Italian Journal of Geriatrics and Gerontology

2016;1(1): 1-3

Editoriale

ASSESSMENT OF IRON OVERLOAD: STUDY OF A GERIATRIC PATIENT AND LITERATURE REVIEW

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Abstract

The effective management of iron overload requires frequent evaluation of body iron stores. Measurement of serum ferritin, although easy to perform, gives results that are too variable for the accurate prediction of total body iron. We took the opportunity of the management of a patient with hemochromatosis to discuss here conditions of studying the quantification of iron overload by invasive (liver and endomyocardial biopsy) or noninvasive assessments (ferritin, CT, MR, SQUID).

Keys words: Iron overload; hemochromatosis; hepatic iron measurements; biopsy; magnetic resonance imaging

Background

The effective management of iron overload requires frequent assessments of body iron stores. The measurement of serum ferritin, although easy to perform, provides results which are characterized by excessive variability for an accurate estimate of total body iron and does not provide any information about such deposits in certain and specific organs and systems. Although determining the iron concentration in the liver is still regarded as the best predictor of total body iron, such a procedure is invasive and not without risk; are beginning to enter in the use of clinical practice also common other non-invasive methods for measuring amounts of iron in the body, as well as having different specificity and sensitivity also evaluate different tissues from the liver. We considered a studied patient for this purpose and we draw some considerations on the latest methods of study of patients with iron overload.

Case report

Patient 65 years old, married, a sister with connectivitis. He suffered of hypertension, diverticulosis, BPH, metabolic syndrome, euthyroid goiter. Diagnosis of hereditary HFE-related hemochromatosis (homozygous mutation C282Y). Xerostomy, worsening fatigue, occasional palpitations. Arthralgias of the pelvis, knees, ankles, with no signs of inflammation. Coopera-

tive patient, alert. Overweight. Blood chemistry and immunoassay tests (antibodies; ReumaTest; Shirmer; capillaroscopy) negative for connectivitis. Neurological examination showed no clear signs of muscular exhaustion. Radiographic and US signs of osteoarthritis of joints, tendon calcifications in all joints, with signs of conflict in the hips; signs of L5 radicular pain and mild to moderate chronic pain of L4 and S1 bilaterally: we diagnosed an osteoarthritis in more skeletal with enthesopathy (while not excluding component due to hemochromatosis). At the cardiac level echocardiogram showed "left ventricle of normal size and contractility (EF 65%), left atrium of normal size for body surface area (Vol LA/BSA 22.4 ml/m^2), aortic root in the limits with calcific cusps, normal forming, valve opening, right-convex interatrial septum (absence of shunts), with the upper right-sided limits of the standard (right atrial area 21.2 cm^2) and a right heart deficit of contractility (TAPSE 1.8 cm), minimum mitral and tricuspid jets, without hemodynamically significant, transmitralic pattern of grade I diastolic dysfunction, mild pulmonary insufficiency". The computerized tomography (CT) did not appreciate altered density areas in pathological significance except a small lump (5mm) payable by the posterior basal segment of the right lower lobe, mediastinal lymph node swelling in the axis without dysmorphia and right atrium, inhomogeneous liver, iconographic finding confirmed by the US for steatosis widespread. The patient was started on cardiac magnetic resonance imaging (MRI) with contrast (with no evidence of signal alterations compatible with previous infarctions and evidence of circumscribed fibrosis rear junctional area) and liver SQUID, which it proves to be negative.

