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Peer-Reviewed Case Report

Left Ventricular Assist Device Thrombosis Treated with Intravenous Tissue Plasminogen Activator in a Patient with COVID-19 Infection

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Abstract

Left ventricular assist device (LVAD) implantation is an established treatment for patients with end-stage, systolic heart failure as a bridge to heart transplantation or destination therapy. LVAD pump thrombosis is a life-threatening complication than can be triggered by prothrombotic conditions such as infection. Management of pump thrombosis presents as both a diagnostic and therapeutic challenge that is associated with a high morbidity and mortality. We report a case of pump thrombosis in a patient with a HeartMate II (Abbott Laboratories, Chicago, IL) and coronavirus (COVID-19) infection that was treated successfully with an intravenous thrombolytic, tissue plasminogen activator.

Background

Patients with heart failure who become infected with coronavirus (COVID-19) are at an increased risk for morbidity and mortality.[1] In this case, we describe a patient with chronic, systolic heart failure with a durable left ventricular assist device (LVAD) who presented with fatigue, malaise, and dark-colored urine found to be positive for COVID-19. He was subsequently diagnosed with LVAD thrombosis and treated successfully with intravenous thrombolytics.

Case Report

This case involves a 33-year-old African American male with morbid obesity and chronic, systolic heart failure secondary to a dilated cardiomyopathy status. The patient was supported by a Heartmate II device (Abbott Laboratories, Chicago, IL) implanted in January 2019. The LVAD implantation was complicated by a methicillin-resistant *Staphylococcus aureus*, LVAD pocket infection that was treated with chronic oral suppressive antibiotics. He also experienced a subdural hematoma after LVAD implantation; thus, warfarin was discontinued. He successfully underwent gastric bypass post-LVAD without complications.

The patient presented to the emergency department 18 months post-LVAD implantation with symptoms of fatigue, malaise, and dark red-colored urine for one week. On presentation, he had a mean arterial blood pressure of 67 mmHg as measured by Doppler. His heart rate was 78 beats per minute, respiratory rate was 18 breaths per minute, temperature was 37.8°C, and oxygen saturation was 96% on room air. Cardiopulmonary examination revealed normal LVAD sounds, and he was euvolemic. The patient was admitted to the medical floor for further management.

During the patient's hospital course, LVAD interrogation showed increasing LVAD power readings consistent with LVAD thrombosis (Table 1).Results of the laboratory analysis can be found in Table 1. A PCR test for COVID-19 was positive.

Table 1. Patient Parameters over Time.

		Hospital Day 0	Hospital Day 7	Hospital Day 14	Hospital Day 21 Post-TPA	2 weeks Post-Discharge
Heartmate II LVAD Parameters	**Power (Watts)**	8.4	10.2	11.8	7.4	6.5
	Pump Speed (RPM)	10000	10800	10800	10800	10000
	Flow (Liter/minute)	6.5	7.8	8.1	6.8	6.6
	Pulsatility index	4.1	3.6	3.3	3.1	3.8
Laboratory Values	**Hemoglobin (mg/dl)**	12.9	8.6	7.4	8.9	10.3
	Platelet (x 10^3 /mcL)	175	105	91	160	183
	White cell count (x10^3/mcL)	4.91	8.41	9.65	4.98	8.0
	BUN (mg/dL)	7	68	80	36	5
	Creatinine (mg/dL)	1.0	5.4	6.48	5.85	1.65
	LDH (U/L)	243	3214	7868	954	468

LVAD-left ventricular assist device; RPM-rotations per minute, BUN-blood urea nitrogen; LDH-lactic dehydrogenase

Since the patient's clinical picture was concerning for LVAD thrombosis, transthoracic echocardiogram imaging with a ramp study was performed and showed a dilated left ventricle and persistent opening of the aortic valve, despite increasing the LVAD speed (Figures 1 and 2).

