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Dysphagia in the Setting of Left Ventricular Assist Device Hemolysis

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Abstract

A 69-year-old man with advanced heart failure treated with a continuous-flow left ventricular assist device presented for evaluation of dark urine and severe dysphagia. Because of evidence of ongoing intravascular hemolysis with device dysfunction, there was a clinical suspicion for pump thrombosis. He had progressive end-organ dysfunction and was therefore treated with tissue plasminogen activator with prompt resolution in hemolysis and dysphagia. Although symptoms of smooth muscle dystonia could represent worsening heart failure in the setting of device failure, the observation may also be related to intravascular hemolysis as described in the prototypic hemolytic disease, paroxysmal nocturnal hemoglobinuria.

Keywords

left ventricular assist device; thrombosis; hemolysis; dysphagia

A 69-year-old man with ischemic cardiomyopathy treated with a continuous-flow (CF) left ventricular assist device (LVAD; HeartWare International, Inc., Framingham, MA) implanted in August 2011 presented for evaluation of dark urine and dysphagia 1 year postimplant. He reported medication compliance, had therapeutic anticoagulation on recent clinic visits, and denied having emerging risk factors for pump thrombosis such as driveline infection. On the morning of admission, the patient noted “tea-colored” urine and increased power readings with alarms on the LVAD controller. In addition, he described abrupt onset dysphagia to liquids. On physical examination, there was no jugular venous distension, no ascites nor hepatojugular reflux; a faint S1 and S2 was auscultated, and there was a continuous LVAD hum. Laboratories demonstrated a rapid rise in serum creatinine from 1.4 mg/dl to 2.6 mg/dl, an international normalized ratio of 2.1, an out of testable range lactate dehydrogenase (LDH) and a plasma-free hemoglobin (PFH) of 466 mg/dl (normal < 6 mg/

dl). A transthoracic echocardiography compared with one taken the previous year showed that the aortic valve was now opening with every cardiac cycle and the left ventricular end diastolic dimension had increased from 6.1 to 6.8 cm. Right ventricular function seemed preserved by echocardiography. Examination of the LVAD confirmed an acute rise in power to maintain a speed of 2660 rpm.

On the basis of echocardiographic evidence of device dysfunction with ongoing intravascular hemolysis (IH), there was high clinical suspicion for acute pump thrombosis. The patient was treated with unfractionated heparin, and the urine was alkalinized, but when renal function continued to decline, intravenous tissue plasminogen activator was administered. LVAD powers and flows returned to baseline within minutes, but increased shortly thereafter, necessitating therapy with a glycoprotein IIB IIIA inhibitor. The next day serum LDH was 2523 units/L (normal 100–200) and declined to 232 units/L over 1 week. Urine color returned to normal and the patient's dysphagia resolved within 24 hours. Two weeks later, the patient was discharged in stable condition on aspirin, clopidogrel, and warfarin. He had a recurrent episode of thrombosis and severe hemolysis 3 months later with identical symptoms (including the dysphagia) and underwent pump exchange in December 2012. He has had no further complications at the time of writing this report; however, his renal function has been compromised by the recurrent episodes of hemolysis (creatinine now > 3 mg/dl).

Despite therapeutic anticoagulation with warfarin, patients treated with LVADs remain at risk for pump thrombosis because of the thrombogenicity associated with artificial surfaces interfacing with the circulatory system. Pump thrombosis may be suspected in the setting of clinical and biochemical evidence for IH related to shear stress on red blood cells propelled through a partially occluded CF pump. Indeed, CF LVADs explanted from patients with marked elevations in LDH and PFH have confirmed the presence of device thrombus.¹ In addition to pump malfunction, the complications of this hemolytic process can include renal failure from pigment nephropathy, as evidenced by the findings in our patient.

In other hemolytic conditions, IH has been linked to smooth muscle dystonia resulting in dysphagia and abdominal pain.² When the levels of hemoglobin released into the plasma overwhelm removal systems, levels of PFH increase and result in the consumption of nitric oxide (NO). NO plays a role in smooth muscle relaxation and vasomotor tone, endothelial adhesion molecule expression, and platelet activation and aggregation. Thus, excessive PFH can result in dystonia of the gastrointestinal system. The clinical sequelae of IH have been described in the prototypic hemolytic disease, paroxysmal nocturnal hemoglobinuria.³ Gastrointestinal dystonia is experienced by ~25–35% of paroxysmal nocturnal hemoglobinuria patients during a paroxysm, particularly those with the highest hemolytic rates, and the episodes generally resolve when hemolysis abates.⁴

This case represents the first of three CF LVAD patients treated at our center, who presented with dysphagia in the setting of severe IH. We present this case as an example of another noncardiac complication of CF devices with interesting pathophysiological consequences. Other examples include the development of arteriovenous malformations in the gastrointestinal tract and acquired von Willebrand syndrome, which have become more

prevalent after the transition away from pulsatile devices.⁵ Although the therapeutic approach for severe IH centers around resolution of pump thrombosis or device exchange, little is known about the management of hemolysis itself in patients with ongoing LVAD therapy. Understanding the pathophysiological consequence of severe IH (*i.e.*, NO consumption) and highlighting the molecular mechanisms that could become deranged may provide clues for adjunctive therapies that may protect other organs.

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