



COVID-19 Associated Left Ventricular Assist Device Pump Thrombosis with Hemolysis and Pigment Nephropathy: Case Report

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Abstract

COVID-19 infection has manifested itself in several ways, most notably respiratory failure. However, this virus has also been shown to induce a hypercoagulable state resulting in myocardial infarction, pulmonary embolism, and stroke. We present a unique case in which a Left Ventricular Assist Device (LVAD) patient became infected with COVID-19 resulting in thrombosis of the LVAD and kidney dysfunction from the hemolysis and pigment nephropathy. Aggressive treatment with lytic and anticoagulant therapy resolved the pump thrombosis and the associated acute kidney injury associated with it.

Keywords: Left ventricular assist device; COVID-19; Pump thrombosis; Hemolysis; Pigment nephropathy

Introduction

The COVID-19 pandemic has disrupted healthcare in profound ways with respiratory impairment representing the most common clinical condition. However, extrapulmonary manifestations have become increasingly reported including myocardial infarction and stroke, consequences of the hypercoagulable state induced by this novel virus. We report a highly unusual case of Left Ventricular Assist Device (LVAD) pump thrombosis with concomitant renal failure due to hemolysis and pigment nephropathy in the setting of a COVID-19 infection. We believe this to be the first reported case of this kind.

Case Presentation

A 32-year-old man with end-stage heart failure was admitted for LVAD placement. His past medical history was significant for morbid obesity (BMI 75 kg/m²), inotrope-dependent (Milrinone 0.375 mcg/kg/min) non-ischemic cardiomyopathy (LVEF <20%), asthma, obstructive sleep apnea, and Deep Vein Thrombosis (DVT).

A Heartmate II™ LVAD (Abbott Laboratories, Abbott Park, IL, USA) was implanted on January 23rd, 2019 without complication. He was discharged on POD #9 with aspirin 81 mg daily and coumadin 4 mg daily with an INR goal range of 2.0 to 3.0. The LVAD speed was set at 10,200 rpm at discharge and increased to 11,600 rpm as an outpatient to optimize flow.

A year later (January 21st, 2020), the patient presented with headache, blurry vision, right lower extremity tingling, and a grand mal seizure. He was found to have a left frontal subarachnoid hemorrhage. His INR at home was reportedly 5 and 5.3; it was 2.9 in the Emergency Department (ED). He was given a prothrombin complex concentrate (KCentra™, CSL Behring, King of Prussia, PA) and Vitamin K to normalize the INR and levetiracetam (Keppra™, UCB Pharmaceuticals, Inc., Smyrna, GA) for seizure suppression. His neurologic symptoms improved and he was transferred to a rehabilitation center where he stayed for nine days. He remained off anticoagulation since the stroke.

Approximately six month later, on July 15th, 2020, the patient was admitted with abdominal pain, lethargy, and hematuric appearing urine. There was neither fever nor respiratory systems. Chest radiography showed no active disease. Laboratory values, however, showed several abnormalities: reduction in Hemoglobin (Hgb), Platelets (PLT), and haptoglobin; elevation in Lactate

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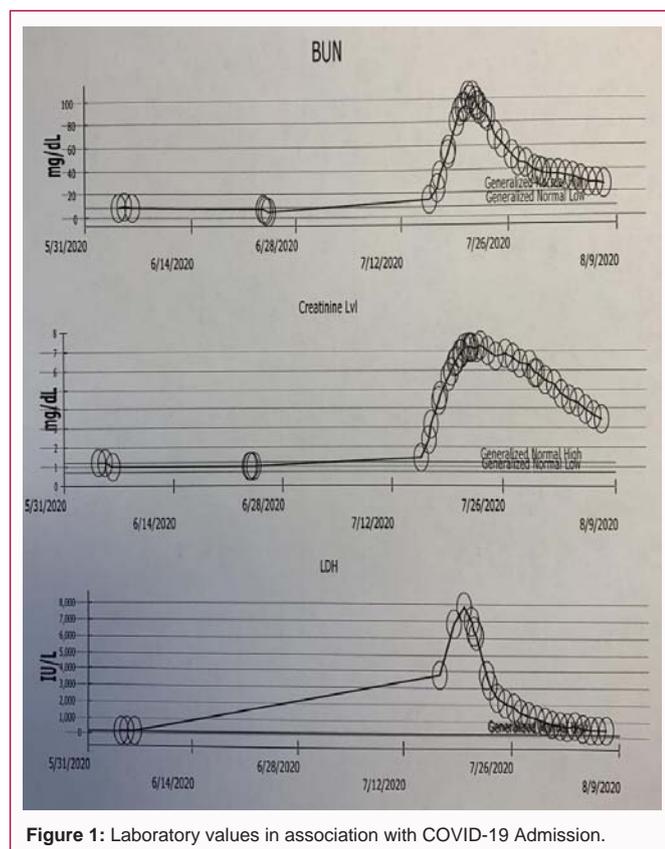


Figure 1: Laboratory values in association with COVID-19 Admission.

