

Bentall Surgery in a Patient with Cold Agglutinin and Antiphospholipid Antibody: Double Trouble

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Abstract: Cold agglutinin disease is an uncommon disease with potential to cause hemolysis and thrombosis during hypothermic cardiac surgery. Antiphospholipid syndrome is also rare disease with hypercoagulation tendency. Perioperative management of both these diseases is challenging. We present suc-

cessful perioperative management of high risk Bentall surgery in patient with both these dreadful diseases. **Keywords:** cold agglutinin disease, antiphospholipid syndrome, Bentall surgery, hypothermia, hypercoagulation, hemolysis, case report. *JECT.* 2016;48:83–85

Cold agglutinin (CA) disease is very rare disorder affecting 15% of patients with autoimmune hemolytic anemia (1,2). It is characterized by the presence of high circulating IgM antibodies directed against red blood cells (RBCs) at body temperatures less than 31°C causing agglutination and then hemolysis (1,2). Antiphospholipid antibody syndrome is an uncommon autoimmune disease causing a hypercoagulable state.

Two common antiphospholipid antibodies include lupus anticoagulant and anti-cardiolipin antibodies, both of which promote clot formation in arteries and veins.

Open heart surgery is generally performed under hypothermic cardiopulmonary bypass (CPB). Presence of CAs in cardiac surgical patients can potentially cause life-threatening hemolysis and intracoronary hemoagglutination/thrombosis causing myocardial infarction (1). Perioperative morbidity and mortality is high in patients with antiphospholipid antibody syndrome. Bentall surgery is generally performed at moderate hypothermic temperature 28°C. Here we present case of Bentall surgery in patient with CA and antiphospholipid antibody.

CASE DESCRIPTION

A 55-year-old female presented with chronic shortness of breath with mild activities. Echocardiographic examination revealed severe aortic stenosis with aortic root dilation. She had been previously diagnosed with autoimmune hemolytic anemia (reticulocyte count 29% with anisocytosis and spherocytosis) due to CA disease (CA titer of 1:1586 at 4°C). She was being treated with steroids for CA disease for 6 months and her most recent CA titer was 1:15 at room temperature and 1:30 at 4°C in the previous month.

Laboratory tests for mycoplasma, infectious mononucleosis, syphilis, cytomegalovirus, rheumatoid factor, and antinuclear antibody were negative. On admission to our center, her reticulocytes count was 2%, and CA titer was 1:2 at room temperature and 1:8 at 4°C. While investigating the patient, lupus anticoagulant was found to be positive by dilute Russell viper venom time and silica clotting time. She was diagnosed as a case of antiphospholipid antibody syndrome. The patient was scheduled for aortic valve and aortic root replacement (Bentall procedure). Baseline activated clotting time (ACT) was 142 seconds. After a smooth induction of anesthesia, a midline sternotomy was performed and heparin was administered in the dose of 400 IU/kg. The initial ACT after heparinization was 824 seconds. CPB was instituted after aortic and bicaval cannulation. Plasmalyte crystalloid solution with added sodium bicarbonate and mannitol were used in priming solution. Priming volume was warmed and warm blood antegrade cardioplegia

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(temperature 34°C) was used. Cold cardioplegia was avoided due to risk of agglutination. Intraoperatively aortic root and ascending aorta was seen to be dilated and thinned out till 3–4 cm below the origin of great vessels. Bentall surgery was performed using 23-mm Medtronic mechanical valved conduit under hypothermic CPB with temperature maintained at 34°C. Operating room and intravenous fluid temperature was maintained accordingly to prevent any fall in patient's core body temperature below 34°C. ACT was maintained above 700 seconds intraoperatively. No agglutinates were observed in CPB circuit. Aortic cross clamp time was 140 minutes and total CPB time was 170 minutes. Patient could be easily weaned from CPB with minimal inotropic support. During the surgery, hematocrit was maintained between 25% and 30% and systemic mean arterial pressure was kept above 60 mmHg. Half dose of protamine was used for heparin neutralization. ACT after neutralization was 178 seconds. Patient received 2 units of packed RBCs transfusion postoperatively. Her reticulocytes count was 2.2% in postoperative period. The patient was started on warfarin and intravenous heparin on postoperative day 1 to maintain an activated partial thromboplastin time between 80% and 90 seconds until the international normalized ratio achieved a therapeutic level of 2.5–3.5.

Postoperative course was stable and patient was discharged on 8th postoperative day.

DISCUSSION

Cold antibodies may have idiopathic origin or may be produced due to an infective process (viral or mycoplasma infections) or a lymphoproliferative disease (2). Clinical implications of cold antibodies depends on titer and thermal amplitude. High titer and high thermal amplitude of cold antibodies may predispose the patient to hemagglutination during induced hypothermia in CPB. Even during rewarming, such cold antibodies may fix complements with risk of catastrophic hemolysis (2). The incidence of detectable cold autoantibody in cardiac surgical patients has been reported to be .8–4% (3).

Intraoperative agglutination should be suspected by the observation of intracoronary thrombus, inadequate delivery of cardioplegia, agglutination seen in the cardioplegia circuit and high line pressures in the CPB circuit (1).

Effective intervention at early detection of agglutination can prevent catastrophic events. Izzat et al. (4) described a case of detection of agglutinates during antegrade cold blood cardioplegia. Prompt insertion of coronary sinus catheter and continuous retrograde warm cardioplegia flushed back agglutinates from coronary arteries to aortic root.

Though the incidence is very less (<5%), cold antibodies before cardiac surgery are detected generally at

the time of blood cross-match screening (5). Patients with low cold antibodies titer (<1:32) and low thermal amplitude (<20°C) are at low risk of agglutination during surgery (3). Preoperative strategies to reduce antibody titer or reactivity include administration of drugs (e.g., steroids, azathioprine, and cyclophosphamide), plasma exchange and IgG therapy (1,5).

