Picture Stories

A case of homozygous familial hypercholesterolaemia

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Sri Lanka Journal of Child Health, 2019; **48**(1): 88-89
DOI: http://dx.doi.org/10.4038/sljch.v48i1.8663
(Key words: Hypercholesterolaemia, homozygous, familial, xanthomas, Sri Lanka)

Introduction

Familial hypercholesterolaemia (FH) is an autosomal codominant condition characterized by a triad of elevated low density lipoprotein (LDL) cholesterol, premature cardiovascular disease (CVD), and tendon xanthomas[1]. The incidence of heterozygous FH is 1:500 whereas homozygous FH (HFH) is rare with an incidence of 1:100,000[2]. We report a 3 year and 6 month old child with HFH presenting with tendon xanthomas from 2 years of age.

Case report

A 3 year and 6 month old boy presented with nodular skin lesions over the extensor aspect of the lower limbs since the age of 2 years. He was followed up at the dermatology clinic and was being treated as viral warts. He was the first child born to non-consanguineous parents following an uneventful antenatal and perinatal period. He has not had any significant illnesses until the appearance of skin nodules. There was a strong family history of ischaemic heart disease where siblings of both parents had died at younger ages due to myocardial infarctions. His growth and development were age appropriate. Examination revealed multiple, small, soft, yellowish nodular lesions over the Achilles tendon, buttocks and the upper part of the shin (Figure 1). Rest of his system examination was unremarkable. There was no corneal arcus.

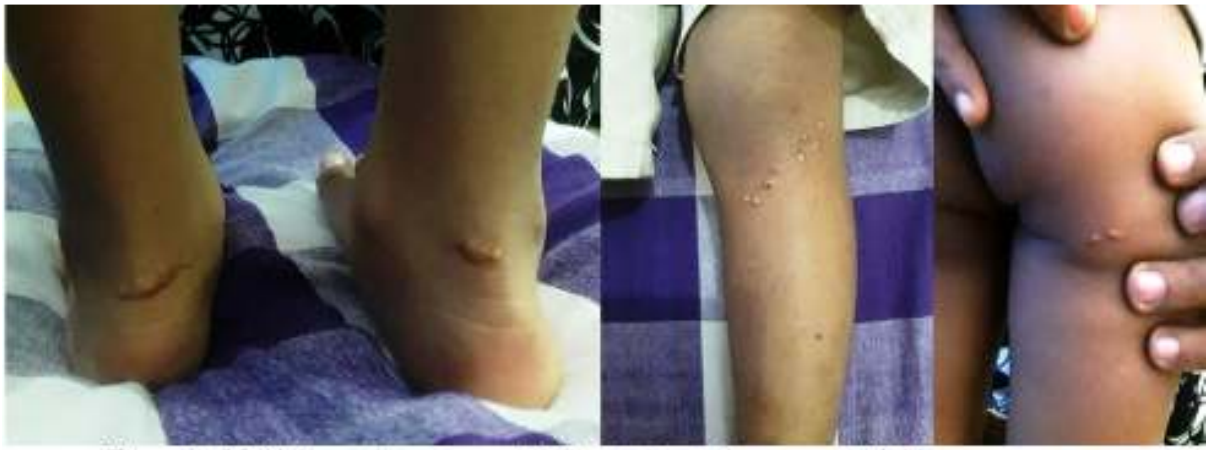

Figure 1: ***Multiple xanthomas over Achilles tendon and upper part of shin***

Lipid profile of the child revealed elevated total and LDL cholesterol (642mg/dl, 570.6mg/dl). Lipid profiles of the other members of the family (Table 1) revealed hypercholesterolaemia in father and mother suggestive of heterozygous FH. The cholesterol level of the younger sibling, though he has no tendon xanthomata, is in favour of another case of homozygous FH.

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(Received on 07 December 2017: Accepted after revision on 19 January 2018)
The authors declare that there are no conflicts of interest
Personal funding was used for the project.
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Table1; *Lipid profile of the family*

Type of lipid (normal range)	Patient	Brother	Mother	Father
Total cholesterol (<200mg/dl)	642	577	314	281
Low density lipoprotein (<130 mg/dl)	578	501	257	215
High density lipoprotein (>45 mg/dl)	51	50	43	42
Triglycerides (<100 mg/dl)	62	129	68	116
Very low density lipoprotein (<40 mg/dl)	12.4	25	13.6	23
Cholesterol/ LDL ratio (mg/dl)	12.5	11.5	7.3	6.6

His basic haematological parameters, liver enzymes, fasting blood sugar levels and thyroid functions were within the normal ranges. 2D echocardiogram (2D Echo) and electrocardiogram (ECG) were normal. Coronary angiogram was not done at this stage. Specific mutational analysis and LDL receptor studies were not done due to limited available facilities. The diagnosis of homozygous FH was made clinically and he was commenced on atorvastatin and a low fat diet.

Discussion

In HFH, there are 2 abnormal LDL receptor genes in chromosome 19[2]. This results in reduced uptake of LDL into the cells resulting in elevated cholesterol levels ranging from 500 to 1,200 mg/dl[1]. In heterozygote individuals, LDL receptor function is not totally impaired. Therefore, the usual serum cholesterol level lies between 200 and 300mg/dl[2]. In this child the diagnosis of HFH was made based on the presence of serum cholesterol levels >500 mg/dl with normal triglyceride levels, appearance of tendon xanthomas in the first decade of life and elevated cholesterol in other family members. The striking clinical presentation of HFH is the tendon xanthomas. They exist in plaques or nodules and consist of a collection of abnormal lipid deposition in foam cells (macrophages with phagocytosed lipid material) and collagen[3].

Familial hypercholesterolaemia (FH) carries a 100 times increased risk of developing atherosclerosis[2]. They can develop coronary artery disease even in early childhood[1]. Aortic root is the most commonly affected site of atherosclerosis in HFH[4]. However, in this patient 2D Echo did not reveal any abnormality. Family history of young cardiac death is a feature in FH[2] and this was evident in this patient.

There are several modalities of treatment for FH such as dietary modification, lipid lowering drugs, LDL apheresis and liver transplantation[1]. In heterozygous FH, treatment should be started at 8-10 years of age whereas in the homozygous variant it should be commenced at the time of diagnosis[4]. Dietary management, statins and ezetimibe are first line treatment modalities[4]. LDL apheresis is indicated when there is a failure in conventional treatment and it has been shown to slow the progression of coronary atherosclerosis[5]. The last treatment modality for homozygous FH is orthotopic liver transplantation[5]. Without treatment, the majority of patients with HFH would die before their twentieth birthday[1]. Since it is the striking physical sign which aids the diagnosis, it is very important to identify xanthomas early in life in order to commence treatment. Family screening would help to diagnose asymptomatic children.

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