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CASE REPORT

LVAD as a bridge to decision complicated with pump thrombosis and infection

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Abstract
Left ventricular assist devices (LVADs) emerged as an effective therapy for the treatment of symptomatic advanced heart failure in spite of maximum tolerated optimal medical treatment. LVADs were initially conceived as a bridge to transplantation, although with the continuing donor shortage, they also serve as a definitive therapy for some patients. Careful evaluation by a multidisciplinary team and proper patient selection are key factors for good outcomes. These patients are very high-risk surgical candidates, and their survival at 1 year after implantation is estimated to be around 81%. We report a unique case of a patient who underwent LVAD implantation as a bridge to candidacy and suffered several complications related to the device. We also present our experience dealing with these complications in a field of limited evidence. This gentleman developed pump thrombosis second- ary to heparin-induced thrombocytopenia, requiring an LVAD exchange during index admission. A year after being discharged from the first episode, he developed mediastinitis, needing removal of the pump, intravenous antibiotics, and veno-arterial extra corporeal membrane oxygenation (VA-ECMO) for hemodynamic support. A new LVAD insertion was required, and the gentleman could be eventually discharged after a prolonged admission.

Keywords LVAD · Pump thrombosis · Pump infection · ECMO

Introduction

For selected patients with advanced heart failure refractory to medical treatment, the development of LVAD technology emerged as a new opportunity for improving their quality of life and increasing their life expectancy. The number of LVAD implantations is growing fast and, although their initial purpose was to serve as a bridge to transplant, the shortage of heart donors makes destination therapy a good alternative for many patients nowadays. They are usually implanted in high-volume centers with trained and experienced staff. During their perioperative course, complications are not uncommon as the complexity of these patients makes them high risk surgical candidates. The creation of dedicated multi disciplinary teams is a key factor for the success of LVAD programs, as the team has to look after a very specific patient population with unique characteristics associated with the pump and new physiology of the heart.

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Case report

A 49-year-old man with long standing heart failure (ischemic cardiomyopathy with severely impaired left ventricular ejection fraction) was under consideration for heart transplantation. His other past medical history included chronic obstructive pulmonary disease and obstructive sleep apnea; he was in poor functional class despite maximum tolerated doses of optimal medical treatment. A right heart catheterization was performed as part of the investigations, which showed pulmonary hypertension (systolic 69, diastolic 26, and mean 42 mmHg) with pulmonary capillary wedge pressure of 25 mmHg and trans-pulmonary gradient of 17 mmHg. His cardiac output was 3.1 L/min and index 1.4 L/min/m^2. After heart team assessment, the patient was considered unsuitable for transplantation at this stage and therefore listed for durable mechanical support.

A HeartWare® LVAD system (Medtronic) was implanted uneventfully. The patient was admitted to the intensive care

unit and was stable on inotropes (0.05 μg/kg/min of adrenaline and 0.5 μg/kg/min of milrinone), with left ventricular assist devices (LVADs) parameters being 4.5 l/min, 2500 rpm and 4.5 W. The patient's progress in the intensive care unit (ICU) was initially satisfactory, being extubated the same day of the operation. Anticoagulation with heparin was started after 24 h of admission, and aspirin was initiated the next day, as per protocol. To offload the right ventricle, our patient was put on continuous veno-venous hemodiafiltration (CVVH) electively and fluid was taken off successfully. He was in the process of stabilization and his inotropic support was weaning well. However on the 9th post-operative day, it was noted that the LVAD power gradually increased to 5.5 W and calculated flows to 8 l/min. Suspecting pump thrombosis, the heparin infusion rate was increased for activated clotting time (ACT) range of 200–220 s and a new dose of aspirin 300 mg was given. The platelet count decreased over the next days. Samples for lactate dehydrogenase (LDH) and anti-Xa levels were sent (LDH was high—808 units/L and anticoagulation was in therapeutic range—0.59 IU/L). Heparin-induced thrombocytopenia (HIT) was suspected, and therefore, a HIT screen was sent, eventually coming as positive 6.52 U/mL (in our biochemistry laboratory, it is done via enzyme-linked immunosorbent assay). In view of pump thrombosis and gradual instability, it was considered prudent to take the patient to operation theatre for an emergency pump exchange (rising lactates and metabolic acidosis). Since it was an emergency procedure and primarily a device issue, in view of the recent insertion of the driveline and outflow graft, it was considered prudent by the surgeons not to change them. After the LVAD exchange (HeartWare® LVAD system—Medtronic), our patient came back from theatre on milrinone 0.7 μg/kg/min, adrenaline 0.08 μg/kg/min, noradrenaline 0.04 μg/kg/min and vasopressin 0.05 units/min.

