CASE REPORTS

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Heart transplantation in a patient with left ventricular assist device after pump thrombosis –The first case report in Serbia

Transplantacija srca kod bolesnika sa ugrađenim uređajem za potporu rada leve komore nakon tromboze uređaja - prvi prikaz takvog slučaja u Srbiji

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Abstract

Introduction. The device thrombosis is one of the most serious complications of the left ventricle assist device implantation with a high mortality and morbidity rate. **Case report.** A 59-year-old male was implanted by left ventricular assist device Heart Mate II as a bridge to transplantation seventeen months before the onset of a potentially fatal complication – the thrombosis with the complete obstruction of the device. Despite the aggressive pharmacological treatment following the initial suspicion of the pump thrombosis, the patient condition got worse with the final "pump off" alarm that marked the discontinuance of the pump work as a result of the complete obstruction by the thrombus. An appropriate occurrence of an adequate donor resulted in a successful surgical treatment – the heart transplantation. **Conclusion.** The urgent heart transplantation by the first priority rank, or the device replacement, although technically extremely demanding procedures, are successful treatment options for these patients.

Key words:
device removal; heart-assist devices; heart transplantation; thrombosis; treatment outcome.

Apstrakt

Uvod. Tromboza implantiranog uređaja za mehaničku potporu leve komore jedna je od najozbilnijih komplikacija sa visokom stopom morbiditeta i mortaliteta. **Prikaz bolesnika.** Bolesniku starom 59 godina implantiran je uređaj za mehaničku potporu rada leve komore kao most do transplantacije srca, sedamnaest meseci pre nastanka potencijalno fatalne komplikacije - tromboze sa kompletnom opstrukcijom pumpe. Uprkos intenzivnom farmakološkom lečenju posle inicijalne sumnje na trombozu pumpe, stanje bolesnika se pogoršavalo do konačnog oglašavanja finalnog "pump off" alarma, koji je signalizirao zaustavljanje pumpe usled potpune opstrukcije trombom. Pravovremena pojava adekvatnog donora rezultirala je uspešnim hirurškim lečenjem – transplantacijom srca. **Zaključak.** Prioritetna transplantacija srca, po prvom redu hitnosti, ili zamena uređaja, iako tehnički ekstremno zahtevne procedure, predstavljaju uspešne terapijske opcije za tu grupu bolesnika.

Ključne reči:
premeštanje implantiranog aparata; srce, implantabilni mehanički aparati; transplantacija srca; tromboza; lečenje, ishod.

Introduction

The left ventricular assist device (LVAD) implantation has emerged as a relevant option for improving quality of life and survival in patients with the end-stage heart failure. The goals of this procedure include bridge to recovery, bridge to transplant, bridge to candidacy and destination therapy. As the current generation of the continuous flow LVADs activate the coagulation system, anticoagulant therapy is recommended in order to minimize the risk of device thrombosis [1]. The device thrombosis may still occur occasionally, and systemic and local thrombolytic agents are usually applied. Surgical interventions to replace the LVAD device or urgent heart transplantation are in some cases required [2].

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Case report

A 59-year-old male with the sudden recurrence of the shortness of breath was admitted to our hospital. Seventeen months before, the patient had been implanted by LVAD Heart Mate II as a bridge to the herat transplantation due to the end-stage heart failure (Figure 1). After the initial uneventful recovery after LVAD implantation, the patient suffered two episodes of gastrointestinal hemorrhage in the fourth and the seventh month postoperatively, which were conservatively, successfully treated. His outpatient anticoagulation regimen was warfarin with a goal international normalized ratio (INR) of 2–3 as well as acetylsalicylic acid, 100 mg daily. His other medications (from last check-up four weeks ago) included ramipril 5 mg daily, amlodipine besylate 5 mg daily, spironolactone 25 mg daily, furosemide 20 mg twice daily, pantoprazole 40 mg twice daily, amiodarone 200 mg daily, levothyroxine 50 mcg daily, atorvastatin 20 mg daily.

