A 51-year-old man with a 2-year history of type II diabetes mellitus, erectile dysfunction, and 3-month history of fatigue was referred in March 2011 to the cardiology department of a local hospital because of 1 week of progressive dyspnea, orthopnea, leg edema, and increasing abdominal girth. His only medication was tolbutamide and metformin. He drank alcohol sporadically with maximum of 1 drink/d and had a history of shoulder arthralgias. On physical examination, the patient had brownish-gray skin pigmentation. He was tachypneic with blood pressure of 105/80 mm Hg and regular heart rate of 118 beats per minute. He had jugular venous distension, bilateral pulmonary crackles, II/VI systolic murmur heard at the apex, ascites, and pitting edema in both lower legs. The ECG showed sinus tachycardia with left atrial and ventricular hypertrophy and repolarization abnormalities. A chest radiograph (Figure 1) revealed cardiomegaly and bilateral pleural effusion. The echocardiogram showed a dilated left and right ventricle with severely compromised systolic function (left ventricular ejection fraction, 20%) and no ventricular hypertrophy. There was moderate mitral and tricuspid insufficiency with elevated right sided pressures (40–45 mm Hg). Coronary angiography was notable for no significant coronary artery disease, and the diagnosis of a nonischemic dilated cardiomyopathy (DCM) was made. Laboratory findings included increased levels of urea 9.3 (2.5–6.4) mmol/L, creatinine 1.0 (0.6–1.4) mmol/L, aspartate amino- transferase 51 (<40) U/L, alanine aminotransferase 52 (<45) U/L, gamma glutamyltransferase 51 (<40) U/L, N-terminal of prohormone brain natriuretic peptide 350 (<12) pmol/L, and glucose 9.6 (3.6–5.6) mmol/L. The patients’ liver enzymes normalized with removal of 7760 mg (Table). Treatment was stopped at an SF level of 41 g/L. Because of slow SF decrease in total iron, the patient recovered rapidly and was discharged from the hospital. Treatment of iron overload was started with phlebotomy, performed once weekly with a removal of 300- to 500-mL whole blood per procedure (Table), decreasing the SF level from 3011 to 1796 μg/L. Because of slow SF decrease and side effects such as frequent palpitations, syncope, and dizziness during phlebotomy, treatment was switched to erythrocytapheresis with a frequency of 1 procedure every 2 to 3 weeks. About 500-mL erythrocytes, fully compensated with the same volume of saline per procedure, were removed. In total, 20 uneventful erythrocytapheresis procedures were performed during a period of 51 weeks. The total removed erythrocyte volume was 9700 mL with an estimated total iron removal of 7760 mg (Table). Treatment was stopped at an SF level of 41 μg/L. The patients’ liver enzymes normalized with time he was in cardiogenic shock with low blood pressure despite inotropic support and subsequently required an intra-aortic balloon pump. Hemodynamic measurements showed a pulmonary artery pressure of 38/24 mm Hg, mean 29, with a pulmonary capillary wedge pressure of 24 and a right atrial pressure of 15 mm Hg and a cardiac output of 3.8 L/min (cardiac index, 1.9 L/min per meter squared). His clinical condition did not improve, so a left ventricle assist device (LVAD) was implanted as a bridge to heart transplantation.

The myocardium tissue of the left ventricular apex, removed during LVAD implantation, showed widespread iron deposition in the cardiomyocytes (Figure 2). These findings were compatible with cardiac hemochromatosis explaining the cause of the DCM. Iron parameters showed elevated serum ferritin (SF) of 3711 (25–250) μg/L and transferrin saturation of 88%. DNA testing confirmed a homozygous substitution of tyrosine for cysteine at position 282 (C282Y) in the hereditary hemochromatosis (HH) HFE protein. After LVAD implantation, the patient recovered rapidly and was discharged from the hospital. Treatment of iron overload was started with phlebotomy, performed once weekly with a removal of 300- to 500-mL whole blood per procedure (Table), decreasing the SF level from 3011 to 1796 μg/L. Because of slow SF decrease and side effects such as frequent palpitations, syncope, and dizziness during phlebotomy, treatment was switched to erythrocytapheresis with a frequency of 1 procedure every 2 to 3 weeks. About 500-mL erythrocytes, fully compensated with the same volume of saline per procedure, were removed. In total, 20 uneventful erythrocytapheresis procedures were performed during a period of 51 weeks. The total removed erythrocyte volume was 9700 mL with an estimated total iron removal of 7760 mg (Table). Treatment was stopped at an SF level of 41 μg/L. The patients’ liver enzymes normalized with
no signs of cirrhosis. After the normalization of SF, while on the LVAD, his heart function gradually recovered. Because of the potential option of explantation of the assist device, heart failure medication such as angiotensin-converting enzyme inhibitors and β-blockers were optimized and repeated echocardiograms and exercise tests were performed while turning off the pump. When these tests all demonstrated sufficient recovery of cardiac function, it was decided to explant the device. This operation, performed 23 months after initial implantation, went uneventful and the patient was discharged from the hospital 8 days after explantation. Echocardiographic measurements post-LVAD removal were left ventricular end-diastolic diameter 47 (versus 64 pre-LVAD implantation), left ventricular end-systolic diameter 32 mm (versus 53 mm pre-LVAD implantation), and mitral deceleration time 170 ms (versus 100 ms pre-LVAD implantation; Figure 3A and 3B). Currently, 12 months after the explantation of the LVAD he remains in good clinical condition, New York Heart Association I, without signs of heart failure and near normal left ventricular function.