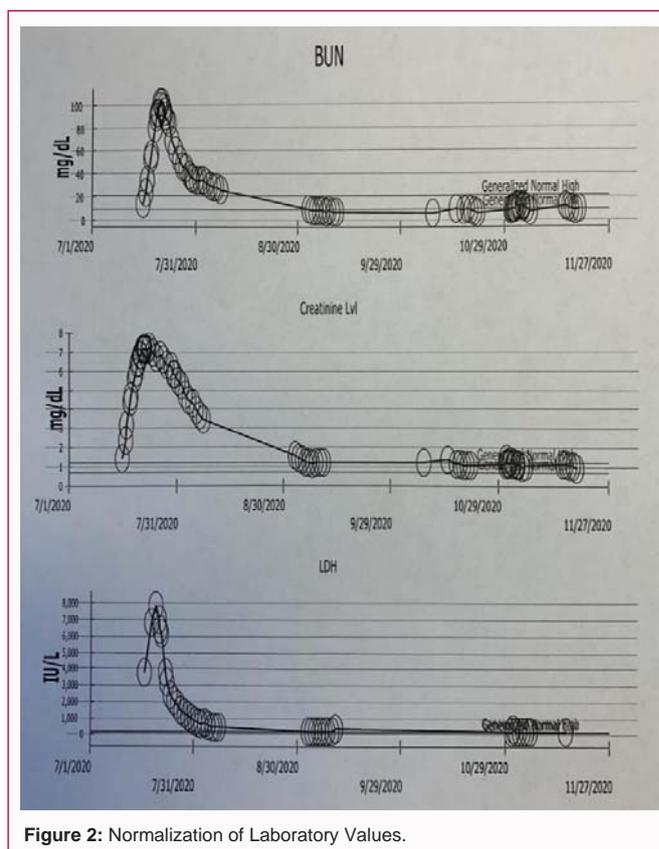


Figure 2: Normalization of Laboratory Values.

Dehydrogenase (LDH), Blood Urea Nitrogen (BUN), Creatinine (Cr), and D-Dimer (Figure 1). These findings were consistent with hemolysis. In addition to the studies, coronavirus surveillance testing was performed and found to be positive. As such, the presumptive diagnosis was COVID-19 associated pump thrombosis resulting in hemolysis, pigment nephropathy, and acute kidney injury.

Treatment was initiated with a Tissue Plasminogen Activator (TPA) protocol 5 mg IV bolus followed by 3 mg/hr infusion for 10 h. Because the clinical and laboratory status did not improve, a second cycle of TPA (1 mg/h) was infused for an additional forty-eight hours. The clinical and laboratory status remained unchanged. A reduction in the LVAD speed (i.e. to reduce the hemolysis) and a heparin infusion to maintain an aPTT between 70 and 90 seconds was initiated. Over the course of the next several weeks, the clinical condition and laboratory values improved (Figure 2) and the heparin was converted to Coumadin. He was discharged on August 07th, 2020 (Hospital Day #24) on Coumadin 5 mg daily and Keppra™ 500 mg BID. All follow-up COVID-19 testing has been negative and no further evidence of LVAD pump thrombosis has been encountered.

Discussion

The LVAD is a mechanical blood pump that is prone to complications, among which is thrombosis. The incidence of pump thrombosis in the continuous-flow type varies depending upon the device, the center(s) reporting their results, and the definition/confirmation of the diagnosis. The initial trials of the HeatMate II™, for example, reported a pump thrombosis rate that ranged from 1.4% at 18 months to 6% at 2 years [1]. Subsequent reports of the same device showed an increased risk of thrombosis with a 1-year incidence of 7% to 11% [2,3]. In a retrospective review of all LVADs at one center, suspected LVAD thrombosis occurred in 20% of patients

over a median follow-up of 275 days [4].

The definition of LVAD pump thrombosis can vary from a suspicion (i.e. based laboratory test and clinical signs) to confirmation (i.e. visual thrombus in explanted pumps). In the absence of visually confirming a pump thrombus, the suspicion is raised in the following settings: Evidence of hemolysis (e.g. hematuric appearing urine, markedly elevated LDH), perturbations in LVAD performance (e.g. inadequate LV unloading and/or changes in pump power), and embolic events. Hemodynamic stability or instability depends upon the degree of pump thrombus (i.e. partial or total), the etiology of the pump thrombus, and the contractile reserve of the native heart.

