case was 725 mL, roughly 100–150 mL/h. The surgery involved revascularization of four coronary vessels (LIMA → LAD, SVG → RCA, OM, Diagonal) with an average of >80 mL/min flow through each.

Anticoagulation was reversed with 300 mg of Protamine returning the ACT to 129 seconds. Post bypass H/H was 7.6 g/dL and 22%. Two units of packed RBC were transfused along with 500 mL of processed autologous blood. Hemostasis proved difficult requiring further blood products: 4 units of fresh frozen plasma, a 10 pack of cryoprecipitate, and a unit of single donor platelets. Once hemostasis was achieved, the chest was closed in routine fashion and the patient transferred to ICU without incident. Plasmapheresis was performed twice more following surgery.

Cardiothoracic ICU nurses report that this patient recovered in the typical fashion. The patient was discharged to a rehabilitation facility on post-operative day seven.

COMMENT

In the administration of CPB on a patient with WM, care should be taken to balance the concerns of hyperviscosity syndrome, hypervolemia, and anemia. A single case study published by Sweeting et al. (4) suggests alteration of protocol for the measurement of viscosity at intervals during CPB similar to those at which arterial blood gases and ACT are monitored. A challenge with this case was that equipment to monitor blood viscosity levels was not available. A preoperative sample was sent to an external laboratory the day before the patient's surgery, but the sample was insufficient for analysis. Fortunately, viscosity issues were not a problem in managing CPB for this patient. This may have been the result of adequate preoperative plasmapheresis and hemodilution with CPB. The type of fluid administered should also be carefully determined to balance the concern of maintaining H/H consistent with adequate tissue oxygenation. Crystalloid (2,000 mL total) was administered to maintain adequate circulating volume. Extensive hemodilution should be avoided but may be necessary to maintain an appropriate physiological viscosity. To further optimize viscosity, the idea of providing these patients with a higher cardiac index may be advantageous for two reasons. At high flow, O_2 delivery is increased correcting for a decrease in O_2 carrying capacity. Also, as flow increases, so does shear stress imparted on the blood. As shear stress increases, blood viscosity will decrease because of blood's behavior as a shear thinning fluid. For this case, high pump flows were not achievable because of minimal circulating blood volume (5).

Hyperviscosity syndrome can also be treated on bypass with the use of mannitol. A dose of 45 g of mannitol was administered on initiation of bypass. Theoretically, with a dose of mannitol at the initiation of bypass, intracellular fluid will be transferred intravascularly, reducing blood viscosity and minimizing the need for crystalloid (6).

In WM patients on CPB, manipulation of acid/base status can be utilized to enhance oxygen delivery. The CDI 500 Inline Blood Gas Analyzer (Terumo Cardiovascular Systems, Ann Arbor, MI) was used to monitor and manage blood gases. PCO_2 was maintained slightly higher than normal. By allowing the patient's pH to run acidotic, hemoglobin's affinity for oxygen is decreased, helping to enhance tissue perfusion. Not only will an elevated PCO_2 induce beneficial acidosis, but it will also vasodilate the cerebral vasculature which may have a neuro-protective effect. As an indicator of appropriate cerebral perfusion, cerebral oximetry saturations were constantly monitored during the case using an INVOS Regional Saturation Monitor (Medtronic). The cerebral saturations were kept at near baseline values throughout the case. PaO_2 was maintained between 250 and 300 mmHg.

In addition, temperature must be carefully controlled because of agglutination concerns. Sweeting et al. suggest maintaining normothermia on bypass if possible, and not cooling beyond 32°C when hypothermia is necessary. It is also suggested that warm cardioplegia should be administered to avoid the potential effects of the cold temperature. Cardioplegia was maintained slightly warmer than normal (25 vs. 20°C). Cooling time was also shortened from normal.

Plasmapheresis was utilized preoperatively twice on the patient. The patient's IgM level was adjusted to <3,000 mg/dL after plasmapheresis from a baseline of >6,000 mg/dL. The decrease in the IgM level may have contributed to minimizing the effects of HVS and associated complications. Anticipating hypervolemia, the decision was made to prepare a hemofilter, but given the low circulating volume present with this patient, it was not used. Retrograde autologous prime was performed in an effort to decrease potential hemodilution. The Sweeting group reports an emergent case and therefore, preoperative plasmapheresis was not able to be performed.

Many of the problems anticipated with this CPB procedure did not materialize. There were no additional blood products required to treat coagulopathy following surgery. Hemoglobin was 7.6 g/dL with a hematocrit of 23% and a platelet count of 113,000. Plasmapheresis was repeated post-operatively to reduce the increasing IgM level and protect the new grafts from the effects of HVS. Research shows that the IgM level will take about 2–3 months to return to baseline for the patient following plasmapheresis (3). The patient was discharged from the cardiothoracic surgery service on post-operative day seven and will be followed by hematology/oncology for the medical treatment of WM. The surgical and perfusion outcome was considered remarkable despite the potential for complications.

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