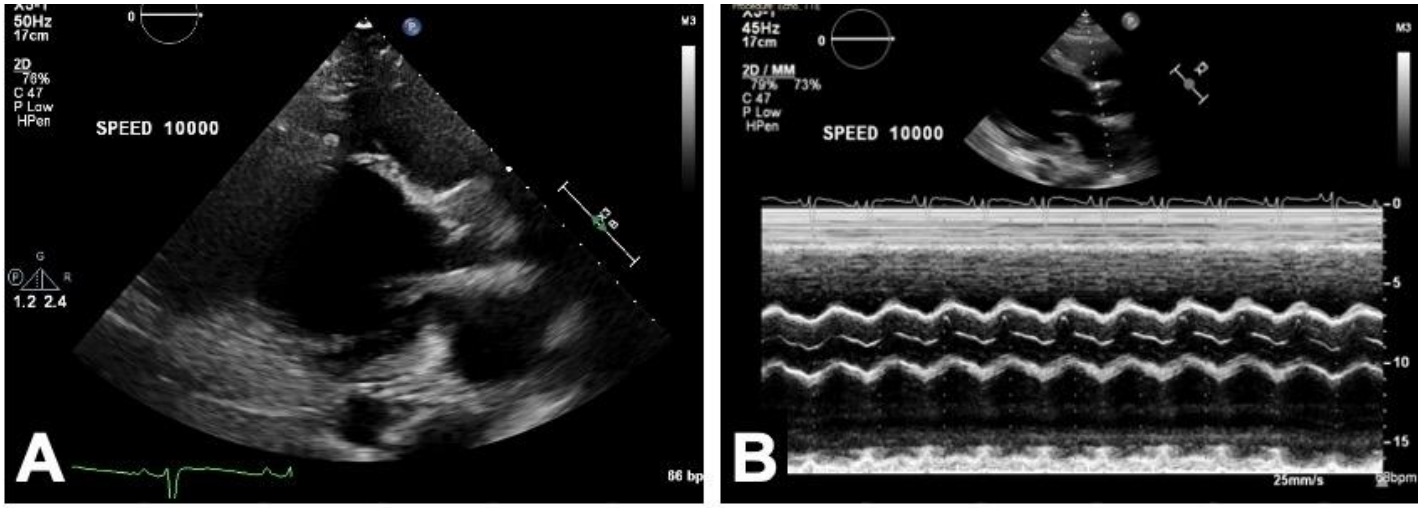

Figure 1. *Transthoracic echocardiogram imaging of Heartmate II LVAD at pump speed 10000 RPM. Parasternal long axis image (panel A) showing severely dilated left ventricular cavity, end diastolic diameter 6.9 cm. M-mode of aortic valve (panel B) shows incomplete aortic valve opening with each heart beat.*

