The Student Section

Clinical Concepts And Treatment For Cold Agglutinin On Cardiopulmonary Bypass

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A fifty-three year old female patient with a weight of sixty-one kilograms, a height of one-hundred fifty-two centimeters, and a body surface area of 1.60 meters squared presented with symptoms which necessitated surgery for a mitral valve repair and removal of a cardiac tumor. Clinical findings included severe mitral regurgitation, mild aortic insufficiency, moderate pulmonary hypertension, rheumatic mitral valve disease, hypertension, myomatous degeneration, and cold agglutinin disease. The paragraphs to follow will describe the pathophysiology and clinical concepts behind cold agglutinin disease and specific modifications in perfusion technique to treat such a patient on cardiopulmonary bypass. The cardioplegia system used for this case is a "coil-in-bucket" blood cardioplegia set. Under normal circumstances when using this system, the blood and cardioplegia solution mix together at a 4:1 blood to cardioplegia solution ratio. The solutions mix and are sent forward with a roller pump through tubing into a metal coil which had been placed inside a bucket full of ice cubes and then continues to travel upward to the patient's myocardium. An alternative delivery technique with this cardioplegia system will be described to follow.

Cold agglutinins are serum antibodies that work on the antigens found on the surface of red blood cells. They are present in all normal, healthy humans but are usually benign unless under extreme cold temperature conditions. The antibodies are usually an IgM immunoglobulin which activates complement and bind to the I-antigens of the red blood cell or anti-I specificity. The IgM antibodies are large proteins used by the immune system to identify and neutralize foreign antigens. The IgM antibody is produced by B cells and is the primary antibody against A and B antigens on red blood cells. IgM antibodies are primarily responsible for the clumping or agglutination of red blood cells. Cold agglutinin disease or hemagglutinin disease is an autoimmune reaction in which antibodies react to a range of cold temperatures which can lead to complement activation, red blood cell agglutination (clumping), hemolysis, and vascular occlusion leading to possible organ ischemia. The main characteristic distinguishing benign and pathologic cold reacting autoantibodies is thermal amplitude which is the temperature at which the antibodies become activated.

With benign autoantibodies, the thermal amplitude is generally less than twenty-two degrees Celsius. Spontaneous autoagglutination does not occur. The antibody titer test is less than 1.64 at four degrees Celsius. The direct antiglobulin test score is usually negative or weak positive with a polyspecific antiglobulin reagent. In contract, the pathologic autoantibodies may have a thermal amplitude as high as thirty-two degrees Celsius, spontaneous autoagglutination can occur until the patient reaches a normal body temperature of thirty-seven degrees Celsius, an antibody titer test with a ratio of one/one thousand at four degrees Celsius, and a direct antiglobulin test score of two to three plus with a polyspecific antiglobulin reagent. The two above antibody tests are described below.

The autoantibody titer test is a measurement of how much antibody an organism has produced that recognizes a particular part of an antigen recognized by the immune system. It is expressed as the greatest dilution ratio that still gives a positive result. For example, a titer of 1:8 compared to a titer of 1:32 means that the patient tested gives a positive result for the antibody at any dilution down to 1:8 (1 part serum to 8 parts solvent). Therefore, at any greater dilution, the test would be negative. Hence, a titer of 1:32 means that the patient produces more of the specific antibody because it now takes a greater dilution (1 part serum to 32 parts solvent) to deem the test negative.

The direct antiglobulin test (DAT), also known as the direct Coomb's test, is used primarily to help determine if the cause of hemolytic anemia is due to antibodies attached to red blood cells. A blood sample

is taken and the red blood cells are washed which removes the patient's own plasma. The blood is then incubated with antiglobulin reagent. If this produces agglutination of the red blood cells, then the DAT test is positive suggesting that antibodies are present on the red blood cell surface. The range for a DAT score is from 0 to 4+. The stronger the DAT result, the more antibodies that are present and the higher the degree of red blood cell agglutination. For example, a DAT score of 3+ would represent a much greater degree of agglutination compared to a DAT score of only 1+.

A patient with cold agglutinin disease can have many potential risks which may occur during cardiopulmonary bypass including hemoagglutination, vascular occlusion with organ ischemia, complement activation, hemolysis, thrombocytopenia, peri-operative myocardial infarction, microvascular thrombosis, renal failure, or cardiac heart failure. Therefore, perfusion technique should be modified to help attenuate any of the above harmful conditions. Two techniques that could be done prior to bypass may include plasmapheresis or plasma exchange.

