

Treatment of Left Ventricular Assist Device Thrombosis With Extended Catheter-Directed Intraventricular Thrombolytic Therapy

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Continuous flow left ventricular assist devices (LVAD) are used in patients with advanced heart failure, either as bridge to transplant or as destination therapy.¹ Because current generation continuous flow LVADs activate the coagulation system, anticoagulant therapy with warfarin is recommended to minimize the risk of device thrombosis.² Occasionally, however, device thrombosis may still occur, which may necessitate surgical LVAD exchange. Because of the relatively high morbidity and mortality associated with a surgical LVAD exchange, alternative methods to abort LVAD thromboses short of surgical intervention would be attractive. Recently, resolution of device thrombosis with catheter-directed intraventricular administration of a single bolus dose of fibrinolytic therapy has been reported.^{3,4} Here, we report the successful resolution of 2 consecutive cases of LVAD thrombosis using continuous catheter-directed intraventricular administration of fibrinolytics for an extended period in patients who did not respond to the initial bolus dose of fibrinolytics without resorting to surgical LVAD exchange.

Case 1

A 45-year-old man with HeartMate II (Thoratec Corporation, Pleasanton, CA) LVAD as destination therapy for dilated cardiomyopathy presented with dark red urine 11 months after device implantation. Further evaluation revealed a subtherapeutic international normalized ratio (INR) (1.4), markedly elevated serum lactate dehydrogenase (LDH; 4010 U/L), low serum haptoglobin (<20 mg/dL), mild hyperbilirubinemia (1.2 mg/dL), and elevated plasma-free hemoglobin (15.4 mg/dL), consistent with hemolysis. Review of logged waveform files revealed no power or flow surges. A transthoracic echocardiogram revealed rightward deviation of the interventricular septum, regular opening of the aortic valve, and mild mitral regurgitation. With gradual increase of LVAD speed to a maximum of 11 200 rpm, the interventricular septum remained rightward and aortic valve opened with every cardiac cycle, suggesting the inability of the device to unload the left ventricle. Both the inflow cannula and the outflow graft seemed appropriately positioned. These findings coupled with his ongoing hemolysis were suggestive of

likely device thrombosis. The patient was initially treated with intravenous heparin and eptifibatid for 5 days with no significant improvement and worsening serum LDH, bilirubin, and creatinine values. Due to lack of clinical response, a trial of intraventricular fibrinolytics was initiated in the cardiac catheterization laboratory. Twenty-five milligrams of alteplase was administered as a bolus dose via a pigtail catheter placed in the left ventricle using the transfemoral approach over 10 minutes. The sheath and the catheter were secured in place, and alteplase was infused continuously at 1 mg/h. An intravenous heparin infusion was used concomitantly with an activated partial thromboplastin time maintained between 50 and 60 seconds. Intraventricular alteplase infusion was continued until serum LDH and bilirubin (surrogate markers for LVAD thrombosis), and creatinine (used as a marker of end-organ perfusion) approached the patient's previous baseline values suggestive of device thrombosis resolution. Position of the pigtail catheter was confirmed daily by chest x-ray (Figure 1). During the course of 30 hours of alteplase infusion, there was normalization of his serum LDH, bilirubin levels, and creatinine (Figure 2). A repeat transthoracic echocardiogram confirmed an unloaded left ventricle with the interventricular

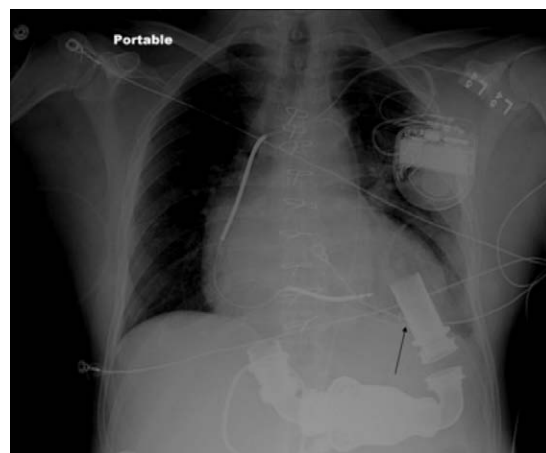


Figure 1. Chest x-ray showing the pigtail catheter and the left ventricular assist device inflow cannula in the left ventricular cavity.

