

Familial Hypercholesterolemia: the Importance of Early Diagnosis and Management

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Introduction

Familial Hypercholesterolemia (FH) is an autosomal dominant hereditary disease, a genetic disease of lipoprotein metabolism, mainly due to a defect in the LDLR gene encoding the LDL receptor.¹⁻⁴ The diagnosis is established by clinical and laboratory criteria and should always be a diagnostic hypothesis in patients with low-density lipoprotein cholesterol (LDLc) levels greater than 190 mg/dL; and can be confirmed by genetic tests that determine the mutation.^{1,2} Some diagnostic criteria have been proposed in an attempt to standardize and formalize the diagnosis of FH, such as the *Dutch Lipid Clinic Network* (Dutch MEDPED).¹ This calculates a patient score based on anamnesis data and physical and laboratory tests such as elevated rates of LDLc; characteristics such as tendinous xanthomas and corneal arch; family history of hypercholesterolemia and/or early coronary artery disease (man < 55 years and woman < 60 years) and identification of genetic mutations.^{1,3} The score determines the probability of an FH diagnosis as possible, probable or definitive FH.¹ The most common mutation related to FH is in the gene encoding the LDL receptor, resulting in LDL receptors with functional reductions in their ability to remove LDLc from the circulation.³ There are two distinct phenotypes: the homozygous form, where two defective genes are inherited and LDL receptors have no functionality; a rare form, 1 in 1 million individuals and in this case are observed LDL levels > 650 mg/dL; and the heterozygous form, where a gene defective to the LDL receptor is inherited from one parent and a normal gene from the other.¹ The absence of a functional gene causes

an increase in the plasma level of LDLc; most frequently affects 1 in 500 individuals with LDL levels > 200 mg/dL.¹ The homozygous form tends to present cardiovascular involvement already in childhood.¹ The mutation may also be secondary to defects in the APOB gene encoding apolipoprotein B100, or by functional gain mutations in the pro-protein convertase subtilisin/kexin type 9 (PCSK) gene. -9).^{1,3,4} In patients with heterozygous FH the LDL particles circulate longer, being more subject to oxidation and chemical transformations that result in high uptake of LDL modified by macrophages, triggering pro-atherogenic mechanisms, causing atherosclerosis, coronary artery disease and arterial disease peripheral.¹ The nutritional therapies, medication, and regular physical exercises help to control LDL levels and to prevent cardiovascular disease.¹⁻³ It is recommended to reduce the intake of foods rich in cholesterol and saturated fatty acids.¹⁻³ Pharmacological therapy is performed with high-potency statins, such as Atorvastatin (10-80 mg) and Rosuvastatin (10-40mg), in order to obtain a reduction of more than 50% of the baseline level.¹ In patients with intolerant to statin therapy, other hypolipidemic agents, such as ezetimibe, niacin or cholestyramine may be used; and may be also combined with each others in patients who are poorly responding to single statin therapy.^{1,3} Drug therapy should be individually prescribed and maintained in the long term, with regular medical follow-up always evaluating liver (TGO/TGP) and muscular (CPK) enzymes.^{1,2} Lipid profile screening is recommended in all individuals over 10 years of age and in all first degree relatives of individuals diagnosed as having FH.¹ In the presence of risk factors, clinical signs of FH or atherosclerotic disease, the lipid profile should be considered from 02 years old on.¹

In this report, we describe the case of a patient in the fourth decade of life with Familial Hypercholesterolemia, who was successfully treated with high-potency statin.

Keywords

Peripheral Arterial Disease; Atherosclerosis; Ankle Brachial Index; Hyperlipoproteinemia Type II.

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Case Report

A 31-year-old female patient from Rio de Janeiro sought outpatient care in March/ 2015 at the General Hospital of Nova Iguaçu with a history of hypercholesterolemia since the age of 16, but had never taken any medication and only had a diet without laboratory improvement. She used to do regular high-intensity physical activity 05 times/week since she was 18 years old. Family history of hypercholesterolemia (Total Cholesterol > 290 mg/dL) in two first-degree relatives (mother and sibling). Maternal grandfather died of AMI before 50 years. Patient presented a February/2015 laboratory test with lipidogram results: CT: 385 mg/dL; HDLc: 86 mg/dL; LDLc: 252 mg/dL and Triglycerides: 92 mg/dL.

