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CASE REPORT

Operative consideration in patient with cryoglobulinaemia undergoing cardiac surgery with use of cardiopulmonary bypass

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Abstract

Cryoglobulinaemia can be defined as the presence of single or mixed immunoglobulins in the serum, which precipitate at sub-homeostatic temperatures and redissolve at higher temperatures. This condition in the context of cardiac surgery can precipitate systemic complications secondary to cold agglutination and lead to significant perioperative problems with the cardiopulmonary bypass machine and the extracorporeal circuit. We present a case of a 74-year-old gentleman with cryoglobulinaemia who underwent mitral valve repair and coronary artery bypass graft surgery. The patient was to undergo preoperative plasmapheresis to reduce circulating levels of cryoglobulin and thereby decrease the risk of potential protein agglutination during cardiopulmonary bypass. Operative considerations included the level of systemic temperature required, the temperature of the cardioplegia solution, level of anticoagulation and the speed and timing of rewarming of the patient to normal homeostatic temperatures. The postoperative management also consisted of early plasmapheresis to further reduce the number of cryoglobulins.

INTRODUCTION

Cryoglobulinaemia can be defined as the presence of single or mixed immunoglobulins in the serum, which precipitate at sub-homeostatic temperatures and redissolve at higher temperatures. This disorder can be observed in a wide array of haematological, rheumatological and infectious disorders. Cryoglobulinaemia can be further subdivided into three subtypes. Type 1 refers to the presence of single monoclonal immunoglobulins whereas Type 2 and 3 tend to form immune complexes consisting of polyclonal antibodies, with Type 2 having the largest representation among the population of patients with cryoglobulinaemia [1].

Within the context of cardiac surgery, the management of these patients can be highly complex due to the nature of the potential complications that could ensue. In patients who require cardiopulmonary bypass, the systemic temperature and temperature of the cardioplegia solution can vary depending on the type of operation and surgeon preference with respect to the method of administration of cardioplegia. In fact, agglutination has been described in the cardioplegia unit in a patient with...
unsuspected cold agglutinin disease [2]. Generally, there is a need for systemic hypothermia often drifting to temperature as low as 30°C for complex or prolonged operations or therapeutic hypothermic to temperatures as low as 18°C to perform operations under circulatory arrest. Hypothermia in itself offers myocardial protection via lowering the metabolic requirements of the myocardium. Furthermore, the form of myocardial protection administered as a solution in the form of cardioplegia can be delivered as warm or cold and either as crystalloid solution or with blood. The potential sequelae of these measures could initiate the cascade of cold agglutination in patients with these cold antibodies, as in present in cryoglobulinaemia. In addition to the systemic complications that could follow, there is also the possibility of cold agglutination occurring within the cardiopulmonary bypass circuit, thus directly impeding the function of the bypass machine and the extracorporeal circuit and thus the operative procedure would be interrupted and could not be performed. There is sparse literature discussing the management of these patients who require cardiopulmonary bypass at hypothermic temperatures.

**CASE DISCUSSION**

We present a case of a 74-year-old gentleman with newly diagnosed idiopathic Cryoglobulinaemia (on no previous treatment for this condition) who required combined mitral valve repair and coronary artery bypass graft surgery. He had presented to the hospital with troponin positive rest pain leading to a diagnosis of non-ST-elevation myocardial infarction. His cardiac risk factors included diabetes mellitus, hypertension and hypercholesterolaemia. His comorbidities included cryoglobulinaemia. He had no previous history of hepatitis and no associated autoimmune condition. Coronary angiography demonstrated triple vessel disease and transthoracic echocardiography confirmed moderate central mitral regurgitation. The patient required combined mitral valve repair and coronary artery bypass graft surgery. Due to the risk of cold agglutination a multidisciplinary strategy was adopted to decrease this risk with specific involvement of the renal and haematology teams to optimize the pre-, peri- and postoperative care of the patient and thus ensure that the risk of cold agglutination was as low as possible. Detailed preoperative investigations were performed including a ‘cryoglobulinaemia screen’ and the measurement of cryoglobulins to elucidate any treatable causes and to assess the level of cryoglobulins, which could indicate the risk of cold agglutination. Following these investigations, in conjunction with the respective teams the patient underwent sessions of plasmapheresis preoperatively with the overall aim of reducing the number of circulating cryoglobulins and was commenced on steroids preoperatively to further reduce this risk. This was performed relatively close the day of the operative procedure, thus ensuring a minimal amount of time for the body to restore and replenish the circulating number of cryoglobulins.

Prior to the operative procedure, the anaesthetists and perfusionists were informed of the significantly increased risk of cold agglutination and that specific measures were in place to avoid this as best possible. In view of this, it was agreed that the systemic temperature would drift to 34°C and use of warm blood cardioplegia, and ensuring that the activated clotting time while on cardiopulmonary bypass was consistently above 440 seconds and use of zero balance ultrafiltration and the careful controlled rewarming of the patient to normal homeostatic temperatures.

The postoperative management also consisted of early plasmapheresis to further reduce the number of cryoglobulins.

**DISCUSSION**

The earliest report in literature discussed the potential of cold agglutination in the context of cold antibodies in patients undergoing cardiopulmonary bypass in 1984 [3]. Furthermore, the technique of using normothermic cardiopulmonary bypass and utilization of warm blood cardioplegia to mitigate the potential risk of cold agglutination has been described [4]. Moreover, when concerning isolated coronary artery disease requiring surgical revascularization the approach of off-pump coronary artery bypass surgery in conjunction with preoperative plasmapheresis and intravascular warming catheter has also been advocated to decrease the risk of cold agglutination [5]. A case series from the Mayo foundation retrospectively analyzed 16 patients identified with cold agglutinins detected either preoperatively or intraoperatively [6]. In patients with cryoprecipitation the clinical manifestation can be variable from clinical signs secondary to skin necrosis, glomerulonephritis and ensuing renal failure to thrombosis of major visceral arteries [7]. There have also been case reports of patients undergoing cardiac surgery with cryoglobulinaemia described as case reports including isolated coronary artery bypass graft surgery [8, 9] and major aortic surgery [10].

Although the perioperative care of the patient was arguably the most challenging aspect of the patient’s management it was critical in ensuring that the postoperative course remained as uneventful as possible. The titre level identified of cold agglutinins preoperatively influences the risk of agglutination occurring at sub-homeostatic temperatures [7].

We recommend the use of a multidisciplinary setting involving cardiac surgeons, anaesthetists, perfusionists, haematologists, rheumatologist and nephrologists in addition to other allied healthcare professions to significantly reduce the preoperative and postoperative complications.

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**CONFLICTS OF INTEREST STATEMENT**

None to declare.

**REFERENCES**


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