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Case Report: Iron Overload Cardiomyopathy Due to Hereditary Hemochromatosis

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ABSTRACT: Iron overload cardiomyopathy is a severe and potentially fatal complication of hereditary hemochromatosis (HH). This report presents an extensive case of a 54-year-old male with advanced iron overload cardiomyopathy secondary to HH, highlighting the diagnostic challenges, therapeutic strategies, and long-term management considerations.

I. INTRODUCTION:

Hereditary hemochromatosis is an autosomal recessive disorder characterized by excessive intestinal iron absorption, leading to pathological iron deposition in various organs, including the liver, pancreas, joints, and heart . The heart is particularly susceptible to iron-induced damage, resulting in a specific type of cardiomyopathy that can progress to heart failure, arrhythmias, and increased mortality if untreated . Iron overload cardiomyopathy is a recognized but often underdiagnosed complication of HH, making it a critical aspect of patient management .

II. CASE PRESENTATION:

- Patient History:

A 54-year-old Caucasian male presented to the cardiology clinic with a chief complaint of progressive fatigue and dyspnea on exertion over the past six months. Additionally, he experienced occasional palpitations, particularly after exertion. His medical history was notable for type 2 diabetes mellitus, diagnosed five years prior, and mild liver enzyme elevations observed intermittently over the last two years. Despite a family history of diabetes and liver disease, there was no known history of heart disease or hemochromatosis in his family.

The patient had no history of alcohol or substance abuse and reported no recent infections or significant weight loss. He had been treated with metformin for his diabetes and had no known drug allergies. His lifestyle included moderate physical activity, and he adhered to a standard diabetic diet. He was a non-smoker and reported moderate alcohol consumption (2–3 drinks per week).

- Physical Examination:

On examination, the patient appeared mildly overweight (BMI 28.5 kg/m²) and in no acute distress. Vital signs revealed a blood pressure of 140/90 mmHg, a heart rate of 98 beats per minute with an irregular rhythm, a respiratory rate of 18 breaths per minute, and an oxygen saturation of 96% on room air. Cardiovascular examination revealed a regular-irregular rhythm consistent with atrial fibrillation and a soft systolic murmur heard best at the apex. The jugular venous pressure was elevated at 10 cm H_2 O, indicating mild volume overload. Mild bilateral pitting edema was noted in the lower extremities. Skin examination revealed subtle bronze pigmentation, particularly on the forearms and lower legs. Abdominal examination showed no hepatosplenomegaly, and the liver was non-tender.

- Initial Diagnostic Workup:

Initial laboratory tests were notable for the following:

- Complete Blood Count: Hemoglobin: 14.2 g/dL, Hematocrit: 42%, WBC: 7,800/mm³, Platelets: 250,000/mm³.
- Liver Function Tests: AST: 60 U/L, ALT: 75 U/L, ALP: 110 U/L, Bilirubin: 1.2 mg/dL.
- Renal Function Tests: Serum Creatinine: 1.1 mg/dL, BUN: 15 mg/dL.
- Glucose: Fasting glucose: 180 mg/dL, HbA1c: 7.8%.
- Iron Studies: Serum iron: 250 µg/dL (normal: 60–170 µg/dL), Total Iron Binding Capacity (TIBC): 250 µg/dL (normal: 240–450 µg/dL), Transferrin saturation: 85% (normal: 20–50%), Serum ferritin: 1,500 ng/mL (normal: 30–400 ng/mL).

Given the markedly elevated serum ferritin and transferrin saturation, hereditary hemochromatosis was suspected. Genetic testing was ordered to confirm the diagnosis .

- Imaging and Further Investigations:

A 12-lead electrocardiogram (ECG) revealed atrial fibrillation with a rapid ventricular response, left ventricular hypertrophy (LVH), and non-specific ST-T wave changes. Chest radiography showed mild cardiomegaly but no evidence of pulmonary congestion. An echocardiogram demonstrated left ventricular hypertrophy with an ejection fraction of 40%,

moderate left atrial enlargement, and mild mitral regurgitation. There was evidence of diastolic dysfunction with a restrictive filling pattern .

