CASE REPORT

Hemochromatosis: Reversible Cause of Heart Failure

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Introduction

GCW, age 33, presents acute heart failure (HF), amenorrhea and darkening of the skin. Three months after this initial situation, the patient is referred to a large cardiology centre and is submitted to HF screening, and the suspicion of hemochromatosis is promptly raised. This disease affects the heart in only 15% of cases. It has been shown that early recognition and intervention may change the prognosis. This is a diagnosis that should be considered in all cases of HF screening since it is easy to diagnose and its treatment can drastically change the prognosis of the disease.

Hereditary hemochromatosis (HH) is a genetic disease of iron metabolism characterized by increased intestinal absorption and progressive accumulation of it in different organs.[1] HH is the most common autosomal disease in Caucasians, particularly those with Nordic or Celtic ancestors, affecting one in each 220-250 individuals.[2] According to the mutations found, HH can be classified as: Hemochromatosis associated with HFE (classical hemochromatosis) and hemochromatosis not associated with HFE: Hereditary hemochromatosis due to mutation at the receptor 2 of transferrin-TfR2, juvenile hemochromatosis (hemojuvelin mutation - HJV gene and hepcidin mutation - HAMP gene), ferroportin disease and African iron overload. The vast majority (80-85%) of HH cases that have northern European ancestors are associated with HFE, while 10-15% of HH cases are not associated with HFE.[3]

Keywords

Cardiac involvement, despite being a low-incidence complication (15%), is the main cause of morbidity and mortality, presenting 1-year survival after diagnosis without treatment.[4]

It is a significant and potentially reversible cause of heart failure which mainly involves diastolic dysfunction and increased susceptibility to arrhythmias and terminal HF, and has a varied spectrum of symptoms.

It was demonstrated that early recognition and intervention can alter the course of the disease. Biochemical markers and tissue biopsy have traditionally been used to diagnose and guide the therapy. More recent diagnostic modalities, such as cardiac MRI, are noninvasive and can assess the quantitative loading of cardiac iron. Phlebotomy and chelating drugs are the main current treatments. Other treatments are being investigated.[5]

Case report

A 33-year-old Caucasian female worker from Alto Jequitiba, Minas Gerais, presented amenorrhea for 3 years and darkening of the skin for 1 year. Progressive dyspnea report for 3 months, associated with gastric fullness, ascites, lower limb edema, orthopnea and NYHA III functional class. Referred to the National Institute of Cardiology for follow-up and etiological investigation.

At the examination she had grayish skin changes, she said she could see her skin more tanned in the last year, but she related it to the fact that she used to work under the sun. In addition to regular heart rhythm in 3 times with presence of 4th accessory sound and symmetrical lower limb edema.

As an initial propaedeutic, the following exams were performed: Ferritin 6073 ng/ml (VR: 20-200 ng/ml), Serum iron 342 mcg/dL (VR: 60 A 180 mcg/dL), Transferrin Saturation 101% VR: 20 to 40%).

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With the suspicion of heart disease caused by iron deposition due to the results of laboratory tests and physical examination, complementary tests were performed to close the diagnosis. Magnetic resonance imaging by the T2* method was suggestive of myocardial and hepatic iron deposition (Figure 1). The pre-treatment cardiac MRI showed a time of T2* 13.0 ms (N: > 20 ms) and an estimated MIC (Miocardial Iron Concentration) of 2.0 mg/g (N: < 1.1 mg/g). After treatment the time of T2* was 17.0 ms, with MIC estimated at 1.3 mg/g. This result was confirmed by endomyocardial biopsy.

Research continued with the exclusion of secondary causes of hemochromatosis and the genetic analysis that excluded HH related to the HFE gene. In conjunction with the clinical data the case is suggestive of Juvenile Hemochromatosis.

The established treatment based on weekly phlebotomies in association with the use of oral and parenteral iron chelators, as well as conventional beta-blocker, ACE inhibitor, spironolactone and furosemide therapy. After 6 months of outpatient follow-up, the patient presented improvement of the functional capacity and improvement of the echocardiographic parameters (figure 2).

Discussion

The main diagnostic hypothesis is non-classical hemochromatosis, or not linked to the HFE gene, the juvenile type being the most compatible with the clinical picture presented. Juvenile HH is characterized by early accumulation of iron in the body, with manifestations between the 2nd and 3rd decades of

life. The manifestations include hypogonadotrophic hypogonadism, heart disease, cirrhosis, diabetes, arthropathy and skin pigmentation. It is characterized by rapid accumulation of iron in the body, early onset, with manifestations of iron overload between the second and third decades of life (15-20 years of age) and functional impairment of affected organs before 30 years of age. Cardiac manifestations with heart failure and arrhythmias are early and are important causes of death.[6]

Cardiomyopathy due to iron overload, whether caused by hemochromatosis or not, is a disease that should always be considered as soon as begins the diagnosis of patients with heart failure. The patient described above manifested the disease with a classic picture of congestive heart failure and already presented a significant iron deposition burden on the heart. Although the disease was no longer at an early stage, the natural history of the disease was modified and there was regression of iron accumulation as well as improvement of ventricular function.

