



Peer-Reviewed Case Report

Chronic LDH Elevation after Left Ventricular Assist Device Implantation

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Abstract

A 61-year-old woman who underwent HeartMate II left ventricular assist device placement for non-ischemic cardiomyopathy developed elevated lactate dehydrogenase within two weeks after implantation. After eight months of observation and several hospital admissions during which there was no evidence of pump thrombosis, she presented with clinically manifest hemolysis. During pump exchange there was notable pannus formation on the inflow cannula of the left ventricular assist device. The pannus around the inflow likely existed for several months, limiting the flow and creating a low-grade hemolysis and this low flow state stimulated thrombus formation triggering gross hemolysis. Thoratec analysis of the pump confirmed that the clot was present for about 5 days. Lactate dehydrogenase normalized after pump exchange.

Key words

left ventricular assist device; hemolysis; heart failure; lactate dehydrogenase



Introduction

Left ventricular assist devices (LVAD) have become an integral tool in the treatment of patients with refractory heart failure [1] as they decrease morbidity, prolong survival [2] and improve the quality of life [3]. According to the INTERMACS registry, more than 10000 LVADs have been implanted since 2006 in yearly increasing increments with nearly 2500 LVADs implanted in 2013 [4]. Recently, several high volume LVAD centers reported markedly increased incidence of pump thrombosis compared with the data from clinical trials [5]. This complication typically presents as hemolysis, and elevated lactate dehydrogenase (LDH) is the most reliable early sign [6]. Therefore, many centers routinely follow LDH level after LVAD implantation and advise immediate hospitalization based on elevated LDH alone. Other causes of LVAD obstruction, resulting in elevated LDH, are less frequent. There is scant data in the literature on hemolysis due to pannus formation. We describe a case of consistently elevated LDH for 8 months after LVAD implant due to pannus formation causing partial obstruction of the inflow cannula followed by gross hemolysis with onset of pump thrombosis.

Case presentation

A 61 year-old-woman with non-ischemic cardiomyopathy had recurrent hospital admissions due to decompensated heart failure and underwent HeartMate II LVAD placement. Preoperative laboratory workup showed no features of hypercoagulability. Heparin infusion was initiated on postoperative day 1 with a target partial thromboplastin time of 55- 65 seconds until an INR level of 2 was achieved. She was discharged on aspirin, persantine, and warfarin therapy. Her baseline LDH ranged between 400 and 500 IU/L. Within the first two weeks after LVAD implantation LDH started rising, never decreased to a level below 600 IU/L, ranging between 652 to 2258 IU/L. Because of this, the goal for INR was increased to 2.5-3.5, and she stayed within the range. Although she felt somewhat better than before surgery, walking longer and further caused lightheadedness, and over the course of several months she had two falls. Her target INR was increased to 2.5-3.5. Two months after this adjustment, she was admitted with gastrointestinal bleeding, and her INR goal was shifted again to 2.0-3.0. In addition we lowered the dose of aspirin from 325 mg/day to 81 mg/day and discontinued persantine.

An echocardiogram showed 2D and color Doppler features consistent with normal appearance of the LVAD device. On ramp study, with the device speed changed from 8000 rpms to 11000 rpms, left ventricular end-diastolic dimension decreased from 5 cm to 4.4 cm, and aortic valve opening time decreased from 230 ms to 100 ms, with both parameters consistent with normal pump function. We were unable to obtain good Doppler flow across the mitral valve in diastole to measure E wave deceleration time. Pump parameters were checked every two to three weeks with no evidence of major power spikes. A computed tomography angiogram (CTA) showed no evidence of thrombus formation in the inflow or outflow cannula. Eight months after device placement and continued LDH elevation, the patient presented with dark cola-colored urine and LDH was 3360 IU/L. She was experiencing shortness of breath and fatigue not different from her



symptoms before LVAD placement. The HeartMate II impeller pump was removed and a HeartWare centrifugal pump was implanted. There was evidence of pannus formation on the inflow cannula of the HeartMate pump (figure 1).

