Case Report

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# A Report of Two Children with Severe Homozygous Familial Hypercholesterolemia

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***Abstract***

Familial hypercholesterolemia (FH) is an autosomal disorder that causes severe elevations in total cholesterol and low- density lipoprotein. FH is one of the primary risk factors for premature coronary artery disease in children and adults which requires early diagnosis and appropriate medical intervention. In this article, we report two cases of homozygous familial hypercholesterolemia.



## Introduction

Hyperlipidemia, in adults, is well known as a primary risk factor for cardiovascular diseases, but various studies on children have shown that increased cholesterol level in various conditions can bring about cardiovascular diseases at older ages, and it may require medical treatment [1]. The homozygous type of hypercholesterolemia is extremely rare and occurs one in a million people worldwide and much more severe than the heterozygous type [2]. This paper introduces two cases of homozygous familial hypercholesterolemia. The purpose of introducing these patients is the rarity of this disease, familiarity with clinical symptoms and therapeutic measures for the prevention of coronary artery atherosclerosis and its side effects.

## Case Report

The first case was a 3-year-old girl (a resident of Khash) who had yellow papular lesions on her hands and legs. Six months before consulting with the physician, these symptoms had gradually shaped. The patient had no other symptoms such as pain, fever, itching, joints swelling and etc. On physical examination, the yellowish orange papular lesions without erythma and tenderness on the dorsal surface of hands, legs, forearms and elbow (3-5 mm, 3-4 numbers) was observed.

The examination of other parts did not reveal any abnormal issue. For the patient and her parents, paraclinical examinations were performed after 12 hours of fasting which is shown in table 1. In paraclinical examinations, the 30-year-old father and 21 year-old-mother who were relatives (paternal cousins), both were found out to have hyperlipidemia. The severity of hyperlipidemia and particularly the low density lipoprotein (LDL) in the child was dramatically high. The patient's paternal uncle had a history of sudden death.

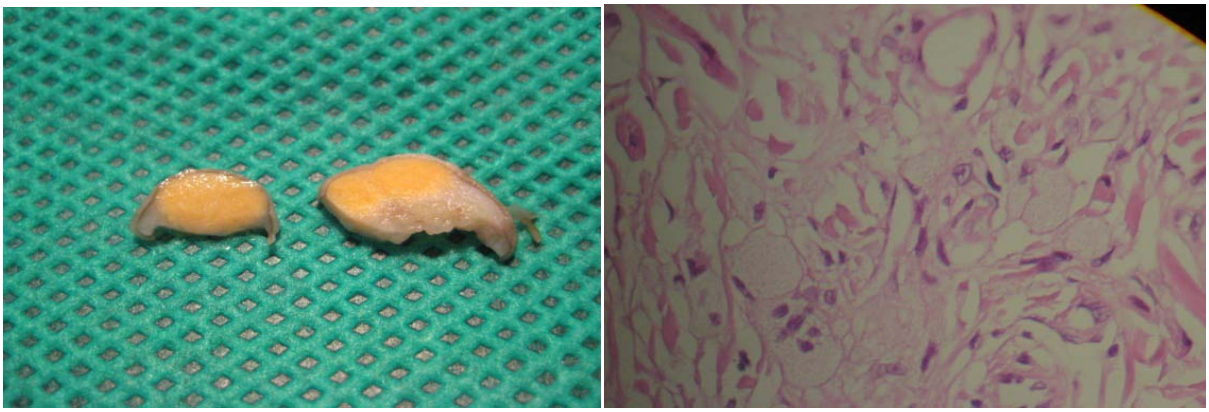
The second case was a four and half-year-old boy (a resident of Khash) with normal growth standards. He came to the clinic with yellowish orange papulonodular lesions on his forearms, hands, buttocks, loin, back and Achilles tendon area which had appeared when he was about 2 years old.