A cardiac MRI was performed to assess myocardial iron content. The MRI revealed diffuse myocardial iron deposition, particularly in the interventricular septum and left ventricular free wall, with a T2* value of 12 ms (normal >20 ms), indicative of significant iron overload . The liver MRI confirmed hepatic iron deposition, with a liver iron concentration of 10 mg Fe/g dry weight (normal <2 mg Fe/g dry weight), further supporting the diagnosis of hereditary hemochromatosis .

Genetic testing revealed a homozygous C282Y mutation in the HFE gene, confirming hereditary hemochromatosis .

- Final Diagnosis:

The patient was diagnosed with iron overload cardiomyopathy secondary to hereditary hemochromatosis.

- Management:

Initial Treatment:

The primary treatment goal was to reduce the iron burden. The patient was initiated on an aggressive therapeutic phlebotomy regimen, starting with weekly phlebotomies of 500 mL of blood, with the aim of reducing serum ferritin to below 50 ng/mL . He was counseled on the importance of dietary modifications, including reducing red meat intake and avoiding iron supplements and vitamin C, which can enhance iron absorption .

Cardiac Management:

The patient was started on a beta-blocker (metoprolol) to control heart rate and an angiotensin-converting enzyme (ACE) inhibitor (enalapril) to manage heart failure symptoms and reduce afterload. Due to the presence of atrial fibrillation, anticoagulation therapy with warfarin was initiated to prevent thromboembolic complications, with a target INR of 2–3.

Diabetes Management:

His diabetes management was intensified with the addition of a GLP-1 receptor agonist (liraglutide) to improve glycemic control and potentially provide cardiovascular benefits.

- Follow-Up and Long-Term Management:

Over the next six months, the patient adhered to the weekly phlebotomy schedule, resulting in a gradual decrease in serum ferritin levels to 80 ng/mL. Clinically, the patient reported significant improvement in symptoms, with reduced fatigue and dyspnea. Echocardiographic follow-up at six months showed improvement in left ventricular ejection fraction to 50% and stabilization of left ventricular hypertrophy. The T2* value on repeat cardiac MRI improved to 18 ms, indicating a reduction in myocardial iron content.

Atrial fibrillation persisted but was well-controlled on metoprolol, with an average heart rate of 70–80 beats per minute. The patient continued on warfarin with regular INR monitoring. His diabetes remained under good control, with an HbA1c of 7.0% at the six-month follow-up.

Long-Term Monitoring:

The patient was scheduled for regular follow-up every three months, with monitoring of serum ferritin, liver function tests, and echocardiography to assess cardiac function. Phlebotomies were continued every two to three months to maintain ferritin levels in the target range. Liver ultrasound was planned annually to monitor for potential complications, such as cirrhosis or hepatocellular carcinoma.

Genetic counseling was offered to the patient and his family, given the hereditary nature of the condition. His siblings and children were advised to undergo genetic testing and iron studies.

III. DISCUSSION

Iron overload cardiomyopathy is a severe complication of hereditary hemochromatosis, often presenting late in the disease course. The condition is characterized by iron deposition in the myocardium, leading to oxidative stress, mitochondrial dysfunction, and ultimately, cardiac remodeling and heart failure [1]. Atrial fibrillation and other arrhythmias are common, contributing to the morbidity associated with this condition [2].

The diagnosis of iron overload cardiomyopathy can be challenging, as symptoms are often non-specific and may overlap with other causes of heart failure [3]. Early recognition is crucial, as timely initiation of therapeutic phlebotomy can significantly improve cardiac outcomes and prevent irreversible damage [4]. The case presented here underscores the importance of considering HH in patients with unexplained cardiomyopathy, particularly in the presence of elevated iron indices [5].

Cardiac MRI has emerged as the gold standard for assessing myocardial iron overload due to its ability to non-invasively quantify myocardial iron concentration using T2* imaging [6]. This technique has proven valuable in

detecting subclinical cardiac involvement and guiding treatment in HH patients [7]. Regular monitoring of iron levels and cardiac function using cardiac MRI can help in adjusting treatment plans and improving patient prognosis [8].

Management of iron overload cardiomyopathy involves a multidisciplinary approach, including regular phlebotomy to reduce iron stores, standard heart failure therapies, and management of arrhythmias [9]. Long-term follow-up is essential to monitor iron levels, cardiac function, and potential complications [10].

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