It is worth mentioning that cardiac MRI using the T2* method was established as a diagnostic method as well as a method for risk stratification in these patients. It can also be used to follow the response to the treatment of the disease.[7]

Iron overload cardiomyopathy is a potentially lethal but treatable disease when diagnosed and treated early in its course. Despite the low incidence of heart disease associated with iron overload in the general population, it is a cardiopathy with potential for treatment and reversal, and its screening tests are easy to perform and inexpensive. Therefore, iron, ferritin and transferrin saturation should be part of the initial propaedeutic routine of patients with dilated cardiomyopathy.
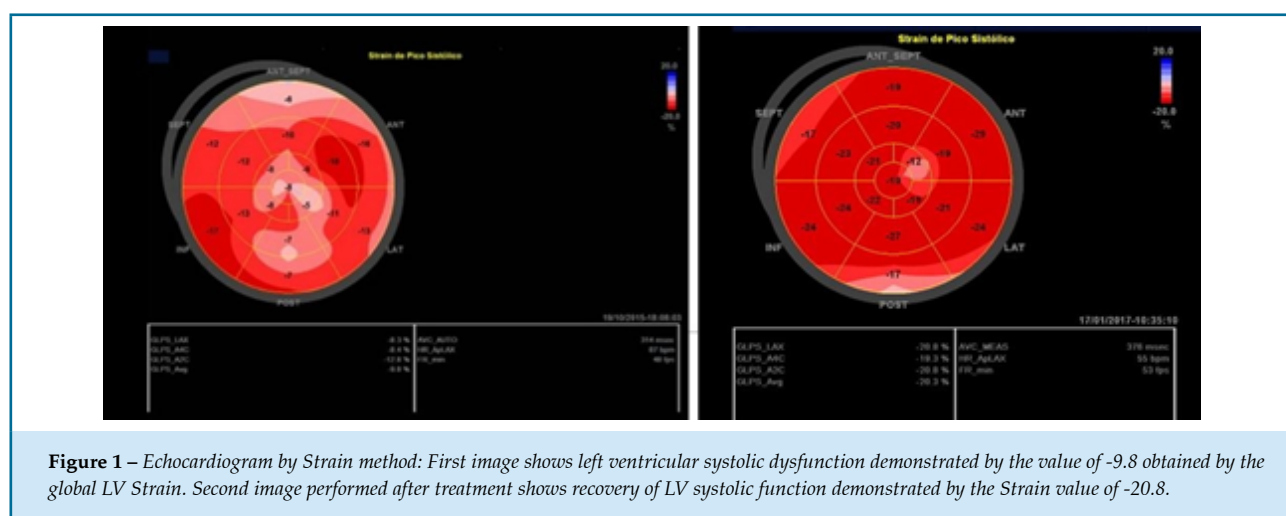

Figure 1 – *Echocardiogram by Strain method: First image shows left ventricular systolic dysfunction demonstrated by the value of -9.8 obtained by the global LV Strain. Second image performed after treatment shows recovery of LV systolic function demonstrated by the Strain value of -20.8.*
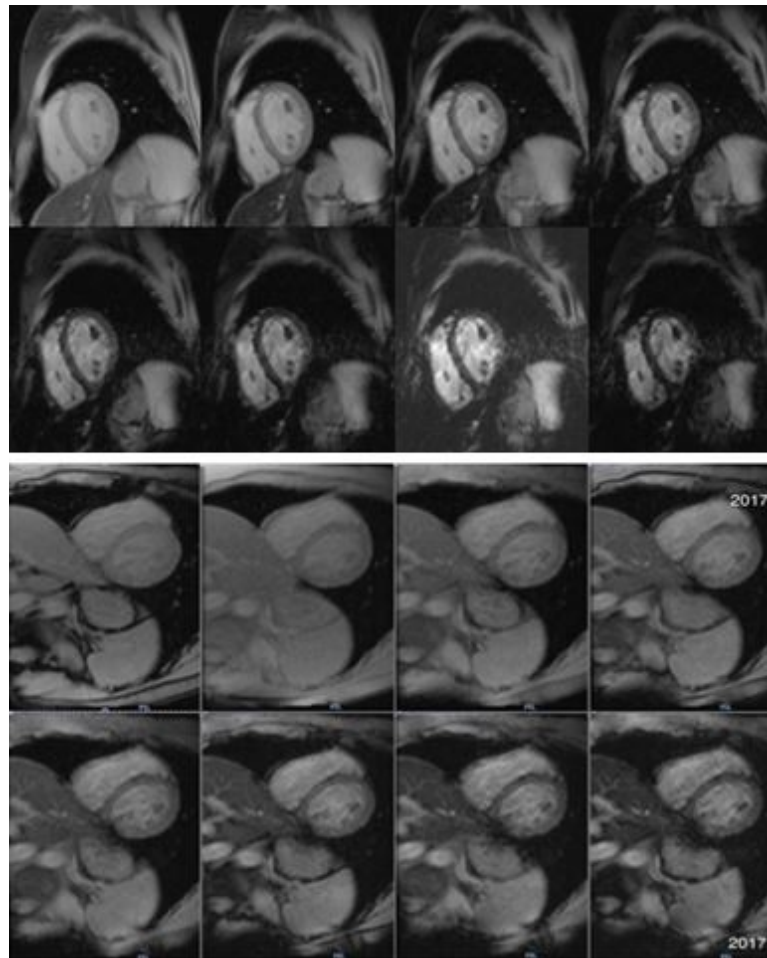
Figure 2 – *Cardiac Magnetic Resonance by T2* method: First image shows iron myocardial deposition feature and the second image shows improvement after treatment.*

Author contributions

Conception and design of the research: Iglesias CPK, Duarte PVF, Miranda JSS. Acquisition of data: Iglesias CPK, Miranda JSS. Analysis and interpretation of the data: Iglesias CPK, Duarte PVF, Miranda JSS, Machado LG, Andrade CRA. Statistical analysis: Iglesias CPK. Obtaining financing: Iglesias CPK. Writing of the manuscript: Iglesias CPK, Duarte PVF, Machado LG, Andrade CRA. Critical revision of the manuscript for intellectual content: Iglesias CPK, Duarte PVF, Miranda JSS, Machado LG, Andrade CRA.

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