These lesions were painless, and without tenderness, erythma and itching. The lesion size varied from 3 to10 mm. The results of other physical examinations were normal. Suspecting xanthoma, caused by hyperlipidemia, lipid profiles were performed after 12 hours of fasting for the patient and her parents as shown in table 1. For the second case, a biopsy of the lesions on the wrist area was performed. There was no evidence of inflammation on histological examination and local accumulation of large macrophages with foamy macrophages was seen, confirming xanthoma (Fig. 1).

The evaluation of hypothyroidism, diabetes mellitus, liver and renal disease and echocardiography showed no abnormalities in both cases.

**Table 1.** Lipid profiles in first and second cases

| Lipid | | Triglyceride mg/dl | Cholestrol mg/dl | low density lipoprotein (LDL)mg/dl | high density lipoprotein (HDL)mg/dl |
|---|---|---|---|---|---|
| Child | Case1 | 110 | 874 | 787 | 65 |
| | Case 2 | 95 | 755 | 685 | 61 |
| Father | Case1 | 165 | 303 | 221 | 49 |
| | Case 2 | 155 | 288 | 212 | 45 |
| Mother | Case1 | 142 | 327 | 250 | 49 |
| | Case 2 | 130 | 310 | 225 | 59 |



**A** **B**

**Figure 1.** The macroscopic and microscopic view of the xanthoma; **A)** the macroscopic view of xanthoma: the yellowish orange nodular lesions with relatively sharp borders in the subcutaneous tissue. **B)** The microscopic view of xanthoma with a magnification of 40, which shows the accumulation of foamy macrophages with clear cyroplasm (foamy cell)

## Discussion

Hereditary hypercholesterolemia was first described by Khachadurian and Kuthman in 1973 as a severe hypercholesterolemia with tendon and cutaneous xanthoma, and a premature atherosclerosis and cardiovascular disease. Then, it was divided into autosomal recessive inheritance and autosomal dominant inheritance [3, 4]. Heterozygous familial hypercholesterolemia is the autosomal dominant inheritance that occurs about 1 in 500 people. The homozygous familial hypercholesterolemia occurs due to the inheritance of two mutant alleles of the LDL receptor which leads to the production of very low levels of the LDL receptors or failure to produce and severe defects in LDL catabolism [2]. In patients with familial hypercholesterolemia, LDL clearance of plasma decreases due to reduced liver LDL receptor [5].

Common symptoms of familial hypercholesterolemia are tendon and skin xanthomas, xanthelasma and corneal arc. xanthoma primarily occurs in the subcutaneous tissues, especially in the Achilles tendon and extensor tendons of hands [5]. Palpable xanthoma in children and adolescents is rare [6]. In familial hypercholesterolemia, cholesterol granuloma can occur rarely in the brain [7].

The homozygous familial hypercholesterolemia should be considered in people with total cholesterol levels over 500mg / dl and relatively normal triglyceride levels, with or without a palpable tendon xanthoma or anyone who has sufficient proofs of the family history of autosomal dominant inheritance but the definite diagnosis is based on the measurements of the LDL receptor activity on skin fibroblasts [8].

The reduced intake of fat and cholesterol and improved diet and paying attention to other cardiovascular risk factors are the cornerstones of hypercholesterolemia treatment. Beneficial effects of medical interventions that result in lowering lipid levels in children with familial hypercholesterolemia are well marked and, if untreated, they rarely survive in homozygous cases in adulthood. Liver transplantation, LDL apheresis, ezetimibe (A selective inhibitor of cholesterol absorption in the digestive tract) and statins are the efficatious factors in lowering LDL cholesterol levels in these patients [8]. In these two cases, although the measurement of the LDL receptor activity on skin fibroblasts was not possible, due to the severe hypercholesterolemia, very severe increase in LDL, normal triglyceride levels, various xanthomatous, especially in Achilles tendon area and ruling out secondary causes of hypercholestrolemia are the most likely diagnosis of homozygous familial hypercholesterolemia.

### Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

### Conflict of Interest

The authors declare no conflict of interest.

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