Plasmapheresis is the removal, treatment, and return of blood plasma from blood circulation. Blood is taken out of the patient's body, plasma is removed from a cell separator, and red blood cells are returned to the patient. The plasma, which contains the antibodies, is treated and then returned to the patient. This technique may be useful if the patient must be cooled to temperatures that would likely cause the autoimmune reaction. Plasma exchange is when blood is taken out of the patient's body, plasma is removed from a cell separator and red blood cells are returned to the patient. The plasma, which contains the antibodies, is completely discarded and the patient receives replacement donor plasma. This technique is useful for rapid removal of the cold-reacting antibodies in short term management.

After a bolus dose of heparin was administered, cannulation occurred. A 20 French aortic arterial cannula was placed. After the cannula was secured and free of any air emboli, a test dose of one hundred milliliters was sent through the arterial line to test that forward flow could be achieved. This was followed by the placement of 26/32 French dual venous cannulas. Once an adequate ACT was established at a minimum of four-hundred and eighty seconds, the initiation of bypass occurred. The patient's temperature was only "drifted" down to a minimum of 35.4 degrees Celsius at its coldest throughout the entire duration of bypass. The cross clamped was placed and the administration of a warm flush followed by the delivery of cold crystalloid was administered. This was given at a four parts blood to one part crystalloid solution ratio. In total, three hundred milliliters of warm and five hundred milliliters of cold solution was given. With the 4:1 ratio, this equaled a total of one-hundred and sixty milliliters of crystalloid. The surgeon first removed some cardiac vegetation and then progressed to repairing the mitral valve. The cross clamp was removed for a total cross-clamp time of 64 minutes. After adequate de-airing and assessment of the mitral repair, the patient was weaned off bypass. The whole duration of bypass lasted for a total of 79 minutes.

The modifications made during bypass for this specific case included "drifting" the patient's core temperature to a lowest recorded temperature of 35.4 degrees Celsius avoiding any potential risk with the use of hypothermia as well as a change with the delivery of cardioplegia solution. An alternative for blood cardioplegia is the use of crystalloid cardioplegia. Therefore, the use of cold crystalloid cardioplegia with a warm flush prior to delivery was administered. A quarter inch "Y" connector is cut into the blood cardioplegia line with one port to the cardioplegia set and the other port to the crystalloid solution. When delivering the initial warm flush to wash out the coronary blood in the myocardium, the ice in the bucket is replaced with warm water kept between 37-40 degrees Celsius. After the flush is complete, the delivery of cold crystalloid is administered through a bucket with ice to maintain heart arrest which can be scavenged away to the cell saver. In total, three hundred milliliters of warm and five hundred milliliters of cold crystalloid was delivered. Other alternative cardioplegia delivery techniques may include continuous warm retrograde delivery with normothermic temperatures or the use of warm blood cardioplegia.

For a standard cardioplegia delivery system without the use of a "coil-in-bucket" system, the same modified approach can easily be achieved. The perfusionist would make sure that the cardioplegia delivery temperature on the heater/cooler unit was set to a normothermic value of at least 37 degrees Celsius before administering the initial dose of warm flush to the coronaries. Once complete, the cardioplegia delivery temperature should be flushed and lowered to a cold cardioplegia delivery temperature before administering the remaining cold crystalloid solution. Alternatively, the continuous warm retrograde delivery technique is easily achieved by setting the cardioplegia delivery temperature to a normothermic value of at least 37 degrees Celsius and delivering the warm crystalloid at a low continuous pressure through the coronary sinus.

The technique proved to be very beneficial to the patient, avoiding any adverse autoimmune reactions due to the cold agglutinin disease while generating very good post-operative outcomes. Since the surgical procedure could be accomplished successfully without cooling the patient to harmful cold temperatures, plasmapheresis was not used in this particular case but is an important concept to understand with cold agglutinin disease patients undergoing cardiopulmonary bypass. Researching and understanding the pathophysiology and clinical con-

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cepts of cold agglutinin disease led to a modification of the normal perfusion technique and cardioplegia delivery for a mitral valve replacement procedure which avoided any adverse risks and reactions that may have caused a detrimental outcome for the patient.

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