Discussion

HH is a common heritable disease, characterized by an increase in iron absorption from the gut inappropriate to body iron stores, resulting in a progressive accumulation of iron in tissues, especially in the liver and pancreas. Cardiac involvement is less frequent, nevertheless can also occur, causing arrhythmias and in rare cases restrictive or DCM.

Standard therapy for patients with primary iron accumulation is phlebotomy. In this case, we described the use of an alternative treatment option, which is erythrocytapheresis. During this procedure, erythrocytes are selectively removed from whole blood by aphaeresis, followed by reinfusion of leukocytes, platelets, and plasma to the patient. This method has been evaluated in 1 randomized1 and a few nonrandomized studies.23 Results from all show that erythrocytapheresis is a much more effective and faster method and removes at least twice as much iron per single procedure compared with phlebotomy. This is especially advantageous in situations of life-threatening organ complications because of iron overload as in this case. The other important benefit of this method is individualized fluid management during the procedure, which makes it more suitable for hemodynamically compromised patients. Prognosis of patients with iron overload cardiomyopathy depends on establishing the diagnosis early and beginning therapy early.3 However, in the presented case, the end-stage DCM with severe systolic dysfunction, requiring support from an LVAD, did fully recover after the treatment with erythrocytapheresis. In addition to showing successful treatment of HH with erythrocytapheresis, this case has 2 other main points: (1) HH may cause a DCM and (2) therapy for HH is still worthwhile even when patients present with cardiogenic shock since the patient improved and was able to be explanted without decompensation ≈1 year after LVAD explant.

Disclosures

None.

References


Key Words: dilated cardiomyopathy • erythrocytapheresis • hereditary hemochromatosis • left ventricular assist device • nonischemic cardiomiopathy
Figure 2. Cardiac tissue removed during LVAD implantation. A, Myocardium of the apex of the left ventricle with brown pigment in the cardiomyocytes. Hematoxylin and eosin staining. Bar, 100 μm. B, Prussian blue iron staining showing the iron in blue. Bar, 100 μm.

Table. Parameters of Treatment of Hereditary Hemochromatosis Patients With Phlebotomy and Erythrocytapheresis

<table>
<thead>
<tr>
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<th>Phlebotomy</th>
<th>Erythrocytapheresis</th>
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<tbody>
<tr>
<td>Serum ferritin at the start of treatment, μg/L</td>
<td>3011</td>
<td>1796</td>
</tr>
<tr>
<td>Serum ferritin at the end of treatment, μg/L</td>
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<td>41</td>
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<td>No procedures</td>
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<td>Treatment duration, wk</td>
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<td>Treatment interval, d</td>
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<tr>
<td>Total volume removed, mL</td>
<td>8800 (whole blood)</td>
<td>9700 (erythrocytes)</td>
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<tr>
<td>Estimated removal of iron per procedure, mg</td>
<td>168</td>
<td>388</td>
</tr>
<tr>
<td>Estimated total removal of iron, mg</td>
<td>3520</td>
<td>7760</td>
</tr>
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</table>

Figure 3. Apical 4-chamber view echo pre and post LVAD. A, Post-LVAD removal and (B) pre-LVAD implantation.
End-Stage Cardiomyopathy Because of Hereditary Hemochromatosis Successfully Treated With Erythrocytapheresis in Combination With Left Ventricular Assist Device Support

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