Tuberous xanthoma – a rare presentation of homozygous familial hypercholesterolaemia

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Sri Lanka Journal of Dermatology, 2005, **9**, 28-30

Abstract

Familial Hypercholesterolaemia is a common autosomal dominant condition characterised by increased low density lipoprotein cholesterol, tendon xanthomas and premature atherosclerosis. We report 10 year old girl with very high LDL cholesterol levels where diagnosis was alerted by the presence of extensive tuberous xanthomas. Family screening revealed high levels of LDL cholesterol in both parents and siblings.

Introduction

Xanthomas are lesions characterised by accumulation of lipid laden macrophages. Xanthomas can be a reflection of alteration of lipid metabolism or a result of local cell dysfunction[1].

Cutaneous xanthoma is mostly a cosmetic disorder. But their presentation might suggest an underlying disorder of lipid metabolism. Mortality and morbidity is related to atherosclerosis and pancreatitis[2].

Equal incidence has been reported in males and females. Xanthomas can occur at any age.

Cutaneous xanthomas can precede the diagnosis of hyperlipidaemia.

Tuberous xanthomas are firm painless red-yellow nodules which can coalesce to form multilobulated tumours. They usually develop in pressure areas such as knee, elbow and buttocks. They can be associated with familial hypercholesterolaemia or familial hyperlipoproteinaemia or secondary hyperlipidaemias such as nephritic syndrome and hypothyroidism[1].

Familial hypercholesterolaemia is an autosomal dominant disorder causing very high levels of total cholesterol and LDL cholesterol.

Familial hypercholesterolaemia is seen in approximately 1:500 persons in the US in its heterozygous state. Because familial hypercholesterolaemia is associated with high risk of premature coronary artery disease, early detection and aggressive management to lower LDL cholesterol levels will reduce the risk[2].

We report a case of familial hypercholesterolaemia where diagnosis was alerted by the presence of extensive tuberous xanthomas and enlarged Achilles tendon.

Case report

Ten year old girl was presented with noduler plaques over elbow, knee buttocks and fingers. (Fig. 1 & 2).

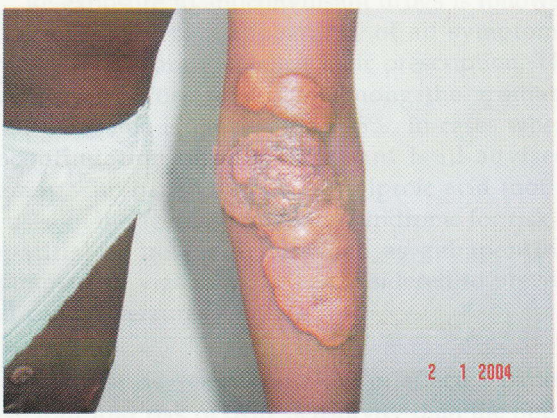

Figure 1

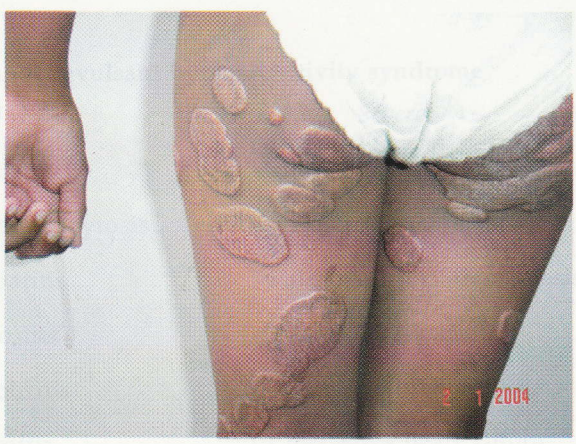

Figure 2

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The lesions started to appear at the age of 5 years. Past medical history revealed no significant illness. Paternal grandfather has died at the age of 45 years from an unknown illness.

Clinical examination revealed the presence of multiple skin coloured plaques on the buttocks, knees, elbows and face. Her Achilles tendon was unusually thick and nodular (Fig. 3).