The anticoagulation in the subsequent post-operative period was changed to bivalirudin. The patient was extubated on the second day, and then gradually over a week, the vasopressors and inotropes were weaned off.

Although his stay in the ICU was prolonged, our patient did well and was discharged to the ward and eventually home. He was closely followed up in clinics by our ventricular assist device (VAD) specialists.

One year after the LVAD pump exchange, the patient presented to the emergency department with signs of infection. He was admitted to the ward with ongoing sepsis; the source of infection could not be isolated initially. Blood cultures, sputum and urine samples were negative. A computed tomography (CT) scan of the chest and abdomen was performed to determine the site of infection, which showed a mediastinal collection. Empirical antibiotic treatment was started with meropenem, teicoplanin and fluconazole. A further positron emission tomography-computed tomography (PET-CT) showed inflammatory activity and mediastinitis was found to be the source of sepsis. The findings were discussed amongst the LVAD team: it was agreed to remove the infected LVAD with the driveline and keep the sewing ring on the left ventricle, temporarily occlude the apical hole with a felt plug, keep the patient on intravenous antibiotics for at least a week while his inflammatory markers settled, and re-insert another LVAD. In the meantime, hemodynamics of the patient would be supported on central veno-arterial extra corporeal membrane oxygenation (VA-ECMO). Ten days after his admission, the patient underwent a third sternotomy. An 8-mm graft was put on the right femoral artery, the femoral vein was cannulated and bypass was started after achieving an ACT target of 480 s (level of heparin-induced antibodies was 0.04 U/mL, which allowed for heparinization just for the surgery). A pre-sternal abscess was found, requiring drainage and washout, and subsequently the LVAD and outflow graft were explanted. The aorta was closed and the driveline removed in toto. There was a collection around the LVAD pump, proximal outflow graft and driveline connecting to the inferior part of the sternum. The sternum was healthy except in the inferior part, where the mediastinal collection was communicating with the pre-sternal abscess at the level of the xiphisternum. Intraoperative transesophageal echocardiography showed very poor left and right ventricular function, with severe mitral and tricuspid regurgitation, but no vegetations or signs of endocarditis. After the procedure, there was significant bleeding from the femoral arterial graft and so arterial cannulation was changed to the ascending aorta using an EOPA® (Elongated One-Piece Aortic Cannula), which was taken out from the suprasternal notch before closing the sternum. The patient was transfered to the ICU on central VA-ECMO and anticoagulated with bivalirudin. His condition stabilized after a re-exploration for bleeding in the mediastinum and left pleura (there was bleeding point from a wire hole and raw area on left chest wall due to adhesions). The patient's condition finally stabilized and was extubated the next day. Surgical pus specimens showed growth of *Fusobacterium nucleatum*, and the patient continued his course of antibiotics for another week.

Finally, a new LVAD system was implanted in an uneventful surgery with good recovery, allowing him to go back home after 2 months of hospital admission. There were no complications regarding the sternal closure or sternal infections, but the hospital stay was quite prolonged due to the time spent during the initial investigations until the diagnosis was made, the multiple times he went to operation theatre (eventually the implantation of the new LVAD), the completion of the prolonged course of intravenous antibiotics, control of his anticoagulation and finally physiotherapy and rehabilitation process.

Recently, our patient had an episode of intracraneal bleed with residual left-sided weakness and dysphagia. However, despite this, he is independent in his daily activities and has

not been readmitted for heart failure. He is currently being followed up by the Heart Failure physicians, stable on NYHA class II, awaiting right heart catheterization and with plans of ongoing evaluation for transplantation in the future.

Discussion

This case highlights the significant amount of challenges the clinicians may face with the management of LVAD patients, from the implantation and peri-surgical period to the long-term follow-up complications. Despite being a well-established therapy that has proven to increase the quality and quantity of life of patients with advanced heart failure, this should be only instituted in expert centres with high-volume cases and well-trained staff. In our centre, we do over 30–35 LVAD cases per year, and since the start of our program, we have implanted more than 300 LVADs.