Discussion

Hemochromatosis is a clinical syndrome characterized by the toxic accumulation of iron in parenchymal cells of vital organs such as liver, heart and endocrine glands caused by different mutations of genes that codified proteins such as HFE (1,2). The diagnostic workup should not only identify the disease but to quantify the iron overload, define the stage of disease and identify risk factors for progression and early complications. The revealed cardiac conformation with the US led us to ask for a new instrumental demonstration by CT, which confirmed the find. This test measures the increase in density X-rays caused by increased iron electron density compared with normal constituents of the liver and myocardial tissue (3). Unfortunately the method is still inaccurate, especially in cases of fibrosis (both in the liver but also of the heart) and for low levels of iron overload, as well as subject to errors for low quantities of metal and for the presence of fat (the patient in question was steatotic). On the contrary, MRI measures the tissue concentration of iron in an indirect way, by detecting the paramagnetic effect, produced by the presence of stored iron (ferritin and hemosiderin), on the behavior of protons in places in resonance tissues. This effect can be evaluated by calculating the longitudinal magnetic relaxation times (T1) and transverse magnetic relaxation times (T2) (4,5). Since the magnetic susceptibility of a tissue is determined by the strength and direction of the magnetic response evoked in the tissue by the application of a constant magnetic field such paramagnetic response of the iron contained in ferritin and ehemosiderin it can also be detected by use of a superconducting device quantum interference (Superconducting Quantum interference Devices, SQUID). This method, not of routine use and affordable for all centers, allows the assessment of liver iron with equivalent results to those obtained by liver biopsy, as demonstrated in the validation experiments (excellent correlations between chemical measurement of liver iron non-tied the heme group and the measurements obtained with, as several limitations magnetic instrumental technique) (inability to assess the iron content at the myocardial level, restricted access of patients for the limited number of instruments, the high cost and the particularity of superconductors used) impede their widespread introduction and widespread use in the clinic (6,7). At the cardiac level considerable efforts are ongoing to evaluate for these purposes the methods of MRI: the evaluation of an hollow organ and mostly the assessment of the moving heart, by its own anatomy, can generate several artifacts, and the uneven distribution of iron can increase the variability of the measurements, as well as the direct validation of the method with chemical measurements of endomyocardial biopsies is problematic for the risk of erroneous sampling given by the uneven distribution of iron in myocardial level. There-

fore, flow and motion artefacts caused by the anatomy of the heart, and the non-uniform iron distribution may all increase the variability of the measurements (8,9).

Conclusions

Subjects with iron metabolism alterations, primitive as in the case of the subject studied, but also secondary (iron overload for transfusions/dyserythropoietic anemia), are likely to experience a life-threatening iron overload (organ damage such as cirrhosis, cardiomiopathy, diabetes, liver cancer - hepatocellular carcinoma - and heart failure). Alongside to now routine exams, such as the US and the CT and MR imaging, magnetic ranging techniques biosusceptometry establishing itself with the intent of ever less invasive evaluation of these patients, in order to supplant the biopsy of various tissues. On the other hand, in these patients the effective management of iron overload requires frequent assessments of these reserves in the body. There is therefore a clinical need for quantitative methods, non-invasive, for the measurement of body iron quantity, they are safe, accurate and readily available.

References

1. Brissot P, Cavey T, Ropert M, et al. Hemochromatosis: a model of metal-related human toxicosis. Environ Sci Pollut Res Int. 2016 Sep 15.
2. Adams PC, Deugnier Y, Moirand R, et al. The relationship between iron overload, clinical symptoms, and age in 410 patients with genetic hemochromatosis. Hepatology 25(1):162–166. 1997
3. Luo XF, Xie XQ, Cheng S, et al. Dual-Energy CT for Patients Suspected of Having Liver Iron Overload: Can Virtual Iron Content Imaging Accurately Quantify Liver Iron Content? Radiology. 2015 Oct;277(1):95-103.
4. Alústiza Echeverría JM, Castiella Eguzkiza A, De Juan Echávarri M, et al. Diagnosis and quantification of iron overload in the liver using MRI. Radiologia. 2008 Jan-Feb;50(1):29-36.
5. Sarigianni M, Liakos A, Vlachaki E, et al. Accuracy of magnetic resonance imaging in diagnosis of liver iron overload: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2015 Jan;13(1):55-63.e5.
6. Fung EB, Fischer R, Pakbaz Z, et al. The new SQUID biosusceptometer at Oakland: first year of experience. Neurol Clin Neurophysiol. 2004 Nov 30;2004:5.
7. Nielsen P, Engelhardt R, Düllmann J, et al. Non-invasive liver iron quantification by SQUID-biosusceptometry and serum ferritin iron as new diagnostic parameters in hereditary hemochromatosis. Blood Cells Mol Dis. 2002 Nov-Dec;29(3):451-8.
8. Jensen PD, Bagger JP, Jensen FT, Heart transplantation in a case of juvenile hereditary haemochromatosis followed up by MRI andendomyocardial biopsies. Eur J Haematol. 1993 Oct;51(4):199-205.
9. Jensen PD, Jensen FT, Christensen T, et al. Evaluation of myocardial iron by magnetic resonance imaging during iron chelation therapy with deferrioxamine: indication of close relation between myocardial iron content and chelatable iron pool. Blood. 2003 Jun 1;101(11):4632-9.