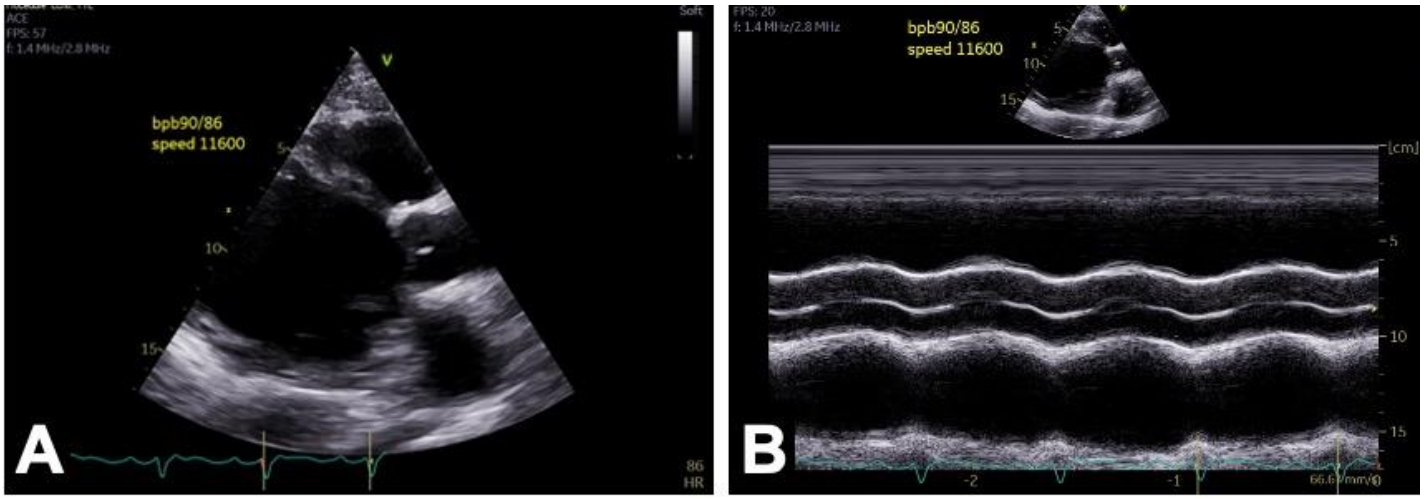

Figure 2. *Transthoracic echocardiogram at Heartmate II LVAD pump speed 11600 RPM. Parasternal long axis image (panel A) shows severely dilated left ventricular cavity with no significant change in end diastolic diameter, 6.8 cm. M-mode of aortic valve (panel B) continues to show incomplete aortic valve opening with each heart beat.*

Computed tomography (CT) without intravenous contrast showed a well-seated LVAD inflow cannula without acute findings. The patient was started on a continuous, intravenous infusion of unfractionated heparin for treatment of LVAD thrombosis. He remained febrile and required multiple blood transfusions for severe anemia. However, his respiratory status remained stable with unremarkable chest radiography.

Due to persistent renal failure and severely elevated lactate dehydrogenase (LDH), the decision was made to administer intravenous tissue plasminogen activator (TPA), utilizing a previously published protocol.[2] The patient was received a 5 mg intravenous bolus of TPA followed by a 3 mg/h infusion of normal saline for 10 hours. The patient received a second intravenous TPA bolus, followed by a continuous infusion for the following 48 hours due to lack of improvement after the first cycle of TPA. The patient was not considered for LVAD pump exchange given his history of chronic LVAD pocket infection. The patient underwent serial head, chest, abdomen, and pelvis CT scans every 8 hours, which were negative for bleeding. Five days following completion of the second TPA infusion, his pump power spikes resolved, and LDH, hemoglobin, and serum creatinine levels improved (Table 1).

He was discharged home after a 4-week hospitalization. At two weeks post-discharge, the patient continued to do well, and serum creatinine levels improved to 1.65 mg/dl with normal LVAD parameters (Table 1).

Discussion

LVAD therapy is a well-established treatment option for patients with advanced, systolic heart failure, particularly given the limited number of available heart transplant donors.[3,4] While individuals significantly benefit from LVAD implantation with dramatic improvement in symptoms and survival, durable LVAD therapy is associated with a number of complications including infection, pump thrombosis, stroke, and gastrointestinal bleeding.[4] Pump thrombosis is a well-known complication of LVAD support that is associated with a high mortality and morbidity.[5] The reported incidence of pump thrombosis of the Heartmate II device ranges from 0.014 to 0.03 events per patient-year.[6] Risk factors for LVAD thrombosis include inadequate anticoagulation, low LVAD speed, infection, poorly controlled blood pressure, and LVAD cannula malposition or kinking.[7,8] While our patient was not on warfarin given his history of subdural hematoma, he remained free of symptoms without evidence of thrombosis for six months prior to becoming infected with COVID-19.