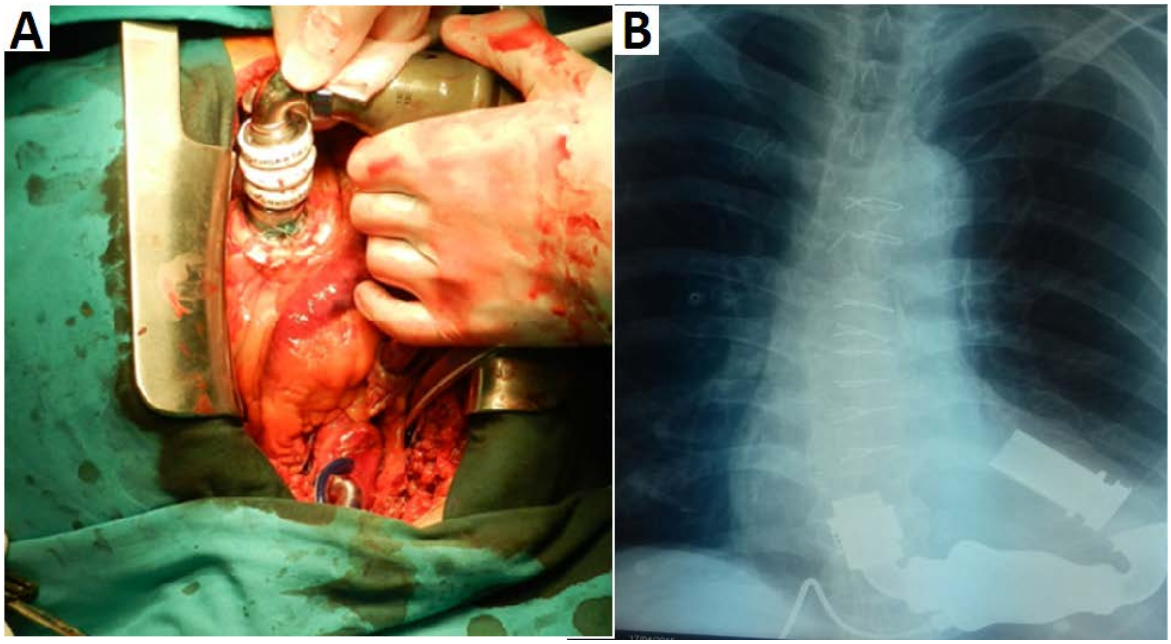

Fig. 1 – A) Left ventricular assist device (LVAD) Heart Mate II implantation as bridge to the heart transplantation; B) Chest X-ray after LVAD Heart Mate II implantation.

At the admission the patient was dyspneic and anxious. The physical examination showed blood pressure of 85/60 mmHg and the heart rate of 80 beats/min. Laboratory tests were consistent with hemolysis. Lactate dehydrogenase (LDH) was elevated at 2,300 IU/L [normal range (nr) 140–280 U/L] (a rise from 400 U/L at the previous check-up four weeks ago), plasma free hemoglobin (pfHGB) 18 mg/dL (does not apear to be above 50 mg/dL) and reticulocytes 2.2% (nr 0.5–2.5%). The INR value was 2.1 (nr 1–2).The LVAD parameters were as following: the pump speed was initially 8,600 rpm but spontaneously dropped down to 8,000 rpm, pump flow (PF) +++ (---), pump power (PP) 15.1–21 W and pulsatily index 1.3. Before the onset of symptoms the LVAD parameters were: pump speed (PS) 8,600 rpm; PF 5.2 L/min; PP 4.6 W; pulsality index (PI) 7.1. The controller device showed a number of "low flow" alarms. The first echocardiogram (ECG) revealed the increase in the dimensions of the left ventricle [both the left ventricular end-diastolic diameter (LVEDD) and left ventricular end systolic diameter (LVESD)] from 6.0 /5.0 cm to 7.3/6.7 cm, respectively. The left ventricle ejection fraction (LVEF) was 15% (Simpson's method). The aortic valve was opening with every beat compared with every third or fourth beat on his last clinic visit. On the color Doppler examination there was no flow through both inflow and outflow cannulas.

