

Cold Agglutinin Disease Detected During Open Heart Surgery

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Abstract Cold agglutinins are commonly found in sera of healthy persons. They rarely become clinically apparent due to their activity at lower temperature. In these patients, cardio-vascular operations requiring hypothermia can result in complications like hemolysis, renal failure, myocardial damage and cause unexpected morbidity and even mortality (Agarwal et al., *Ann Thorac Surg* 60:1143–1150, 1995). Ideally, all patients should be routinely screened pre-operatively for antibodies and management plans made accordingly but the low incidence of the disease, cost of screening tests and the lack of direct relationship between the titers, thermal threshold and risk of complications makes the screening an uncommon practice.

Keywords Cold Agglutinin · Cardiac surgery · Cardiopulmonary bypass · Hypothermia

Introduction

Cold agglutinin disease is an autoimmune phenomenon in which incomplete antibodies present in various clinical settings directly agglutinate human red cells at low temperatures. Appearance of I Ag on human RBCs in post natal period leads to modification in fetal i antigen leading to development of low levels of antibodies which agglutinate at low temperatures. Open heart surgery with hypothermia in patients with cold reactive proteins can cause hemolysis, inadequate cardioplegic distribution, MI, renal and hepatic insufficiency and cerebral damage [1].

Case Report

A 38 year old female presented to our hospital with complaints of fever, dyspnoea and cough since 1 month. She had two episodes of fever in 1 month and her cough and dyspnoea were waxing and waning since 1 month.

The patient was a known case of rheumatic heart disease with MS and MR since 6 years (diagnosed during pregnancy). She came for a mitral valve replacement to our hospital. Pre operatively, her Hb was 14.3 g%, Hct was 41.1 %, MCV 98.7 fl, MCH 38.0 pg, TRBC 5.6 million/dl, total proteins were 7.1 g/dl (albumin 3.8 g/dl and globulin 3.3 g/dl). AST was 25 IU/l, ALT was 41 IU/l, total bilirubin 1.5 mg/dl (direct –0.2 mg/dl and indirect 1.3 mg/dl). ESR was 30 mm 1st h. X-ray chest showed ++ rotation and showed mild cardiomegaly. ASLO and CRP were within normal limits. Her blood group was A+ve.

During surgery, while preparing for cardioplegia at 4 °C, her blood started agglutinating. It was picked up immediately by the anesthetist and a normothermic cardiopulmonary bypass was done. The case was immediately informed to the blood bank and her blood samples were sent. Her indirect Coomb's test was negative. Direct Coomb's test and auto-control were found to be positive. Cold antibody titer was positive (1:8) at 4° C. The peripheral blood film was examined and it did not reveal any abnormality. The reticulocyte count was 1.8 %.

Subsequent patient evaluation included lab tests for Infectious Mononucleosis, CMV, Syphilis, RA factor, ANA and an abdominal ultra sound which did not reveal any infection, malignancy or auto-immune phenomenon. The disease was idiopathic. The sample was also sent to Biorad laboratories where C3d was found 1+. The patient was stable intra operative and post-operative. One unit of packed red cells was transfused after surgery, which was uneventful.

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Discussion

Cold agglutinins are predominantly IgM antibodies directed against the RBC I or i antigen. These are commonly found in sera of healthy individuals but the clinical importance depends upon the titer and thermal threshold (the highest temperature at which the antibody is active). The thermal amplitude of cold agglutinins is rarely more than 30 °C and usually less than 25 °C [2]. The patient with low-titer, low-thermal amplitude antibodies are usually asymptomatic. Symptomatic patients are frequently with high-titer, high-thermal-amplitude antibodies. However, the clinical course of a patient with high-titer, high-thermal-amplitude antibodies might be completely silent [3]. Cold agglutinins are usually of little clinical importance, with diagnosed disease having an approximate incidence of 1:75,000 [2]. In the setting of cardiac surgery, it may be of greater clinical importance due to the use of hypothermia for myocardial protection. The complications such as acute hemolytic reaction have been reported after exposure to hypo-thermic cardioplegia.

Cold reactive antibodies may be benign or pathological depending upon the thermal reactivity. Benign ones are often seen in healthy individuals, are reactive below 22 °C and have a titer of less than 1:64 as was seen in this case. The pathologic cold antibodies have high thermal amplitude and manifest as chronic cold agglutinin disease or acute transient hemolytic anemia [4].

Clinically significant clod agglutinin (CA) disease may occur as a primary or secondary process. Primary or idiopathic CA disease usually occurs in the seventh or eighth decades, affecting women more often than men. It is frequently chronic in duration, well tolerated, and is often asymptomatic. Secondary CA disease usually occurs as sequelae of an infectious process (e.g., mycoplasma pneumonia, cytomegalovirus) or an underlying lymphoproliferative disorder. Cold agglutinins have also been

demonstrated in patients infected with human immunodeficiency virus independent of other infections or neoplasm [5].

It is not uncommon for cold antibodies to initially manifest during surgical hypothermia in patients with no previous known history of CA disease. The low incidence of CA disease, screening test costs, and the lack of a direct relationship among antibody titer, thermal threshold, and the risk of complications makes routine preoperative screening of CA titers uncommon [2]. In the case of the patient with known CA disease, preoperative determination of the thermal threshold of the CA antibody may improve patient management, as the temperature at which agglutination is likely to occur may be avoided. Cooling the perfusate in the blood cardioplegia system and watching for agglutination before systemic cooling of the patient has been suggested as one alternative to preoperative screening. If agglutination is detected in the blood cardioplegia system, the cardioplegia apparatus should be warmed to room temperature and the blood flushed from the cardioplegia apparatus and catheters.

References

1. Agarwal SK, Ghosh PK, Gupta D (1995) Cardiac surgery and cold-reactive proteins. *Ann Thorac Surg* 60:1143–1150
2. Fischer GD, Claypoole V et al (1997) Increased pressures in retrograde blood cardioplegia line: an unusual presentation of cold agglutinins during cardiopulmonary bypass. *Anesth Analg* 84:454–456
3. Baltalarli A, Keskin A, Sirin B (2000) Warm heart surgery for the patient with cold agglutinins. *Internet J Thorac Cardiovasc Surg* 3(2)
4. Basu S, Saifuddeen A, Kaur P (2009) Transient cold agglutinin disease with mycoplasma infection. *JAPI* 57:653–654
5. Nagarajan M, Manickavasam M et al (2002) Cold agglutination in open heart surgery. *Indian J Thorac Cardiovasc Surg* 18(3): 121–122