A 60-year-old man was admitted to our hospital because of aortic stenosis with a peak pressure gradient of 61 mmHg, moderate aortic regurgitation, and a dilatation of the ascending aorta of 50 mm in diameter, which had grown 5 mm in 2 years. Because of severe aortic stenosis with a bicuspid valve and fast progression of the ascending aorta in size, replacements of both the aortic valve and the ascending aorta were planned.

He had experienced severe acute renal failure with hemolysis because of cold agglutinin one year before the operation. The hemoglobin had decreased to 4.3 g/dL during hemolytic attack. His titer of cold agglutinin was extremely high. The titer of cold agglutinin has kept above than 1:131072 at 4 degree Celsius. It once increased to 1:524288.

Both the replacement of the aortic valve and the ascending aorta under normothermic cardiopulmonary bypass using intermittent warm blood cardioplegia were completed uneventfully. He was discharged from the hospital on postoperative day 11.

Keywords: aortic valve, ascending aorta, cardiopulmonary bypass, cardioplegia, cold agglutinin

Case Report

Aortic Valve Replacement to a Patient with High Titer of Cold Agglutinin

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Introduction

Cold agglutinins are antibodies that react with red cells at low temperatures, producing hemagglutination with resultant microvascular occlusion and hemolysis.1 During hypothermic surgical procedures such as cardiopulmonary bypass, careful perioperative management is required for patients with cold agglutinins.

We report on a patient with an extremely high titer of cold agglutinin who successfully underwent replacement of both aortic valve and ascending aorta under normothermic conditions.

Case Report

A 60-year-old man was admitted to our hospital because of aortic stenosis with a peak pressure gradient of 61 mmHg, moderate aortic regurgitation, and a dilatation of the ascending aorta of 50 mm in diameter, which had grown 5 mm in 2 years. An echocardiographic examination suggested a bicuspid aortic valve. Because of severe aortic stenosis with a bicuspid valve and fast progression of the ascending aorta in size, replacements of both the aortic valve and the ascending aorta were planned.

The presence of cold agglutinin had been diagnosed 2 years prior to surgery during close examination following hemolytic anemia. His titer of cold agglutinin had previously been extremely high and increased up to 1:524288 at 4 degree Celsius. Since the diagnosis, he had been treated solely by keeping warm except infusion of rituximab, a monoclonal antibody that selectively targets CD
20-positive B-cells. In spite of treatment with rituximab, however, the titer of cold agglutinin remained elevated at above 1:131072 at 4 degrees Celsius. He has had hemolytic anemia with gross hematuria every winter. One year prior to surgery, flu-related infection had introduced subsequent anemia and acute renal failure. The hemoglobin had decreased to 4.3 g/dL. Urine nitrogen and creatinine had increased to 157 mg/dL and 19.87 mg/dL, respectively. He had been received emergency treatment including transfusion and continuous hemodialfiltration.

At the time of surgery, the titer of cold agglutinin was 1:131072 at 4 degrees Celsius. Careful attention was paid to the temperatures of CPB, transfusions, infusion fluids, and the operation room in particular throughout the surgery. The patient was anticoagulated with heparin of 3 mg/kg. Once an activated clotting time of 300 seconds had been achieved, normothermic CPB was initiated. The aortic cross clamp was applied, and warm blood cardioplegia was delivered retrogradely into the coronary sinus at a temperature of 37 degrees Celsius. After a transverse aortotomy, warm blood cardioplegia was applied through a selective antegrade approach. Throughout the procedure, warm retrograde cardioplegia was intermittently delivered within 20 minutes.

The aortic valve was bicuspid with a fusion of the right coronary cusp and the non-coronary cusp. Calcification of the aortic annulus was resected using an ultrasonic surgical system (Olympas, Center Valley, PA). An aortic valve replacement using a 23-mm On-X valve (MCRI, Austin, TX) was performed with interrupted sutures in supra-annular position. Subsequently, an ascending aorta was replaced with a 28-mm UBE-Neo graft (Ube Industries, Ube, Japan). The CPB weaning was accomplished without trouble. Total cross-clamp time was 120 minutes.

The lowest core temperature was 37.1 degree Celsius in the rectum. The lowest peripheral temperature was 35.3 degree Celsius on the left foot (Fig. 1).

The postoperative maximum concentration of blood creatine kinase MB was 62 U/L. The postoperative hemodynamics was stable. The patient was moved from the intensive care unit within a day. The postoperative course was uneventful except for the microscopic hematuria which was successfully treated with haptoglobin. The blood hemoglobin concentration decreased to 8.0 g/dL on the operation day. Red blood cells and fresh, frozen plasma were transfused. No transfusion was performed beyond postoperative day 1. The maximum blood concentration of lactase dehydrogenase and total bilirubin were 703 IU/L on the postoperative day 3 and 3.44 mg/dL on the postoperative day 2, respectively (Fig. 2). After anticoagulation had been controlled with warfarin, he was discharged from the hospital on postoperative day 11.
**Discussion**

The clinical importance of cold agglutinins depends on two factors: The plasma titer of cold agglutinins and the thermal amplitude at which hemagglutination occurs. Moore reported that a patient with nonspecific cold agglutinins whose presentation is characterized by a low titer, a low thermal amplitude, and a lack of clinical symptomatology can undergo hypothermic CPB without increased threat of a hemolytic or vascular occlusive crisis. However, if any of one of the factors mentioned is beyond the limitation above, careful perioperative management is required. Even though the patient was careful with daily living, he had a severe hemolytic attack, so he was expected to have a high thermal amplitude. In addition, the titer of cold agglutinin (1:524288) was extremely high, thus, we decided to present a case with unusual circumstances.

Various approaches for management of patients with cold agglutinins during cardiac surgery using CPB have been demonstrated. These approaches can be divided into two distinct ways: One, to decrease the titer of cold agglutinins and two, to maintain blood temperature above the thermal amplitude. Although preoperative, total exchange transfusion or plasmapheresis would decrease the titer of cold agglutinins, transfusion or plasmapheresis with a sufficient quantity of plasma carry the risk of associated infection or graft versus host disease.

An alternative approach, which we have chosen for the present case, is normothermic CPB with warm blood cardioplegia. To minimize myocardial injury, we selected warm blood cardioplegia. A strict adherence was preserved to supply cardioplegia within 20 minutes during 120 minutes of the aortic cross clamp time. Although some cases with relatively low titer of cold agglutinins (1:8 to 1:1024) employing warm blood cardioplegia were publicized, a case with an extremely high titer as the present case (1:524288) has not been reported. Under our strategy, the perioperative course was uneventful.

While many studies have suggested that continuous normothermic perfusion with oxygenated potassium-enriched blood provides the ideal state for the heart during a cardiac operation, the credibility of intermittent warm cardioplegic solution is not still established. To use the warm blood cardioplegia intermittently, special attention needs to be given to the interruption time of providing cardioplegia compared to cold blood cardioplegia. Intermittent supply of cardioplegia, however, allows for a clear surgical view during aortic valve replacement.

**Conclusion**

Even in a patient with an extremely high titer of cold agglutinins and a history of severe hemolysis, a surgery using CPB was performed safely under normothermic CPB with intermittent warm blood cardioplegia.

**References**