Current literature indicates that COVID-19 plays a pivotal role in the pathogenesis of coagulopathy via various mechanisms including tissue factor release, endothelial damage caused by inflammatory response and hypoxia, and platelet activation.[9] Recent data shows that the proinflammatory cytokine release seen in patients infected with COVID-19 is associated with an upregulation of procoagulants such as factor VIII, P-selectin, and von Willebrand factor as well as downregulation of anticoagulants such as endothelial protein C receptor and thrombomodulin.[10]

LVAD pump thrombosis can manifest with LVAD power elevations, dark or tea-colored urine, elevated serum LDH, low plasma haptoglobin, elevated indirect bilirubin, and elevated plasma free hemoglobin.[6,11] Echocardiogram imaging with ramp study can assist with the diagnosis. Management of LVAD pump thrombosis remains a major challenge, and a multidisciplinary approach should be implemented in patients with suspected pump thrombosis to determine the best treatment approach ranging from escalation of anticoagulation to LVAD exchange.[6] Aggressive management of pump thrombosis is critical given the high risk of complications and death.[12] Medical treatment consists of high dose unfractionated heparin infusion which was implemented in our case.[5,6]

In a prior systematic review of this topic, escalation of antithrombotic therapy by adding direct thrombin inhibitor or glycoprotein IIb/IIIa inhibitor resulted in complete resolution in 49% (25/51) of thrombosis and no or partial resolution in 51% (26/51) of cases.[5] Use of a glycoprotein IIb/IIIa inhibitor or direct thrombin inhibitor therapy alone resulted in complete thrombus resolution in 49% (19/39) of patients.[5] A recent case study reported a similar presentation of LVAD pump thrombosis in the setting of COVID-19 infection that was successfully treated with aspirin, unfractionated heparin, and cangrelor.[13] Failure to improve with full anticoagulation should trigger consideration for thrombolysis or pump exchange.[14,15] Although pump replacement remains the definitive treatment for LVAD thrombosis, it is limited by the increased risk associated with redo-cardiac surgery.

While there is limited data on the use of TPA for the treatment of LVAD thrombosis[16], more recent published medical literature suggests a potential role for TPA as salvage therapy in refractory COVID-19 acute respiratory distress syndrome to treat the hypercoagulable state triggered by the infection.[17] Published reports show that TPA can be administered intravenously or intra-ventricularly by a catheter-based approach, or in combination with unfractionated heparin, glycoprotein IIb/IIIa inhibitor, or direct thrombin inhibitor.[2,16,18,19] Treatment with TPA carries a high risk of life-threatening bleeding; reports of upwards of 20% incidence has been documented.[5] In a recent case series on three patients with severe COVID-19 acute respiratory distress syndrome and coagulopathy, treatment with TPA was associated with improvement in respiratory status.[20] Further investigation into the potential benefit of TPA administration to treat COVID-19 respiratory failure is warranted given the high mortality and morbidity of this disease and current limited treatment options.

Conclusion

LVAD pump thrombosis is associated with significant morbidity and can be fatal when provoked by prothrombotic states such as those seen with COVID-19 infections. Cardiologists and cardiac surgeons caring for LVAD patients must have a high index of suspicion for this complication in order to quickly diagnose and determine the best treatment approach to optimize patient outcomes. Optimal management of VAD pump thrombosis remains challenging, and a multidisciplinary team approach is recommended to guide treatment. As our case demonstrates, thrombolytics should be considered as a potential treatment option for patients presenting with LVAD thrombosis.

Our patient was successfully treated with a combination of intravenous TPA and unfractionated heparin with resolution of LVAD thrombosis and renal failure. Importantly, the patient did not experience any bleeding complications. Our case highlights that COVID-19 is a risk factor for precipitating LVAD thrombosis that can successfully be treated with thrombolytics.

References

1. Chatrath N, Kaza N, Pabari P, et al. The effect of concomitant COVID-19 infection on outcomes in patients hospitalized with heart failure. ESC Heart Failure. 2020;7:4443– 4447.

2. Nair N, Schmitt AA, Rau EM, Anders S, Sandler D, Icenogle TB. Thrombolytics in VAD management - A single-center experience. IJC Hear Vasc. 2016;11:49-54.

3. Slaughter MS, Rogers JG, Milano CA, et al. Advanced heart failure treated with continuous-flow left ventricular assist device. N Engl J Med. 2009;361(23):2241-2251.

