Warm Heart Surgery for the Patient with Cold Agglutinins
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Citation

Abstract
Cold-reactive antibodies may cause complications such as hemolysis and myocardial damage due to their activity at low temperatures during cardiac surgery. The detection of cold agglutinins in a patient before the operation may change the operative strategy. This report describes a case with coronary artery disease in which the cold agglutinins with high-titer and high-thermal amplitude were detected preoperatively. The operation was conducted with normothermic cardiopulmonary bypass and warm blood cardioplegia. The management of this rare situation remains controversial but currently, warm heart surgery appears to be the most expedient method.

Keywords: Cold agglutinin; Cardiac surgery; Cardiopulmonary bypass, Hypothermia.

INTRODUCTION
Cold agglutinin disease is an autoimmune phenomenon in which antibody directly agglutinates human red cells at low temperatures. In these patients, open heart operations with hypothermia carry the risk of red cell agglutination resulting in complications such as hemolysis, myocardial infarction, renal insufficiency and cerebral damage,

Various approaches for management of these patients have been described in some previous case reports. Preoperative plasma exchange, intraoperative total blood exchange, use of warm crystalloid cardioplegia followed by cold crystalloid cardioplegia infusion have all been used in an attempt to decrease the concentration of the cold-reactive antibody

Alternatively, surgery may be conducted at normothermia or moderate hypothermia depending on thermal amplitude and titer of antibody.

Because of the limited number of cases reported, the optimal guidelines for detection and management of this uncommon clinical problem remains controversial. This report describes a case with coronary artery disease in which the cold agglutinins with high-titer and high-thermal amplitude were detected preoperatively. The operation was conducted with normothermic cardiopulmonary bypass and warm blood cardioplegia.

CASE REPORT
A 63- year-old man presented with moderate stable angina and a markedly positive response on exercise tolerance test but no history of other illness or blood transfusion. Cardiac catheterization revealed an ejection fraction of 60 per cent and severe proximal lesions of the left anterior descending, proximal diagonal, and circumflex marginal arteries. Angioplasty of these long tight lesions were considered unsafe and the patient was admitted for coronary artery bypass grafting.

The patient’s initial preoperative routine laboratory findings were within normal limits. However, autoagglutination was noticed during the test procedures at room temperature in the blood bank. Antibody screening tests showed cold reactive antibodies in the patient’s blood. Agglutination was completely resolved by warming the blood sample to 37oC . Patient was blood type 0 Rh+. The titer of the cold agglutinin was 1/1024 at 4oC, showing anti-I blood group specificity. The thermal amplitude for agglutination was determined as 30oC. Subsequent patient evaluation including laboratory tests for infectious mononucleosis, mycoplasma pneumonia, cytomegalovirus, syphilis, rheumatoid factor, antinuclear antibody and abdominal computed tomography revealed no viral infection, malignancy, or autoimmune disorder. The disease was considered idiopathic. The reticulocyte count was 2.1
percent, plasma bilirubins, LDH and SGOT were in normal limits.

Compatible units of blood were obtained and operation was planned using systemic normothermia with warm blood potassium cardioplegia infusion. Priming volume was warmed, two stage venous and arterial cannulas were inserted and cardiopulmonary bypass instituted at 37oC. The operation was performed with special precautions to avoid exposure of the patient’s blood to temperatures within the active range of the cold agglutinin. The temperature of the operating room was raised to 30oC, anesthetic agents and all intravenous fluids were warmed. During the operation, hematocrit levels were kept between 25 and 30 per cent, and systemic hypotension under 60 mm Hg was not allowed. Oxygenated blood, transferred from the oxygenator, was made cardioplegic by the dilution with 1:4 ratio of warmed crystalloid cardioplegic solution (Plegisol), and the addition of sufficient potassium chloride to bring the potassium concentration to about 25 mmol/L. Cardioplegic solution was infused through the aortic root after the cross-clamp. The initial dose was 15 ml/kg, subsequent doses of 5 ml/kg cardioplegic solution with 15mmol/L potassium concentration was given intermittently about every 15-20 minutes.

