Intra Operative Massive Graft Thrombosis and Failure after Heart Transplant in LVAD Assisted Patients: Report of Two Cases

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Abstract

Left Ventricular Assistance Devices (LVAD) is an increasingly used option for advanced heart failure patients on waiting list for cardiac transplantation (C-Tx). LVAD recipients are prone to thromboembolic complications caused by blood activation and systemic inflammation. Even though similar survival has been observed with or without LVAD at the time of transplantation, particular LVAD-related morbidity may occur. Herein we describe two unique cases of acute intra cavitary cardiac graft thrombosis and fulminant heart failure, occurring peroperatively, after weaning from cardiopulmonary bypass, in heart transplant recipients who had benefited of an LVAD as bridge to transplantation.

Introduction

Long-term mechanical circulatory support using left ventricular assist devices (LVADs) is a routine strategy to bridge patients to cardiac transplantation (C-Tx) especially in severely ill or hyperimmuned patients; a significantly improved survival on waiting list being reported [1]. However, LVAD recipients are prone to infectious, hemorrhagic and thromboembolic complications caused by systemic alterations of coagulation and fibrinolysis, inflammation and immune responses [2]. Even though the survival of transplanted is reportedly not influenced by the previous use of Mechanical Circulatory Support (MCS) [3], its potential impact on imbalances of the coagulation system early after C-Tx outcome is scarcely known. Herein we describe two unique cases of highly acute intracavitary cardiac graft thrombosis and failure in two heart transplant recipients who had benefited of an LVAD as a bridge to transplantation.

Case Presentation

Case 1

A 48 years-old woman sustained an acute coronary syndrome requiring placement of a LVAD as bridge to transplant (HVAS, Heart Ware Inc., Framingham, MA) for severe heart failure. After 23 months on LVAD supports he received orthotopic C-Tx. Donor was an iso group 61 years-old woman. Recipient's preoperative tests revealed no anomalies in platelets count, but increased APPT (1.7 ratio), reduced prothrombin (38%) and coagulation factors II, VII and X (respectively 29%, 52% and 19%) were noted. Fibrinogen level was 5.65 g/l. INR was 2.3. Although the chosen graft was compatible, she had high levels of anti-HLA antibodies and was therefore highly sensitized. Intracavitary inspection of the graft at the time of transplantation in the operating room revealed no anomalies. After clamp removal, the graft showed good contractility On Transesophageal Echocardiography (TEE) while still under Cardiopulmonary bypass (CPB). After weaning from bypass and infusion of 18 000 UI of protamine, a progressive hemodynamic deterioration developed despite increasing doses of catecholamines. TEE showed at this moment reduced biventricular contractility, and a massive thrombosis of the left atrium, left and right ventricles (Figure 1a,1b, Video 1a-1c).

Hemodynamic collapse ensued, requiring implantation of central veno-arterial Extracorporeal Life Support (ECLS).

After multidisciplinary discussion, the decision was made to perform medical treatment alone (heparin anticoagulation) rather than immediate surgical thrombus removal. Graft ischemia time was 3 hrs and 30 min, total CPB duration was 122 min. During surgery, the patient was transfused with 14 RBC units, 10 units of fresh frozen plasma, 4 units of fibrinogen and two concentrate
of apheresis platelets. CPB circuit and reservoir were free of any thrombus. Early postoperative tests revealed an increased APPT (4.6 ratio), reduced prothrombin (30%) and coagulation factors II and V (34% and 32%). Fibrinogen level was 0.59g/l, platelets dropped to 26 Giga/L. Despite mechanical support, the patient passed away the day after due to graft and multi organ failure. Pathologic study of the native heart showed old infarct sequelae but no sign of inflammatory lesions.