The patient was treated by heparin infusion, followed by the infusion of alteplase through the central venous line (started with bolus of 10 mg alteplase during 10 min period, followed by the infusion of 10 mg *per* hour). During the application of the second dose of alteplase on the day 2 after the admission, the patient complained of the acute severe pain on the left side of his chest. At that moment the "pump off" alarm occurred on the monitor display, marking the spontaneous discontinuance of the pump. The patient's LVAD controller was turned off and double drug support with norepinephrine and milrinone was started.

ECG performed after the pump stopped and the inotrope support started showed the mild decrease in the left ventricle dimensions (LVEDD 5.9, LVESD 4.7 cm) with the LVEF in the basal part of 22%. There was a trace of mitral regurgitation. The aortic valve was normaly opening with every beat. There was no flow through both inflow and outflow cannulas as well as through the outflow graft. The chest computed tomography (CT) scan showed the competent outflow graft anastomosis on the ascending aorta as well as the free inflow cannula in the left ventricle. The outflow graft was of substantially narrow lumen with no

signs of kinking. The inflow cannula was in the correct position placed in the direction of the posterior leaflet of the mitral valve. There were no signs of infection around the pump and the drive line (Figure 2).

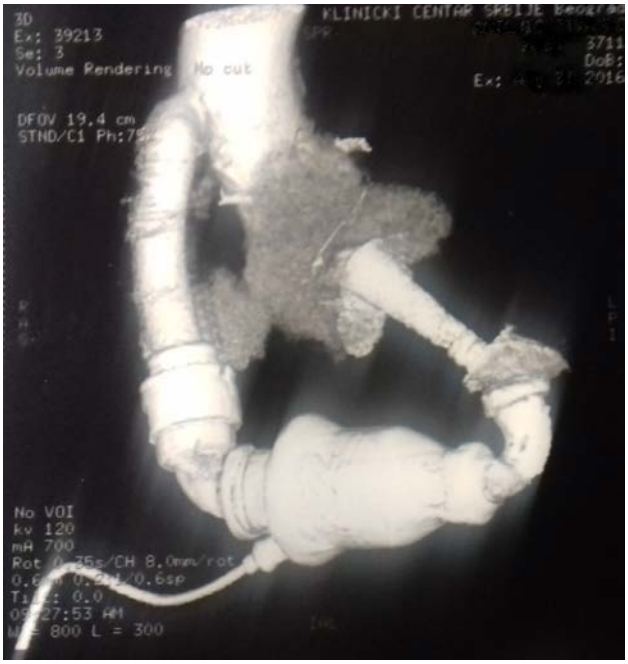

Fig. 2 – Multislice computed tomography (MDCT) of the chest – the outflow graft connection to the ascending aorta and the inflow cannula to the left ventricle are competent.

The haemodynamic inotrope support was continued for the next nine days. The vital sings in that time were: temperature 36.5°C, heart rate of 90 beats/min, mean respiratory rate 24 breaths/ min (nr 12–16 breaths/min) mean arterial pressure of 70 mmHg (nr 70–100 mmHg) and oxygen saturation of 95%. (nr 97–100%). Despite the risks presented, the patient refused suggested pump replacement surgery. He was then en listed on the priority waiting list for the heart transplantation.

At the day 11 upon admission, the favorable occurrence of the adequate donor resulted in the succesfull surgical treatment – the heart transplantation. The operation was carried out as usual under the extracorporeal circulation with the arterial cannulation of the left femoral artery and separate venous cannulation of both caval veins performed after chest reentry. Following resternotomy, it was proceded with the extensive adhesiolysis of the very tough pericardial adhesions. The heart was explanted “en block” with the device**.** After the preparation of the donor heart, the transplantation was performed by biatrial technique (Figure 3). Later inspection of the explanted device confirmed the thrombotic masses in both the inflow and the outflow cannulas and the completely clogged pump rotor.

The operation was completed without complications and the uneventful recovery followed. During the postoperative period the patient was hemodynamically stable, anicteric, eupneic, with good tolerance of physical stress. The regular myocardial biopsy was performed two weeks and one month after the operation. There were no signs of cell or humoral rejection of the transplanted heart.