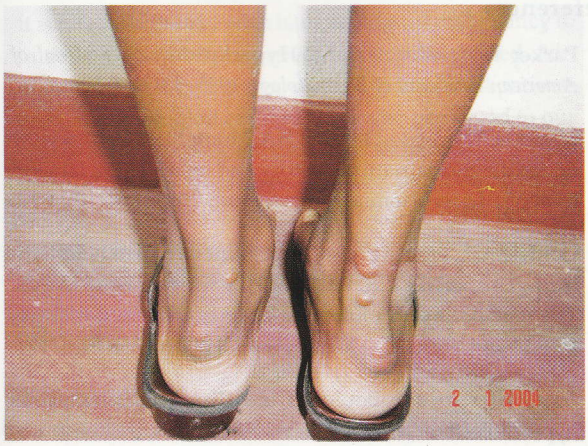

Figure 3

There were no xantholesmas or arcus cornea. Her blood pressure and weight were within normal limits (BMI 20). Peripheral pulses were normal and auscultation of the heart was normal.

Her lipid profile showed total cholesterol of 611 mg/dl,

LDL cholesterol 568mg/dl

HDL cholesterol 43 mg/dl,

Triglyceride 78mg/dl (normal).

Screening for secondary causes of hyperlipidaemia was negative. Echocardiography of the heart revealed myxomatous mitral valve with mild MR and sclerotic aortic valve with mild AS and AR.

Screening of the family members revealed high levels of total cholesterol and LDL cholesterol (Table 1).

All of them were normal on clinical examination. There was no obesity, xantholesma, arcus cornea or tuberous xanthoma. There was no past history of chest or abdominal pain. But their Achilles tendons were thicker than normal.

The presence of the triad of type IIa hyperlipidaemia, tendon xanthoma and positive family history supported the diagnosis of familial hypercholesterolaemia. The presentation at very young age, very high cholesterol levels (over 600 mg/dl) and high LDL cholesterol in both parents favours the diagnosis of homozygous state.

Discussion

Familial hypercholesterolaemia is an autosomal dominant disorder characterised by elevated LDL cholesterol levels with or without concurrent elevation of triglycerides. It is due to absent or grossly malfunctioning LDL (low density lipoprotein) receptors. The LDL receptor is the primary determinant of hepatic LDL uptake, which normally processes approximately 70% of circulating LDL. Any major change in the number or functional state of LDL receptors directly affects serum cholesterol levels. If an individual inherits 2 defective alleles of LDL-R gene (homozygous state) LDL production will increase by 200-300%.

Therefore patients who have homozygous state for familial hypercholesterolaemia demonstrate 5-6 fold high total cholesterol levels (600-1000 mg/dl)[3].

High levels of LDL cholesterol causes enhanced cholesterol in non-hepatic cells independent of LDL receptors. These scavenger pathways allow cholesterol uptake by monocytes and macrophages leading to 'foam' cell formation and plaque deposition in endothelium in coronary arteries. Therefore it is highly hazardous condition because atherosclerosis affects

Table 1

Family member	*Total cholesterol*	*LDL cholesterol*	*HDL cholesterol*
Father	371 mg/dl	328 mg/dl	43 mg/dl
Mother	311 mg/dl	266 mg/dl	45 mg/dl
Brother	268 mg/dl	218 mg/dl	50 mg/dl
Sister	245 mg/dl	192 mg/dl	53 mg/dl

large blood vessels relatively early and extensively. However, homozygous familial hypercholesterolaemia is very rare affecting only 1:1 million persons in the general population[4].

Cholesterol also accumulates in other areas such as skin, tendons and heart valves. In the skin it causes xantholesma and variety of xanthomas. Tendon involvement, particularly the Achilles tendon, is the hallmark of familial hypercholesterolaemia[5]. Heart valve involvement causes valvular dysfunction particularly aortic stenosis.

In familial hypercholesterolaemia all affected family members display high LDL cholesterol concentration. Death from homozygous familial hypercholesterolaemia typically occurs when individual is aged 20 years or younger. Whereas a heterozygous form the mean age of death is around 45 years.

Management of children with LDL cholesterol levels higher than 130mg/dl includes a combination of dietary measures, exercise and healthy low fat, low cholesterol diet with balanced energy intake. The objective is to achieve a LDL cholesterol level of 110 mg/dl or lower. The child should engage in regular aerobic exercises.

Ideal weight should be maintained. Lipid lowering drugs as single drug therapy with statins such as Atorvastatin has shown considerable efficacy in homozygous familial hypercholesterolaemia[4,6].

Screening of first degree relatives is worthwhile as the treatment for elevated LDL cholesterol levels lowers the risk of premature coronary heart disease.

References

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