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Case Report

Deep Hypothermic Circulatory Arrest for Emergency Repair of Type A Aortic Dissection in a Patient with Cold Agglutinins

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Abstract: Cold agglutinins (CA) are auto-antibodies that adhere to erythrocytes in cold temperatures, and can result in agglutination of red blood cells. This process can cause complement-mediated intravascular hemolysis, which can be catastrophic. We describe a patient who developed CA during initiation of deep hypothermic circulatory arrest for emergent repair of Type A aortic dissection. The patient was found to have anti-I and anti-C antibodies and a positive direct Coombs test. CA resolved with re-warming, and resulted in no adverse events.
Keywords: cold agglutinin, deep hypothermic circulatory arrest, cardiopulmonary bypass, circulatory arrest, type A dissection, cardiac surgery. *J Extra Corpor Technol. 2021;53:299–301*

Cold agglutinin disease (CAD) is a rare clonal lymphoproliferative B-cell bone marrow disorder that results in an autoimmune hemolytic anemia in the setting of cooler temperatures (1–3). Though uncommon, it accounts for 15–25% of autoimmune hemolytic anemias and is observed more in Northern Europe, with a prevalence of 13–16 per million individuals (2,4,5). Cold agglutinins (CA) are autoantibodies that bind to red blood cells (RBCs) at a temperature between 3°C and 4°C, but can also bind at higher temperatures depending on the thermal amplitude (TA) (1,2). Thermal amplitude is the highest temperature at which CAs react with erythrocytes (1,2,5). The mechanism of agglutination, and hemolysis is entirely complement dependent (1,2). At the TA, CAs begin binding complement factors, which can result in agglutination and intravascular hemolysis (1,2).

Although CAD is rare and largely asymptomatic, CAD becomes pertinent in rare clinical situations, such as deep hypothermic circulatory arrest (DHCA) and cardiac surgery when hypothermia induces CA (1–6). It can be potentially catastrophic if not detected early, leading to complications associated with cardiopulmonary bypass (CPB) resulting from agglutination and hemolysis (1,2). Herein, we describe a patient who presented for emergency repair of Type A and Type B aortic dissection, and underwent CPB and circulatory arrest for repair of the proximal aortic arch. Upon initiation of DHCA to 19.7°C, clumped RBCs were noted in the cardioplegia heat exchanger of the bypass machine. Written consent for publication and HIPAA authorization were obtained from the patient.

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CASE DESCRIPTION

Patient

The patient was a 62-year-old man with past medical history of hypertension, who presented after a syncopal event in addition to chest and back pain. He underwent CT of chest, abdomen, and pelvis which revealed type A and type B aortic dissection with involvement of the innominate artery, occlusion of the left subclavian and vertebral arteries, with extension to the level of the right renal artery. Bedside ultrasound revealed cardiac tamponade with right venal (RV) collapse on systole.

Intraoperative

Patient was taken to the operating room for ascending aortic dissection repair with graft and aortic valve

replacement. He was intubated uneventfully. Multi-lumen access catheter with Swan-Ganz catheter was placed. Temperature probe placed in the nasopharynx. Artic Sun, a noninvasive temperature management device, was used for cooling and rewarming. Blood pressure was maintained primarily with norepinephrine infusion. Pre-CPB activated clotting time (ACT) was 138 seconds.

Surgery was initiated and patient was heparinized with 20,000 IU for an ACT of 553 seconds. A 17-Fr. arterial cannula was inserted into the right femoral artery and a two-stage venous cannula was inserted into the right atrial appendage. An LV vent was placed via the right upper pulmonary vein. A retrograde cannula was placed into the coronary sinus via the right atrial wall. CPB (Medtronic Bio-Console 560) was initiated at 27 minutes after surgical incision. Regarding the CPB, the extracorporeal prime volume was 1,110 mL using a balanced salt solution with high potassium, magnesium, dextrose, tromethamine in normal saline. The oxygenator was ventilated with 100% oxygen at a sweep of 2.5–3.5 L/min. Pump flow was approximately 3.5–4.5 L/min pre-DHCA and post-DHCA. Mean arterial pressures were maintained at approximately 50 mm Hg pre-DHCA and post-DHCA.