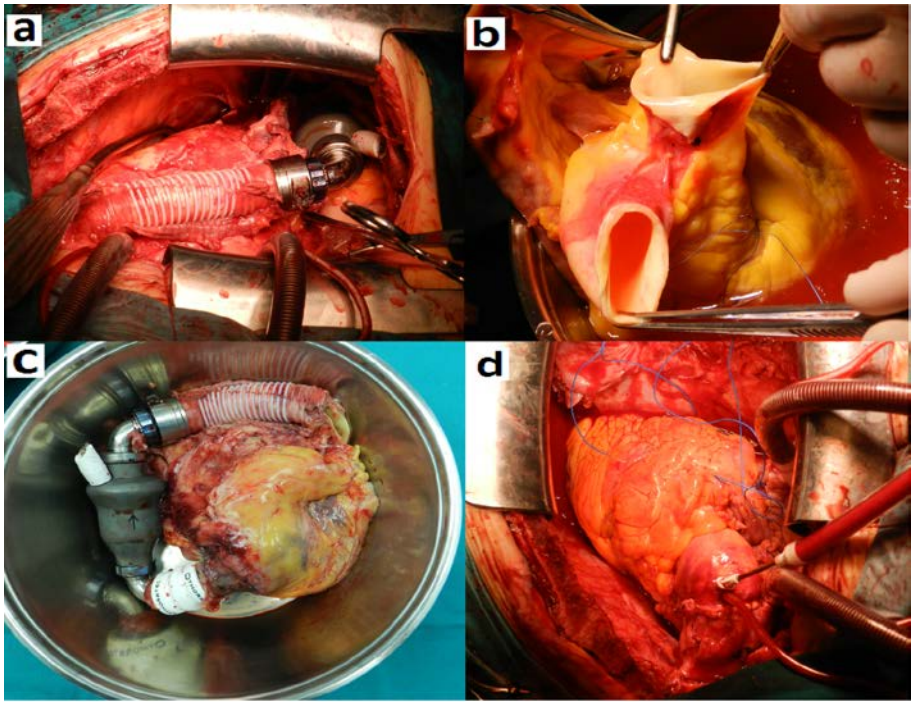

Fig. 3 – Heart transplantation.
a) dissected recipient`s heart with previously implanted left ventricular assist device; b) preparing donor heart; c) explanted heart with the device; d) final result – transplanted heart.

Echocardiography showed normal width of the aorta of 3.1 cm, the normal dimensions of the left ventricle (LVEDD 4.7 cm, LVESD 2.9 cm), excellent systolic function, LVEF 75% by Teicholz, 80% by Simpson. The left atrium size was 3.2 cm. The right ventricle was 2.5 cm with normal tricuspid valve function and morphology.

On the hospitalization day 36 (25 days after the transplantation), the patient was transfered from the isolated care unit to the general care unit and on the day 44, he was discharged home in good general condition. In the regular monthly check-ups, the patient did well. All clinical, histological and laboratory parameters were in the therapeutic range 14 months after the transplantation.

