Case Report

Homozygous familial hypercholesterolemia

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ABSTRACT

Familial hypercholesterolema (FH) is an inherited autosomal dominant disorder of lipid metabolism. We report a 3 years old female child who presented with multiple eruptive xanthomatosis of skin since 6 months of age and had deranged lipid profile consistent with FH.

Key words: Familial hypercholesterolemia, homozygous and heterozygous state, low density lipoprotein cholesterol, xanthoma

Introduction

Familial hypercholesterolemia (FH) is an autosomal disorder of lipid metabolism characterized by strikingly elevated levels of low density lipoprotein (LDL) cholesterol, cutaneous xanthomas, and family history of premature atherosclerosis.[1] Such patients are at increased risk of developing coronary artery disease and also sudden death unless the condition is recognized and treated promptly.[2] A 3 years old female child having clinical and biochemical findings consistent with homozygous FH is reported here for academic interest and its rarity.

Case Report

A 3 years old girl born of non-consanguineous marriage presented with multiple yellowish papular lesions and plaques over Achilles tendons, wrists, knees, and gluteal folds [Figure 1a] and also involving gluteal cleft [Figure 1b]. Lesions were asymptomatic and started when she was 6 months old. They have progressively increased in size and extent thereafter. Her father also had multiple nodular swellings over elbows [Figure 2] and legs. The

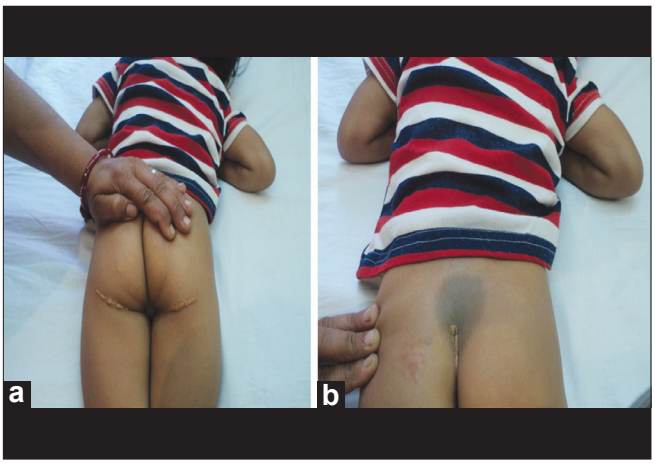

Figure 1: (a and b) Xanthmatous lesions over gluteal folds and cleft

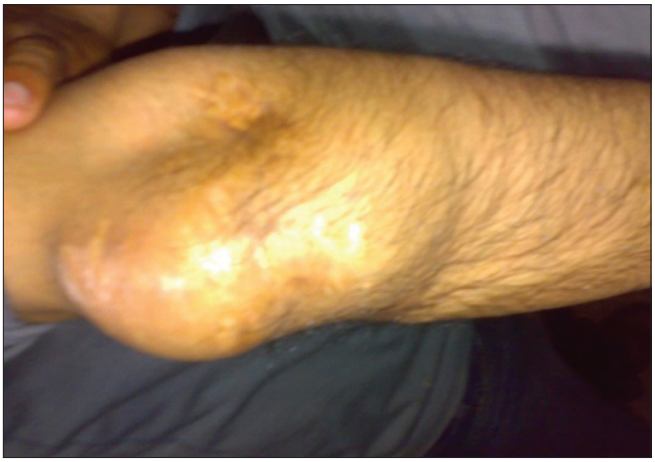

Figure 2: Nodular lesions over elbow of the father

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lipid profile of the child showed serum cholesterol level 760.3 mg/dl (normal < 200), HDL cholesterol 35.3 mg/dl (normal 45-65), LDL cholesterol 598.6 mg/dl (normal <100), VLDL cholesterol 126.4 mg/dl (normal <40) and serum triglyceride 117.7 mg/dl (normal <140). Serum cholesterol level and triglyceride level in her father were also deranged, i.e., 240mg/dl and 237 mg/dl respectively. A skin biopsy of both showed eruptive xanthomas. Her elder male sibling and mother had a normal lipid profile. On eliciting further history from other members of the family, the maternal sister of her father had similar complaints and died of acute myocardial infarction at the age of 40.

This girl was developmentally appropriate for her age with no significant history of loss of weight or appetite. There was no lymphadenopathy or organomegaly. CVS and CNS examination was normal. X-ray chest, ultrasound abdomen, ECG, echocardiogram, blood sugar, and LFTs were all normal. A diagnosis of homozygous FH was made on the basis of family history, characteristic cutaneous xanthomas since early childhood, and elevated levels of cholesterol and LDL cholesterol. After consultation with a cardiologist, the child was started on atorvastatin 10 mg daily besides dietary control of fats. The parents were counseled about the facts related to the disease and advised for regular follow up.