Physical examination at the first consultation: Abdominal Waist: 72 cm, Weight: 66 kg, Height: 1.68 m, BMI: 23 kg/m², BP: 110/70 mmHg, HR: 68 bpm. Presence of tendinous xanthoma (Figure 1). Corneal arch absent. No changes in cardiovascular, respiratory and abdominal examination. Electrocardiogram performed at the 1st consultation without alterations. Laboratory tests were requested to assess dyslipidemia and imaging tests.

According to the criteria of Dutch MEDPED the patient has 13 points (Relative of 1st degree TC > 290 mg/dL - 2 points, tendinous xanthoma - 6 points, LDLc 252 mg/dL - 5 points), being considered as definitive diagnosis of FH.

Atorvastatin 20mg was started at the first visit, but the patient irregularly used it and returned to the doctor's office after three months with the results of laboratory and imaging tests: Carotid echocardiography and abdominal USG. These tests didn't show significant alterations. Atorvastatin was prescribed at 40 mg and reassessment scheduled for three months. Patient returned in September/15 with laboratory tests, showing a decrease of Total Cholesterol and LDLc levels (Figure 2) and unchanged hepatic and muscular enzymes (TGP 19U/L, TGO 23U/L, CPK 117U/L); and exercise test without alterations.

Lipidogram was requested to first-degree relatives with the following results: Mother - TC: 205 mg/dL and LDLc 125 mg/dL and Brother - TC: 193 mg/dL and LDLc 89 mg/dL; Both on statin therapy for more than two years. Brother has tendinous xanthoma. Genetic testing without possibility of accomplishment in public health service until the moment.



Figure 1 – Xanthoma in the calcaneus.

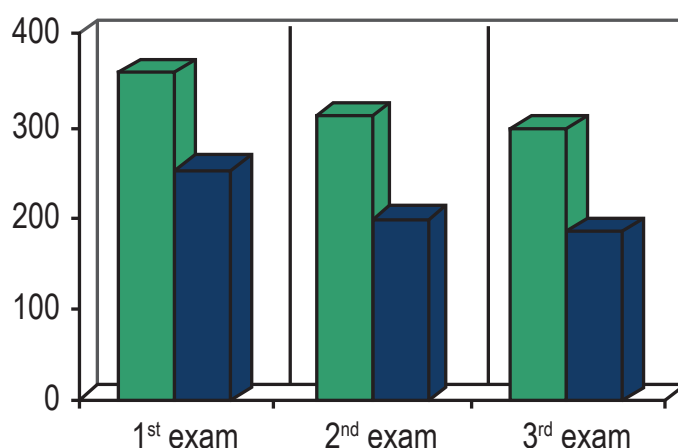


Figure 2 – Evolution of total cholesterol and LDLc values.

Discussion

The findings described in literature show that FH is a worldwide health problem, with a high risk of early cardiovascular diseases. Early identification of disease carriers contributes to the reduction of morbimortality, through appropriate guidelines and necessary therapeutic measures. The heterozygous form affects one in 500 individuals, corresponding in Brazil to 400,000 people with HF. The described patient was classified as a definitive diagnosis of FH by the Dutch MEDPED criterion, although this has not yet been validated for the Brazilian population. The reported case showed the good result with the use of high-potency statin and the importance of regular medical follow-up. It should be noted that the homozygous form is severe and affects children as early as the first decade of life, so early diagnosis can ensure that these children have the same life expectancy as the general population.

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Author contributions

Acquisition of data: Menezes IRR, Cunha AFC. Analysis and interpretation of the data: Menezes IRR, Cunha AFC. Writing of the manuscript: Menezes IRR, Cunha AFC. Critical revision of the manuscript for intellectual content: Menezes IRR, Cunha AFC.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