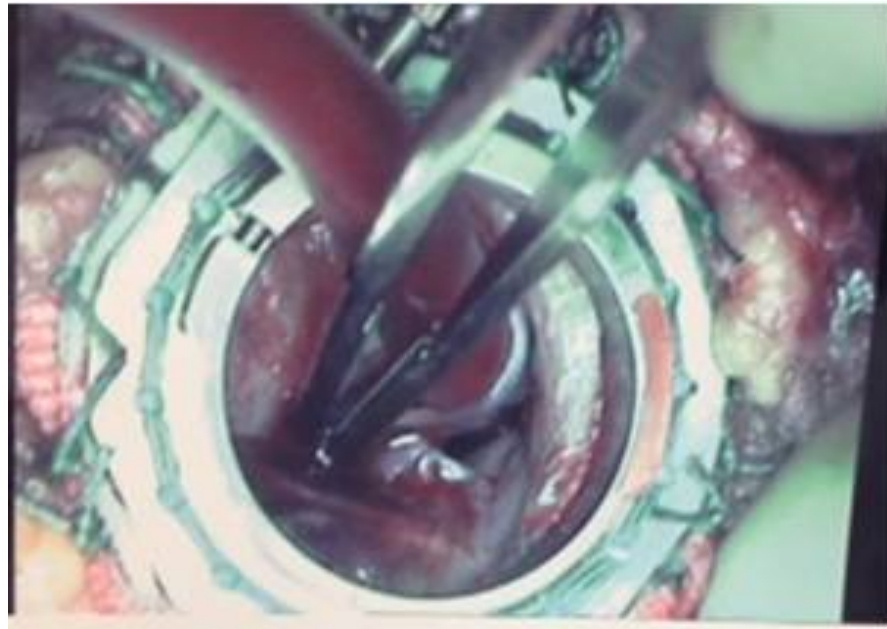


Figure 1. Intraoperative direct view illustrating pannus formation at LVAD inflow cannula

The device was sent to Thoratec for analysis who confirmed that a thrombus aged about 5 days was present. The pannus around the inflow cannula likely existed for several months, limiting the flow and created low-grade hemolysis (evident as continued LDH elevation). This low flow state stimulated thrombus formation triggering gross hemolysis. Lactate dehydrogenase returned to normal level after LVAD exchange. Figure 2 illustrates the longitudinal LDH values from the onset of LVAD implantation till its replacement.

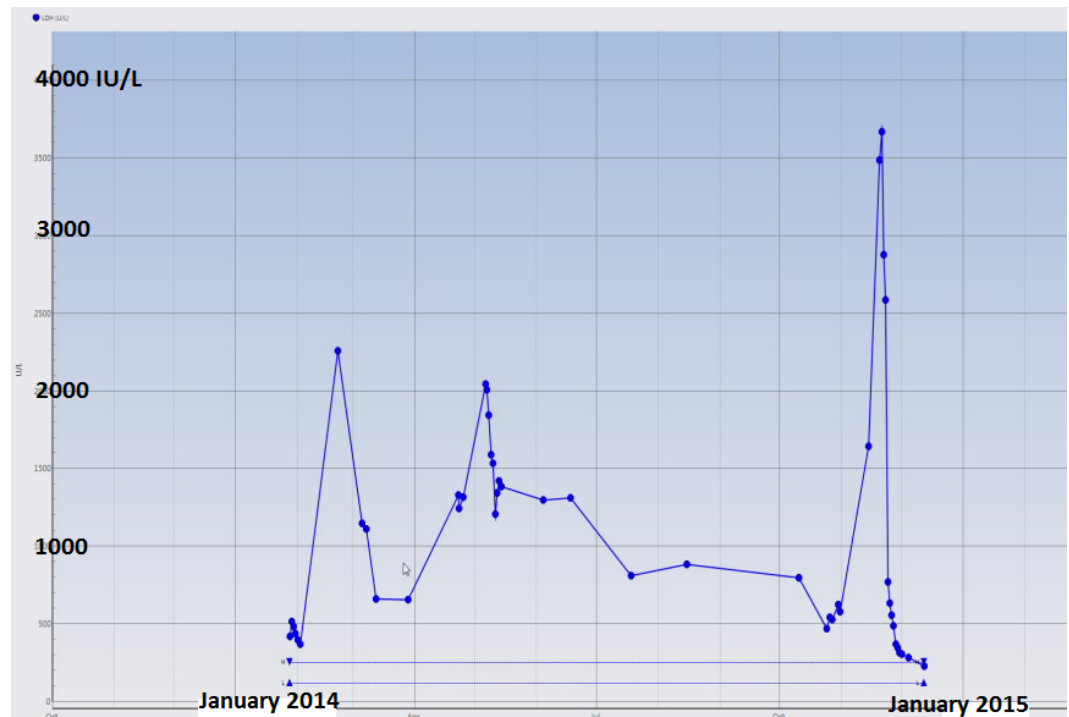


Figure 2. Longitudinal values of lactate dehydrogenase after HeartMate II placement from device implantation till explant