The consequences of pump thrombosis can be life-threatening and pump exchange may be the only solution [5]. In other instances, non-surgical management with thrombolytics and IV anticoagulants may salvage the device and the patient. This is analogous to a thrombosed prosthetic heart valve. In the previously mentioned report [4], medical therapy led to resolution of hemolysis and discharge to home in 60% of the cases. Thrombolytics and/or device exchange was reserved only for unstable patients. In our case, we used a combination of thrombolytic and anticoagulant therapies with success, avoiding a formidable device exchange.

The causes of pump thrombosis are several, including anything that may alter the flow characteristics through the pump (e.g. shift in position of the pump inflow or outflow), clots entering the pump from any vascular source that can enter the left heart or from the left heart itself, accumulation of blood elements on 'vulnerable' pump surfaces (e.g. rotors, stators Figure 3), and alterations in the coagulability/anti coagulability of the blood-device interface. It is noteworthy to comment that some patients may never form pump thrombus in the absence of any anticoagulation while others develop thrombus

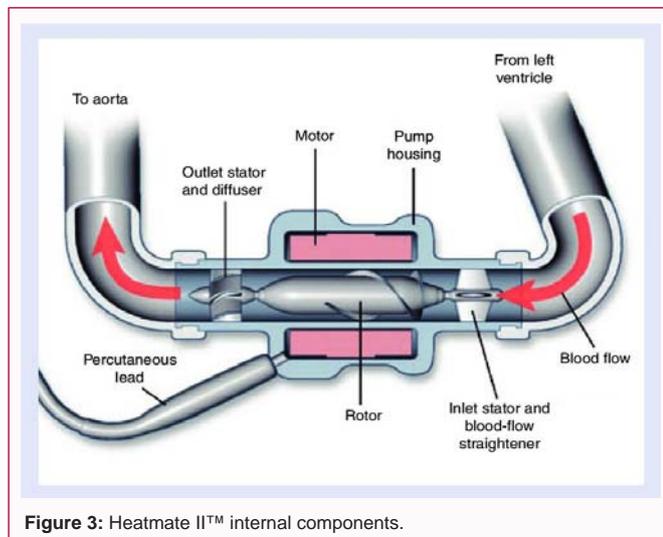


Figure 3: Heatmate II™ internal components.

while therapeutically anticoagulated. In this case, the etiology of the pump thrombosis was believed to be an acute hypercoagulable state induced by a COVID-19 infection. Although the patient had been off anticoagulation for six months following the intracranial bleed, the timing of the pump thrombosis in association with the COVID-19 infection suggests a correlation. Furthermore, the success of the thrombolytics and anticoagulants support the notion that the thrombus was relatively fresh and amenable to lytic and anticoagulant therapies. Chronic thrombus formation would have manifested itself differently and not have responded to this treatment strategy.

The association of a hypercoagulable state in COVID-19 infections has been recently published by Abou-Ismaïl and others [6]. The mechanism is believed to be a severely heightened inflammatory response that leads to thrombo-inflammation through mechanisms such as cytokine storm, complement activation, and endotheliitis. Various elevations in biomarkers have been found during acute COVID-19 infections supporting the theory of a thrombo-inflammatory etiology for the hypercoagulability. In our case, we observed elevations in several biomarkers: The ferritin level was measured at 2,238 (normal range 22 ng/mL to 275 ng/mL) and the D-Dimer registered >25,000 (normal range 270 ng/mL to 490 ng/mL). In addition, the troponin value was six-fold greater than the upper limit of normal. The absence of another cause for pump thrombosis, the timing of the event in association with the infection, and the success of medical therapies with resolution of the hemolysis and pigment nephropathy strongly favors the diagnosis of COVID-associated LVAD pump thrombosis.

The purpose of this paper is to bring awareness to the healthcare community managing patients on LVADs. While the COVID-19 pandemic is still active, patients supported on LVADs are at risk for pump thrombosis if infected. Several authors have begun publishing

their experience of LVAD patients with COVID-19 [7,8], and one manuscript is credited with the first reported of an LVAD pump thrombosis in the setting of the coronavirus epidemic [9]. As the pandemic continues to affect vulnerable patients, it is prudent to maintain a heightened sense of vigilance in LVAD patients as they are vulnerable to the hypercoagulable state associated with the illness. Therapeutic levels of anticoagulation in LVAD patients during this pandemic may need to be confirmed more frequently and clinicians need to have a low threshold to test for COVID-19 in LVAD patients since the consequences of pump thrombosis are life-threatening. Lastly, if an LVAD patient presents with any signs, symptoms, or laboratory values suggestive of hemolysis, rapid initiation of lytic and anticoagulant therapy may mitigate the effects of pump thrombosis and avoid pump exchange.

This case report serves to add further information on the effects of COVID-19 on LVAD patients and promotes aggressive testing and treatment.

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