4. Hanff TC, Birati EY. Left ventricular assist device as destination therapy: a state of the science and art of long-term mechanical circulatory support. Curr Heart Fail Rep. 2019;16(5):168-179.

5. Dang G, Epperla N, Muppidi V, et al. Medical management of pump-related thrombosis in patients with continuous-flow left ventricular assist devices: A systematic review and meta-analysis. ASAIO J. 2017;63(4):373-385.

6. Goldstein DJ, John R, Salerno C, et al. Algorithm for the diagnosis and management of suspected pump thrombus. J Hear Lung Transplant. 2013;32(7):667-670.

7. Park SJ, Milano CA, Tatooles AJ, et al. Outcomes in advanced heart failure patients with left ventricular assist devices for destination therapy. Circ Hear Fail. 2012;5(2):241-248.

8. Webber BT, Panos AL, Rodriguez-Blanco YF. Intravenous thrombolytic therapy for patients with ventricular assist device thrombosis: An attempt to avoid reoperation. Ann Card Anaesth. 2016;19(1):192-196.

9. Whyte CS, Morrow GB, Mitchell JL, Chowdary P, Mutch NJ. Fibrinolytic abnormalities in acute respiratory distress syndrome (ARDS) and versatility of thrombolytic drugs to treat COVID-19. J Thromb Haemost. 2020;18(7):1548-1555.

10. Roberts KA, Colley L, Agbaedeng TA, Ellison-Hughes GM, Ross MD. Vascular manifestations of COVID-19 - thromboembolism and microvascular dysfunction. Front Cardiovasc Med. 2020;7:598400.

11. Akin S, Soliman OI, Constantinescu AA, et al. Haemolysis as a first sign of thromboembolic event and acute pump thrombosis in patients with the continuous-flow left ventricular assist device heartmate II. Netherlands Hear J. 2016;24(2):134-142.

12. Al-Quthami AH, Jumean M, Kociol R, et al. Eptifibatide for the treatment of heartmate ii left ventricular assist device thrombosis. Circ Hear Fail. 2012;5(4):68-70.

13. Frick MD W, Mallory R, Guglin M, et al. Unusual case of pump thrombosis in LVAD patient with COVID-19 — Diagnostic Challenges. VAD J. 2020;6(2):2.

14. Stulak JM, Cowger J, Haft JW, Romano MA, Aaronson KD, Pagani FD. Device exchange after primary left ventricular assist device implantation: Indications and outcomes. Ann Thorac Surg. 2013;95(4):1262-1268.

15. Moazami N, Milano CA, John R, et al. Pump replacement for left ventricular assist device failure can be done safely and is associated with low mortality. Ann Thorac Surg. 2013;95(2):500-505.

16. Jabbar AA, Yau R, Frazier OH, Delgado R. Direct thrombolytic therapy for thrombosis of a centrifugal flow left ventricular assist device. ASAIO J. 2013;59(5):530-532.

17. Choudhury R, Barrett CD, Moore HB, et al. Salvage use of tissue plasminogen activator (tPA) in the setting of acute respiratory distress syndrome (ARDS) due to COVID-19 in the USA: a Markov decision analysis. World J Emerg Surg. 2020;15(1):29.

18. Bellumkonda L, Subrahmanyan L, Jacoby D, Bonde P. Left ventricular assist device pump thrombosis: Is there a role for glycoprotein iib/iiia inhibitors? ASAIO J. 2014;60(1):134-136.

19. Hayes H, Dembo L, Larbalestier R, O'Driscoll G. Successful treatment of ventricular assist device associated ventricular thrombus with systemic tenecteplase. Hear Lung Circ. 2008;17(3):253-255.

20. Wang J, Hajizadeh N, Moore EE, et al. Tissue plasminogen activator (tPA) treatment for COVID-19 associated acute respiratory distress syndrome (ARDS): A case series. J Thromb Haemost. 2020;18(7):1752-1755.