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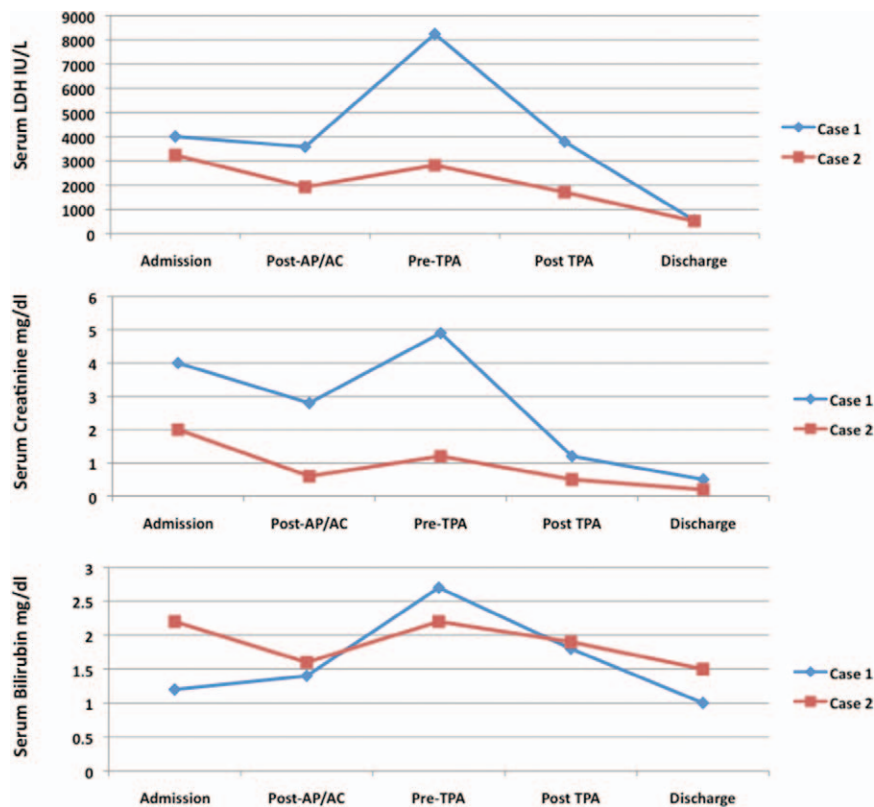


Figure 2. Comparison of serum lactate dehydrogenase (LDH), bilirubin, and creatinine pre- and postfibrinolytic therapy. AC indicates anticoagulation therapy (intravenous heparin); AP, antiplatelet therapy (intravenous eptifibatide), and TPA, tissue-type plasminogen activator (alteplase). Blue represents case 1 and red represents case 2.

septum in the midline, only trace mitral regurgitation, and intermittent opening of the aortic valve. The patient developed a groin hematoma around the arterial sheath site, which was controlled with manual compression.

Case 2

A 46-year-old man with HeartMate II LVAD for dilated cardiomyopathy presented with dark red urine 8 months after his LVAD implantation. On cardiac auscultation, he had abnormal LVAD tones. Further evaluation revealed a significantly elevated serum LDH (3237 U/L), low serum haptoglobin (<20 mg/dL), and elevated unconjugated bilirubin (2.2 mg/dL) consistent with hemolysis. His INR was subtherapeutic at 1.6. LVAD logged waveform files revealed recent intermittent power surges. A transthoracic echocardiogram revealed inadequate unloading of the left ventricle with shifting of the interventricular septum to the right and moderate mitral regurgitation, despite a gradual increase in his LVAD speed to 10 600 rpm. Cardiac computed tomography excluded inflow cannula and outflow graft obstruction. On the basis of these findings, LVAD thrombosis was suspected, and he was initially treated with intravenous heparin and eptifibatide. Due to lack of clinical response, he was treated with catheter-directed alteplase infusion as described in case 1 for 96 hours until normalization of serum LDH, bilirubin, and creatinine values were achieved (Figure 2). A repeat transthoracic echocardiogram suggested an unloaded left ventricle with the interventricular septum in the midline and a reduction in the severity of the mitral regurgitation to mild. The patient tolerated the alteplase infusion well without any complications. The pigtail catheter position was stable in

both of the patients throughout the duration of therapy and there was no evidence of infection.

Discussion

This case series illustrates the feasibility of aborting an evolving LVAD thrombosis with prolonged catheter-directed administration of intraventricular fibrinolytics. An LVAD thrombosis may result from the development of an in situ thrombosis on the impeller itself or by ingestion of an existing thrombus from the left atrium or the left ventricle. Device thrombosis was reported in 4% of patients with destination LVADs and in 1.5% of patients with LVADs as a bridge to cardiac transplant in the HeartMate II clinical trials.^{1,5} Although both of our patients in this case series presented with a subtherapeutic INR, LVAD thromboses may occur at any INR, including supratherapeutic INR. Resolution of device thrombosis with catheter-directed administration of a bolus dose of fibrinolytic therapy has been reported.^{3,4} However, the patients in the current case series did not respond to the initial bolus fibrinolytic injection, perhaps attributable to the slower, chronically developing in situ thrombosis. The eventual complete resolution of the LVAD thrombosis in response to prolonged, catheter-directed fibrinolytic therapy in both patients (30 and 96 hours, respectively) suggests that a longer duration of fibrinolytic infusion could be considered in patients with lack of an immediate response to bolus fibrinolytics before resorting to surgical device exchange.

Prolonged catheter-directed administration of fibrinolytics could be associated with serious bleeding complications, especially given the inherent bleeding risks associated with

continuous flow LVADs. Another potential concern would be dislodgement of the pigtail catheter into the LVAD inflow cannula. Meticulous efforts must be taken to ensure that the pigtail catheter is well secured and in a proper position. Thus, despite our successful outcomes, further studies using prolonged catheter-directed fibrinolytic therapy are warranted to determine the feasibility, safety, and efficacy more completely of this novel technique in cases of refractory VAD thrombosis.

Disclosures

V. Jeevanandam is a scientific advisor for Thoratec and HeartWare. The other authors have no conflicts to report.

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KEY WORDS: catheter ■ heart failure ■ thrombolysis ■ thrombosis, ventricular assist device

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