Discussion

Thromboembolic events in patients who recived LVAD are common despite the anticoagulant therapy. The most frequent presentations are: cerebrovascular accident, transient ischemic attack, arterial noncentral nervous system embolism, or pump thrombosis. The device thrombosis of a certain degree was reported in 4% of patients with LVAD implanted as a destination therapy and in 1.5% of patients with LVAD implanted as a bridge to transplantation [3]. There are two main categories of risk factors that predispose to the LVAD thrombosis: device-related and non-device-related [4]. In the screening for and the diagnosis of LVAD thrombosis, laboratory tests are crucial. LVAD thrombosis cause hemolysis and in the early stages it can be identified by elevated LDH, plasma-free hemoglobin and indirect bilirubin levels. Noninvasive diagnostic tests alone are of limited accuracy. Under the certain circumstances, echocardiography can give some indirect evidence like the reduction in diastolic flow velocity through the cannula and/or increased systolic to diastolic flow ratio. Rarely, the direct presentation of LVAD thrombus can be seen. But, the ultrasound “ramp study” is highly sensitive and specific in the detection of axial pump thromosis when used in conjunction with LDH levels [5]. The exact role of routine CT angiography is unclear. Multislice computed tomography (MSCT) is helpful in patients with an unexplained elevated LDH, in order to rule out other causes that may increase this marker and in order to assess patients with a suspected malposition of one of the pump parts. Furthermore, the routine use of MSCT may require a skillful cardiovascular imager with LVAD experience for interpretation [6]. LVAD pump parameters will demonstrate increased pump power or intermittent power spikes. The PF rate will be overestimated with a concomitant decrease in the PI resulting from the reduction of the flow through the LVAD [7]. Ideal strategy for the treatment of LVAD thrombosis is yet to be defined. Medical therapy usually includes the unfractionated heparin infusion, thrombolysis, glycoprotein IIb/IIIa inhibitors, and thrombin inhibitors. These medications are associated with many side effects, mostly bleeding. Most centres weigh the risks associated with the pump replacement vs. thrombolytic therapy in an individualised manner, because it is unclear which patients will have good reponse to medical therapy. If a patient is hemodynamically unstable, the recommended treatment is the pump replacement. On the other hand, if the patient can be hemodynamically stabilized, the other option is the priority heart transplantation [8].

Goldstain et al. [9] formed the algoritam for the diagnosis and therapy of thrombosed LVAD. Patients with LDH elevations or *de novo* power elevations that appear late in the clinical course should be promptly evaluated for frank hemolysis. In the case of the appropriate left ventricle unloading detected by the echocardiography and rump study, the other causes for hemolysis and heart failure symptoms should be searched for. If adequate left ventricle unloading is not confirmed, a MSCT angiogram to evaluate the position of the inflow cannula and outflow graft is indicated. Furthermore, the evidence of unimpeded flow of the contrast from the left ventricle cavity through the outflow graft and into the aorta should be obtained. In the presence of inflow cannula malposition or kinking of the outflow graft, surgical correction should follow. In the absence of pump inflow or outflow abnormalities, the inability to unload the left ventricle on the rump study points to the pump thrombosis. In that case, a patient should be transferred to the intensive care unit for close monitoring and initiation of intravenous heparin and inotropic/diuretic therapy as needed depending on heart failure symptoms. Persistent hemolysis, heart failure symptoms, and/or power spikes may be addressed with more aggressive antithrombotic therapy with direct thrombin inhibitors. If the hemolysis persists despite aggressive antithrombotic therapy, then LVAD replacement should be considered. A patient could be put on the urgent listing for the heart transplantation if the estimated waiting time is no more than a few days and heart failure symptoms can be readily controlled. If the low output state persists and the heart failure progresses, the urgent LVAD replacement is mandatory. If a patient is not potential surgical candidate, in the presence of end-organ dysfunction or hemodynamic compromise, the systemic thrombolytic therapy may be attempted but the prognosis is poor. Some authors advise that patients with pump thrombosis with red alarms-pump stoppage, and in shock unresponsive to battery and controller exchanges, require urgent LVAD replacement [9].

In our clinic, the preffered first line treatment in hemodynamically stable patients with pump thrombosis is thrombolytic therapy with Actylisis®. In the patient reported above, the initial aggressive medical treatment was not successful. On the day 2 following admission, there was a total thrombotic occlusion of the LVAD. After the pump stopped, it was disconnected from the controller and the inotropic support initiated. As the patient was hemodynamically stable and not motivated for the pump replacement, despite the risks presented, he was put on the priority list for the heart transplantation. Nine days later, the adequate donor appeared and the patient underwent the heart transplantation. The operation was successfully completed.

Conclusion

The LVAD thrombosis with total occlusion is one of the most serious complications with a high morbidity and mortality and the treatment must be started immediately. The urgent heart transplantation by the first priority rank or the replacement of the device, although technically extremely demanding procedures, are for the present the successful treatment options for these patients. While our patient had an excellent outcome considering his grave presentation, it again brings up the issue of the optimal management of the LVAD thrombosis.

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