Intraoperative strategies include warm blood antegrade/retrograde cardioplegia, warm ischemic arrest, limiting systemic hypothermia, warming operating room, anesthetic gases, intravenous fluids, blood, and warming mattresses. The aim is to keep the systemic perfusion temperature above the thermal threshold of agglutinin activity (5).

Management of patients with cold autoantibodies needs meticulous planning before cardiac operations. In the present case, patient was optimized by preoperative steroid therapy for 6 months which reduced cold antibodies titer to sufficiently low level. Bentall surgery was successfully performed at temperature of 34°C without any evidence of thrombosis or hemolysis perioperatively.

The incidence of antiphospholipid syndrome (APS) is 1–5% in young, healthy people and 30% in patients with systemic lupus erythematosus (SLE) (6). The APS can manifest as vascular thrombosis, pregnancy loss, renal thrombotic microangiopathy, cardiac valvular disease, thrombocytopenia, and hemolytic anemia. Catastrophic APS is an accelerated form of APS with multiorgan failure (7). It can cause mortality in nearly 50% of patients. APS is paradoxical disease showing delay in coagulation in laboratory tests despite a thrombotic tendency in vivo.

APS criteria for definite APS include one or more episodes of thrombosis, a symptom related to thrombosis, and a positive antiphospholipid antibody test (aPL test) result on two or more occasions that are at least 12 weeks apart (8). Such patients are more susceptible to cardiac valvular disease because endocardial injury due to blood flow exposes phospholipids in the cells and induces microthrombi and fibrotic changes (9). In the present case, patient had history of spontaneous abortions and aortic valvular disease along with positive lupus anticoagulant. Considering the symptoms and urgency of surgery, we could not repeat antiphospholipid antibody test after 12 weeks of first positive test preoperatively. It was prudent decision to presume such case as APS and manage accordingly.

ACT is common test of anticoagulation done during cardiac surgery with CPB. ACT measurement in APS patients may be variable like raised baseline ACT values varying heparin response due to decreased antithrombin III level. There has been no consensus regarding the best method of anti-coagulation in such patients during CPB. Different case studies and reports have used different anti-coagulation regime, e.g., 1) using standard heparin dose (3 mg/kg) or an raised dose (5 mg/kg) irrespective of the ACT (8), 2) using heparin dose that doubles the baseline

ACT level (10), 3) maintaining plasma heparin level more than 2.5 IU/mL, and 4) measurement of the antifactor Xa level (11). We used heparin in the dose of 4 mg/kg and maintained ACT above 700 seconds intraoperatively in this case.

After the completion of CPB, neutralization of heparin with protamine should be carefully done. We initially intended not to reverse heparin effect; however, considering diffuse bleeding, we neutralized heparin by half dose of protamine. After the surgery, one should be cautious about catastrophic APS. Incidence and mortality of catastrophic APS is about 1% and 50%, respectively (11). Surgery and infections can trigger it, hence appropriate antibiotics and anticoagulants should be administered postoperatively.

CONCLUSION

Cardiac surgery in presence of cold antibodies can be potentially fatal event. APS patient can have lethal consequences during cardiac surgery. It is unusual coincidence of combination of both these diseases in the present patient. Preoperative optimization, and judicious intra- and postoperative management can bring successful outcomes in such patients with double troubles during high-risk cardiac surgery.

REFERENCES

1. Park JV, Weiss CI. Cardiopulmonary bypass and myocardial protection: Management problems in cardiac surgical patients with cold autoimmune disease. *Anesth Analg*. 1988;67:75–8.
2. Fischer GD, Claypoole V, Collard C. Increased pressures in the retrograde blood cardioplegia line: An unusual presentation of cold agglutinins during cardiopulmonary bypass. *Anesth Analg*. 1997;84:454–6.
3. Agarwal SK, Ghosh PK, Gupta D. Cardiac surgery and cold-reactive proteins. *Ann Thorac Surg*. 1995;60:1143–50.
4. Izzat MB, Rajesh PB, Smith GH. Use of retrograde cold crystalloid cardioplegia in a patient with unexpected cold agglutination. *Ann Thorac Surg*. 1993;56:1395–7.
5. Shah S, Gilliland H, Benson G. Agglutinins and cardiac surgery: A web based survey of cardiac anaesthetic practice; questions raised and possible solutions. *Heart Lung Vessel*. 2014;6:187–96.
6. Shi W, Krilis SA, Chong BH, Gordon S, Chesterman CN. Prevalence of lupus anticoagulant and anticardiolipin antibodies in a healthy population. *Aust N Z J*. 1990;20:231–6.
7. Asherson RA, Cervera R, de Groot PG, et al. Catastrophic antiphospholipid syndrome: International consensus statement on classification criteria and treatment guidelines. *Lupus*. 2003;12:530–4.
8. Miyakis S, Lockshin MD, Atsumi T, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). *J Thromb Haemost*. 2006;4:295–306.
9. Hojnik M, George J, Ziporen L, Shoenfeld Y. Heart valve involvement (Libman-Sacks endocarditis) in the antiphospholipid syndrome. *Circulation*. 1996;93:1579–87.
10. Sheikh F, Lechowicz A, Setlur R, Rauch A, Dunn H. Recognition and management of patients with antiphospholipid antibody syndrome undergoing cardiac surgery. *J Cardiothorac Vasc Anesth*. 1997;11:764–6.
11. Cho H, Jeon Y, Man Hong D, Kim HJ, Min JJ. Anesthetic management of antiphospholipid syndrome patients who underwent cardiac surgery—three cases reports. *Korean J Anesthesiol*. 2014;66:164–8.