Heparin was administered intermittently to keep ACT >450 seconds. After 18 minutes following the initiation of CPB, the patient was slowly cooled to 19°C. Upon reaching 19.7°C, the perfusionist noted RBC "clumping" in the cardioplegia heat exchanger, which was at a lower temperature (15°C) than the rest of the circuit. Cardioplegia temperature was 2°C upon observing clumping. Further cooling was halted, surgeon was informed, and the temperature was increased to slowly to 20.2°C over 4 minutes with resolution of clumped RBCs. Slow rewarming was trialed until resolution of clumping was seen given that clumping was not observed at warmer temperatures. Cardioplegia temperature was also increased to 7°C. Circulatory arrest at 20.2°C was initiated 6 minutes later for 30 minutes during ascending aortic dissection repair with a 32-mm Gelweave straight graft. An attempt was made to wean patient off CPB at normothermia (37.1°C), however mild to moderate aortic regurgitation was noted with significant hypotension. A decision was made to reinitiate CPB. The temperature was decreased to 35.8°C as DHCA was not anticipated. Aortic valve replacement with a 23-mm Edwards Lifesciences Magna Ease tissue was performed. After rewarming to normothermia, bypass was discontinued, and heparin was reversed with protamine 180 mg resulting in an ACT of 125 seconds.

Several type and screens were sent to the blood bank immediately before surgery and peri-induction, which required pre-warming, to remove antibodies from the RBCs, from room temperature to 37°C. After multiple blood samples, the patient was found to have anti-I antibodies in addition to a positive direct Coombs test to anti-C3. The patient was type and crossmatched during the surgical case, and prior to the administration of blood products. Perioperative coagulopathy was noted by the surgeon and through laboratory findings with hematocrit 23.5%, platelet 96–109,000/L, fibrinogen 104 mg/dL, and INR 2.4. The patient was transfused a total of 1 unit RBCs, 3 units fresh frozen plasma (FFP), 2 units cryoprecipitate, and 1 unit of pooled platelets. TA and titers were not obtained.

At the completion of the surgery, the patient was transferred to the cardiovascular intensive care unit (ICU), where he was extubated. Postoperatively, the patient was found to have confusion with multiple cardiovascular infarcts due to extensive aortic dissection extending to the left vertebral artery. This was managed conservatively. He had also developed acute kidney injury, which resolved within 5 days. He had a transient minimal increase in his troponin to .03 ng/mL. Total postoperative ventilation time was 1 day; total length of ICU was 4 days; total length of hospitalization was 14 days. The patient was eventually discharged for rehabilitation 2 weeks later. Follow-up several months later revealed resolving neurological deficits.

DISCUSSION

Deep hypothermic circulatory arrest is necessary for the repair of acute Type A aortic dissection (7,8). The concept involves decreasing core temperature to as low as 14°C to decrease cerebral metabolic demands and provide a bloodless surgical field for aortic arch repair (7,9). This decrease in cerebral metabolic rate offers a significant degree of neuroprotection and diminished excitatory neurotransmitters, which lowers inflammatory markers in the brain (8,10,11).

Given the urgency of the operation, there was minimal history available. The patient was difficult to crossmatch given the presence of antibodies. Blood samples sent to the blood bank and required pre-warming to 37°C to remove the coating of anti-I to assess the blood type. At this point, it was noted the RBCs also had anti-C3 coating the erythrocytes. Difficulty with crossmatching raised the suspicion of CA as blood matching occurred prior the initiation of bypass and DHCA. Anti-I is associated with largely viral infections as well as *Mycoplasma pneumoniae,* with up to 80% of patients with CAD having a previous *M. pneumoniae* infection (5,12,13). Both anti-I and anti-C are considered to be cold antibodies (5,12,13). Furthermore, the majority of CA are anti-I, as seen in this patient (5). These CA pose a considerable risk during CPB, causing a range of complications such as hemolysis and hemagglutination leading to embolisms, thromboses, infarctions, and hemolysis (14). Postoperatively, the patient denied a history of pneumonia and notable viral

infections. He also denied symptoms of Raynaud's disease or acrocyanosis.

Risk stratification is difficult in these patients as CA are typically asymptomatic (5,6). Identification of high-risk individuals involves questioning about signs and symptoms of hemolysis and agglutination (14). High-risk patients would benefit from obtaining titers, determining TA, and obtaining a hematology and/or anesthesiology consultation (3,4,14). If titers are as low as <1:40 and TA is <20°C, no further workup is needed (3,4). Management strategies include reduction of antibody levels through plasma exchange, administration of steroid, azathioprine, cyclophosphamide, or rituximab, in an effort to mitigate the likelihood of clinical significance (3,4). Other strategies during surgical interventions include avoiding hypothermia, temperatures above the TA, warm blood cardioplegia, moderate hypothermic CPB with systemic circulatory arrest (4,6,14–17). If agglutination occurs intraoperatively, warming the core temperature until resolution of agglutinins and utilizing warm retrograde myocardial washout are possible options (4). In addition, it is recommended to limit transfusion of FFP given it is a complement-rich blood product which can replete C3 and C4 levels and possibly increase hemolysis in patients with CAD (1,2).

CONCLUSION

Although a rare condition, it is important to recognize the signs early to mitigate the life-threatening complications that arise from CAD, such as hemolysis, thrombosis, and embolism. Early identification and appropriate planning can prevent some of the complications.

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