Discussion

Primary hypercholesterolemia occurs as a monogenic defect in lipoprotein catabolism by a mutation in the LDL receptor gene. The rate at which the LDL is removed from the plasma is determined by the heterozygous or homozygous state of the individual.[3,4] Heterozygous FH occurs with prevalence of approximately 1:500 individuals, manifesting clinically between the third and sixth decades. In contrast, homozygous FH occurs very rarely with prevalence of one in million persons. FH homozygotes inherit two abnormal LDL receptor genes, resulting in markedly elevated plasma cholesterol levels ranging between 500 and 1200 mg/dl. Triglycerides are normal to mildly elevated and HDL may be slightly decreased. Receptor negative patients have < 2% normal LDL receptor activity whereas those who are receptor defective may have as much as 25% normal activity and a better prognosis. LDL cholesterol is removed from plasma in the heterozygous state at 2/3 of the normal rate resulting in 2 to 3 fold elevation of LDL cholesterol, whereas in the homozygous state, it is removed at 1/3 of the normal rate resulting in 6 to 8 fold elevation of plasma LDL.[3-5] Clinically homozygous children usually present with cutaneous xanthomas during early childhood and cardiovascular abnormalities in the second or third decade of life[5] as happened with our patient who had almost all of these features except the CVS abnormalities which usually manifest in second decade. Similar instances of homozygous FH have also been reported by others also.[6,7] Family history is informative because premature heart disease is strongly prevalent among relatives of both parents.

The management of FH patients especially homozygotes has been a challenging job. Besides dietary control, a number of therapies have been advocated and early institution of such therapy may increase the long-term survival rates.[8-10] HMG COA reductase inhibitors known as statins are remarkably effective in lowering the LDL cholesterol levels. Combination therapy with ezetimibe, selectively blocking cholesterol absorption in the gut results in further modest decline in LDL levels. It has largely replaced the bile acid sequestrants. Other cholesterol lowering medications like nicotinic acid and fibrates have less often been used in children.[5] The NCEP expert panel for children and adolescents recommends that consideration may be given to pharmacologic treatment of hyperlipidemia if the child is at least 10 years of old and the adequate period of dietary restriction, at least 6 months, has not achieved therapeutic goals. The guidelines further specify that in rare cases an individual may begin therapy earlier when there is an extremely high level of cholesterol and family history of early coronary disease is prevalent.[5] Considering the above fact, we have put our patient on atorvastatin 10 mg once a day, besides dietary control, though safety and efficacy of statins have yet not sufficiently been supported by the available literature in the age group < 10 years. Further follow up of the patient will make clear the effect of the above mentioned therapy in lowering the serum levels of LDL cholesterol, reducing the size of xanthomas and also in preventing the complications such as coronary artery disease and premature death.

References

1. Goldstein JL, Brown MS. Metabolic basis of inherited disease. In: Stanbury JB, editor. New York: McGraw Hill; 1983. p. 672.
2. Risk of fatal coronary heart disease in familial hypercholesterolemia. Steering committee of the Simion Broome Register Group. BMJ 1991;303:893-6.
3. Parker F. Disorders of metabolism. In: Moschella SL, Hurley HJ, editors. Dermatology. 3rd ed, Vol. 2. Philadelphia: WB Saunders Company; 1992. p. 1653.
4. Brown MS, Goldstein JL. The hyperlipoproteinemia and other disorders of lipid metabolism. In: Wilson JD, Braunwald E, Isselbacher KJ, Peterdorf RG, Martin JB, Fauci AS, *et al*. editors. Harrison's Principles of Internal Medicine. 12th ed, Vol. 2. New York: McGraw-Hill; 1992. p. 1820.
5. Neal WA. Disorders of lipoprotein metabolism and transport. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BF, editors. Nelson Text book of Pediatrics. 18th ed. Philadelphia: Saunders; 2007. p. 580-93.

6. Lahiri BC, Lahiri K. Homozygous hypercholesterolemia with cutaneous and tendinous xanthoma in a child. Indian J Dermatol 2000;45:205-7.
7. Somwanshi PR, Agarwal SN. Homozygous familial hypercholesterolemia. Indian J Dermatol Venereol Leprol 2000;66:331-2.
8. Thompson GR. The hyperlipidaemias. In: Uyod JK, Scriver CR, editors. Genetic and metabolic diseases in pediatrics. London: Butterworth; 1985. p. 211-33.
9. West RJ, Lloyd JK. Hypercholesterolemia in childhood. Adv Pediatr 1979;26:1-34.
10. Lavie CJ, Gau GT, Squires RW, Kottke B, Management of lipids in primary and secondary prevention of cardiovascular diseases. Mayo Clin Proc 1988;63:605-21.

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