Two saphenous vein grafts were used for revascularization of the large diagonal and the circumflex marginal arteries. The left internal mammary artery was anastomosed to the left anterior descending artery. After the completion of distal anastomoses aortic cross-clamp was released and the proximal anastomoses were done under side-clamp. A second aortic cross clamp application with cardioplegia was needed for re-anastomosing internal mammary artery to left anterior descending artery because of anastomotic tear and bleeding. The total cross-clamp time was 95 minute. The heart started beating spontaneously and the patient was successfully weaned from bypass without any pharmacological support. No evidence of in vivo hemolysis or agglutination was found during the operation. The patient was kept warm in the recovery room with a heated mattress. All intravenous solutions were warmed. The postoperative course was free of cardiac complications. No electrocardiographic or enzymatic evidence of myocardial injury was apparent. The reticulocyte count was 1.8 percent, no important increase was found in plasma bilirubins postoperatively. The patient was clinically well and was discharged from the hospital on the seventh postoperative day.

**COMMENT**

Cold agglutinins, predominantly IgM antibodies mediated against the red blood cell I or i antigens, are not uncommonly found in otherwise healthy adults and children. Their clinical importance depends on their titer and thermal amplitude, the highest temperature at which the antibody is active. The thermal amplitude of cold agglutinins is rarely more than 30oC and usually less than 25oC. The patient with low-titer, low-thermal amplitude antibodies are usually asymptomatic but may serve hemolytic anemia or peripheral vessel occlusive phenomenons such as acrocyanosis, livedo reticularis and skin ulcers when exposed to low temperatures. Although agglutination may be reversible in vitro, ischemia and gangrene may occur in vivo if capillary sludging has been prolonged. These findings may alert the clinician against to the possibility of the disease. Symptomatic patients are frequently with high-titer, high-thermal-amplitude antibodies. However, like the reported case, the clinical course of a patient with high-titer, high-thermal-amplitude antibodies might be completely silent. This fact supports the policy of routine testing for cold agglutinins before the cardiac surgery in which the systemic or topical hypothermia is routinely used. The disease may be associated with infection or with lymphoproliferative or autoimmune disorders. The related laboratory tests should be included to preoperative screening in the patients with cold agglutinins. The idiopathic form has a peak incidence after age 50 years, a usual age for cardiac bypass procedures.

The management protocol during the open heart surgery in the patients with cold agglutinins is still controversial. The complications such as acute hemolytic reactions, and intracoronary agglutination have been reported after exposure to hypothermic cardiopulmonary bypass and cold cardioplegia. Earlier, preoperative plasma exchange was the preferred method in an attempt to decrease the antibody concentration. The total washout method introduced by Lee and associates has the disadvantages of massive transfusion. Alternatively systemic normothermia or mild hypothermia depending on thermal amplitude of the antibody is an available method.

For myocardial protection, crystalloid/blood cardioplegia at higher temperature has been the most common strategy. Intermittent cross-clamping with/without induced ventricular fibrillation has also been used for coronary surgery. Warm crystalloid washout technique provides myocardial cooling.
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but requires isolation of the heart from the remaining circulation, which is not achievable because of noncoronary collaterals. Shahian and associates have reported 3 case in which this technique was used, but the myocardial injury with enzymatic evidences were described in 2 of them.

The operative strategy for a patient with cold antibodies needs some changes in routine management plan. Agarwal and associates have reviewed 50 cases appeared in the literature between 1969 and 1995, and managed with various techniques. The patient reported here has one of the highest value of thermal amplitude and titer in the literature. They recommended warm heart surgery as the method of chose for these kind of patients. The general precautions such as a warm operating room and warming of intravenous fluids should not be ignored. The normothermic operation with warm blood cardioplegia obviates the need for hypothermia and prevents activation of the cold agglutinins. Additionally, it may provide excellent myocardial protection in the patients with long cross clamp time like the patient reported here.

References
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