Unfractioned heparin is the anticoagulant of choice in the setting of immediate post-op LVAD patients due to the extensive clinical experience of the ICU teams with it, the titratable control in the intensity of anticoagulation and the easiness of its reversal in the event of a life-threatening haemorrhage. However, typically during first 5 to 10 days, between 1 and 5% of exposed patients develop HIT. It is an auto-immune phenomenon that makes the patients more prone to bleeding and thrombotic events [1]. This complication is specially dramatic after LVAD surgery, not only because of its direct effects (in our case a device thrombosis) but also because of the indirect consequences (changing heparin to bivalirudin, which has higher bleeding risk and is more difficult to titrate with the routine tests for anticoagulation). Our centre has more experience with bivalirudin than with argatroban.

LVAD pump thrombosis is a devastating complication that usually occurs months or years after the implant. The best approach to deal with it is still a matter of ongoing debate: while medical management can be established successfully with the addition of platelet glycoprotein IIb/IIIa inhibitors or thrombolysis on top of aspirin and heparin, other experts recommend a surgical approach [2]. In our case, the very early timing of the thrombosis, which is unusual, is most likely related to HIT. Due to the extremely high bleeding risk of adding increased anticoagulation or thrombolytics during the first peri-operative days, our team felt more comfortable dealing with this complication with a pump exchange even accepting that, according to the registries, the long-term survival could likely be less after subsequent implants. Of note, the surgical option for the HeartWare system might be more challenging, as the intrapericardial location of the pump forces the surgeons to perform another sternotomy, while in the case of other devices, a less invasive subcostal approach has been described [3].

LVAD-associated infections are relatively common, affecting nearly 30% of the patients during the first year, and being the most vulnerable period, the first month following surgery [4]. The severity of these infections is variable (from percutaneous driveline infection to pump/outflow graft), and the most common pathogens are *S. aureus*, *P. aeruginosa*, and *Enterobacteriaceae*. The diagnosis of LVAD infection is specially challenging as the patients have usually poor echocardiographic window, computed tomography may be limited by artifacts and magnetic resonance is not a possibility [5]. Positron emission tomography with F18-fluorodeoxiglucose and computed tomography is a well-established technique for the diagnosis of cardiovascular implantable device infection [6]. This technique has been used with good results for identifying the location, extent and severity of LVAD-associated infection, and may guide the need for surgical intervention. Our patient presented with a collection of pus in the mediastinum and device infection, which warrants invariably surgical treatment. As there is lack of available data in the literature for this situation, the best treatment of this life-threatening condition remains uncertain. In this peculiar case, there was a theoretical significant risk of early reinfection of the pump, if it was exchanged during the same procedure. Therefore, our team decided to perform a surgical washout and drainage of the abscess, and to add an extended course of antibiotics while supporting the circulation with central VA-ECMO. *Fusobacterium nucleatum* is an opportunistic pathogen present in the oral cavity frequently associated with gingival and periodontal infections. It can cause severe infections and abscesses that can be local (including Lemierre syndrome) and systemic by hematogenous dissemination [7].

ECMO as a bridge to LVAD is a consolidated approach for patients with cardiogenic shock or decompensated end-stage cardiomyopathy who are potential transplant candidates [8], which also worked well in our patient despite his peculiar characteristics. To our knowledge, there are no previous reports in the literature where a patient with an explanted LVAD for infection is bridged to central VA-ECMO as a bridge to durable LVAD for transplant candidacy.

In conclusion, we describe the case of a patient with end-stage cardiomyopathy who, not being a transplant candidate due to high transpulmonary gradient, was bridged to candidacy with a long-term LVAD, and required 2 pump exchanges and a support with central VA-ECMO in between due to significant complications related with the devices. Adequate patient selection and the concentration of cases in expert centres with dedicated facilities facilitate the successful institution of these therapies [9]. Multidisciplinary teams, specifically dedicated to mechanical circulatory support, are required to lead the management, promptly identify complications and provide decision-making in order to improve the outcomes of this population [10].

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Informed consent Our patient understood and agreed to participate in this research and signed an informed consent for its elaboration.

Human and animal rights No infringements of human/animal rights occurred in this investigation.

Ethical committee approval There was no change in the treatment protocol and ethical clearance by a committee was not required.

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