Case 2

A 55 years-old woman suffered from left main coronary artery dissection at coronary angiography, with consequent acute coronary syndrome and heart failure requiring LVAD placement (HVAS, Heart Ware Inc., Framingham, MA). Orthotopic C-Tx was performed two months later. Donor was an iso group 37 year-old male. Recipient’s preoperative tests revealed no anomalies in platelets count, increased APPT (1.8 ratio), reduced prothrombin (23%) and factors II, VII and X (respectively 30%, 15% and 17%). Fibrinogen level was 5.45g/l and INR was 3.38. She had no Anti-HLA hyper immunization. Intracavitary inspection of the graft at the time of transplantation revealed no anomalies. At weaning from bypass and after infusion of 20 000 UI of protamine, severe biventricular graft failure led to the implantation of peripheral veno-arterial ECLS. Perioperative TEE revealed extensive thrombosis of the left cardiac chambers with obstruction of the mitral valve orifice (Figure 2a, 2b, Video 2). The initial decision was in favor of medical treatment alone. Total graft ischemia time was 2 hours and 14 minutes. CPB time was 3 hrs and 5 min and during surgery the patient was transfused with 6 units of red blood cells, 6 units of human prothrombin complex concentrate, 1 unit of fibrinogen and one concentrate of apheresis platelets. CPB circuit and reservoir were free of any thrombus. Early postoperative tests showed reduced prothrombin (39%), elongated APPT (3.9 ratio). Factors V, VII and X were diminished (36%, 29% and 53%), fibrinogen level was 2.03 g/l, and platelets dropped to 68 Giga/L. Given the persistence of thrombus and concomitant severe bleeding under efficient anticoagulation (heparin), reoperation was decided 6 hours later. At surgery, left atrial and ventricular thrombectomy were performed through the mitral and the aortic orifice. Concomitant bioprosthetic mitral valve replacement was required because of extensive impingement of valve structures in the thrombi. Pathologic
study of the intra cardiac thrombus revealed a typical fibrinolytic cruronic aspect. The graft myocardial function ultimately recovered, allowing ECLS weaning at day 8, with a 70% left ventricular ejection fraction.

Discussion

Thrombus formation within the left atrium is relatively common late after orthotopic heart transplantation [4]. The two cases reported herein represent a completely different phenomenon. Our two patients received standard immunosuppressive and open standard non heparin-bonded circuit CP Banti coagulation protocols (350 UI/kg of heparin). Reversal of Heparin with protamine was based on ACT control. They had no inherited or acquired hematologic disorders. No histological element supporting hyper acute rejection was found, especially in our anti-HLA hyper immunized patient. Furthermore, cross-match tests were negative in both cases. A pathophysiologic hypothesis might be represented by the prothrombotic status due to systemic inflammatory response and blood activation associated with CPB and long-term LVAD support. CPB and blood contact with artificial surfaces and air are known triggers of a complex coagulopathy cascade. Shear stress applied to blood cells, loss of pulsatility and acquired von Willbrand disease are LVAD-associated factors that may contribute to such events [5]. Moreover, preoperative Warfarin use for LVAD, prolonged CPB, hemodilution due to perioperative filling and CPB priming solution, hypothermia, massive transfusions, high doses of heparin and protamine, and blood stagnation (notably in the graft) contributed to a multi factorial coagulopathy state. High doses of heparin are associated with antithrombin deficiency and hyper coagulability states, while protamine in excess could lead to an antiplatelet effect (observed combination of bleeding and thrombus) [6,7]. Others patient-related prothrombotic factors such as genetic modulation of inflammatory response can be advocated [8]. One should consider the role of continued intra operative TEE surveillance for weaning from CPB and diagnosis of such complication. Treatment should be discussed case-by-case in a multidisciplinary fashion. Medical treatment with efficient anticoagulation, early surgical thrombectomy or even emergency re-transplantation is the available options.

References

1. Zuckermann A, Bodhjalian A, Dunkler D. Waiting list survival and cardiac transplant outcome of patients supported on left ventricular assist device Vs inotropic support: Comparison of two eras. J Heart and Lung Transplantation. 2004;23(2):S120.