Discussion

A low level of hemolysis is common in all extracorporeal circuits with a rotatory pump. Clinically significant hemolysis is one of the feared complications that is increasingly recognized after LVAD support and is associated with increased mortality. Ravichandran et al. [7] compared patients with Heartmate II with and without hemolysis and found that survival in the hemolysis group was markedly decreased at one year (38.9% vs. 89.3% in those with and without hemolysis, respectively, $p < 0.001$). Hemolysis is suspected when a patient develops new onset anemia in absence of a bleeding source and manifest with dark cola-colored urine, elevated plasma free hemoglobin (PFHb), hyperbilirubinemia with undetectable haptoglobin and elevated LDH [8]. Shah et al. found that an LDH > 600 IU/L for HeartMate II is a superior marker of hemolysis [9] compared with a PFHb > 40 mg/dl which has been used to define significant hemolysis in the INTERMACS registry [10]. Other features of hemolysis –as a result of pump malfunction- include a new palpable pulse, the development of heart failure symptoms, increased pump power, new opening of the aortic valve and worsening of mitral regurgitation on echocardiography [11].

The most concerning cause of hemolysis in LVAD patients is pump thrombosis which should prompt pump replacement or cardiac transplantation to reduce mortality [5]. Other treatment options include thrombolytic therapy which has a 54.3 % success rate and glycoprotein IIb/IIIa antagonist which has a 39.3 %



success rate compared with 75.5 % success rate with pump exchange [8]. In the study by Ravichandran et al., all patients with evidence of hemolysis had partial to complete pump thrombosis at explant and they concluded that hemolysis likely serves as a marker of pump thrombosis [7]. Other less common causes of hemolysis include cannulae/device malpositioning or migration and kinking or pannus formation on the inflow or outflow cannula. There is little data in the literature on hemolysis due to pannus formation on the inflow cannula of HeartMate II. Pannus is an avascular mass of fibrous tissue and its pathogenesis is not fully understood [12]. Comparison between pannus and thrombus formation was better studied with prosthetic heart valves. Unlike in thrombus formation, suboptimal anticoagulation did not appear to be a risk factor for pannus development; in addition, a longer period is required for pannus formation, usually 6 months or longer [13]. However, a shorter time interval for pannus formation has also been reported [14]. In the presented case, pannus formation likely occurred in the early postoperative period as evident by elevation of LDH within 2 weeks after LVAD implantation and was responsible for persistent LDH elevation for 8 months. The onset of clinically manifest hemolysis occurred with the development of LVAD thrombus due to the continued low flow state which prompted pump exchange.

In the presented case, preoperative imaging failed to delineate a cause for the continued LDH elevation. The capacity of echocardiography to evaluate the inflow and outflow cannula is limited by acoustic window/shadowing and cannula artifact. Uriel et al. demonstrated that their “ramp” test protocol reliably detected LVAD thrombosis and malfunction through attenuated reduction in LV dimensions and increased power detected by the LVAD console with increasing LVAD pump speed [15]. Estep et al. showed that the best diagnostic parameters included changes in the LV end-diastolic diameter (<0.6 cm), aortic valve opening time (<80 msec), and deceleration time of mitral inflow (<70 msec) from lowest to highest pump speed [16]. Although CTA is an important tool to delineate the anatomy of the inflow cannula within the left ventricle, the extracardiac portion cannot be assessed with imaging and intraoperative inspection is needed. Moreover, it is unable to detect thrombus within the LVAD pump itself. Identifying the cause of hemolysis using echocardiography, CTA, or cardiac catheterization may not be definitive and occasionally intraoperative examination with extensive dissection to visualize the entire system is mandatory. Mechanical pump or inflow graft failure is therefore a diagnosis of exclusion and has been identified as the “black box” area that cannot be examined with preoperative imaging [17]. The presented case highlights one of the rare causes of chronic hemolysis after LVAD placement which is inflow cannula pannus formation.



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