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Case Report

Tuberous xanthoma in type 1 familial hypercholesterolemia

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ABSTRACT

Familial hypercholesterolemia (FH) is a genetic disease in which there is high low-density lipoprotein cholesterol levels due to mutation in the gene encoding the receptor for low-density lipoprotein (LDL) located on chromosome 19 and the patients are at high risk for cardiovascular disease, cerebrovascular accidents, metabolic syndrome, and premature coronary death. We present this rare genetic disorder in a 7-year-old boy. The clinicians should be aware of this condition as early diagnosis and treatment can reduce the morbidity and mortality rate associated with the condition.

Keywords: Tuberous, Xanthoma, Familial, Hypercholesterolemia, LDL

INTRODUCTION

Familial hypercholesterolemia (FH) is a genetic disease in which there is high low-density lipoprotein cholesterol levels due to mutation in the gene encoding the receptor for low-density lipoprotein (LDL) located on chromosome 19 and the patients are at high risk for cardiovascular disease, cerebrovascular accidents, metabolic syndrome, and premature coronary death. Xanthomas are localized lipid deposits which occurs due to alterations in lipid metabolism. They can be the presentation of a serious underlying lipid abnormality. In children, they are mostly associated with abnormalities of cholesterol metabolism with hypercholesterolemia and high LDL cholesterol.[1]

CASE REPORT

A 7-year-old male child, 2nd born of non-consanguineous marriage presented with asymptomatic raised lesions over buttocks, ankle, knee and elbow since 3 years of age which was slowly increasing in size. There was no history of any unexplained or early deaths in family. Examination revealed weight of 22 kg (-1.2 SD score for age) and height of 128 cm (-0.27 SD for age) and head circumference 51 cm (-1 SD). There was no pallor, clubbing, cyanosis, icterus, lymphadenopathy. There were no dysmorphism or neurocutaneous markers. He was afebrile with a pulse rate of 96/minute, respiratory rate of 24/minutes and blood pressure of 100/60 mmHg (25-50th centile) measured on right arm in supine position. The cardiovascular examination was essentially normal. There were diffuse, flat xanthomas on his buttocks, elbows and large tuberous xanthomas on his ankle (Figure 1a and b). The patient had a serum LDL cholesterol level of more than 840 mg per deciliter (21.8 mmol per liter); the LDL cholesterol level was 440 mg per deciliter (11.4 mmol per liter). Father had total cholesterol level of 350 mg per deciliter (9.09 mmol per liter) and LDL cholesterol level 254 mg per decilitre (6.59 mmol per liter). The mother and other sibling had normal report. The blood sugar, thyroid profile, liver function test and ultrasonography of the abdomen were normal. The echocardiography was normal. The eye and hearing assessment was normal. The skin biopsy showed sheets of foamy histiocytes admixed with fibroblast (Figure 1c). The whole exome sequencing identified two heterozygous pathogenic indel variant (variant 1 (c.1246_1249delCGGA: p.Arg416fs and variant 2 (c.2416dupG; p.Val806fs) in LDLR gene.

Genetic testing for familial hypercholesterolemia (FH) revealed compound heterozygous pathogenic variant in LDLR gene. Parental testing was not done due to resource constraints. The secondary causes of hyperlipidemias such as hepatic disease, diabetes mellitus, nephrotic syndrome, hypothyroidism, and drug-induced was ruled out and a diagnosis of FH type 1 was made based on the clinical presentation of xanthoma, lipid profile testing and positive genetic report.

The child was prescribed daily treatment with atorvastatin (10 mg) and ezetimibe (10 mg) along with strict dietary restriction of saturated fatty acid and lifestyle modification, which resulted in a moderate reduction in their LDL cholesterol levels.

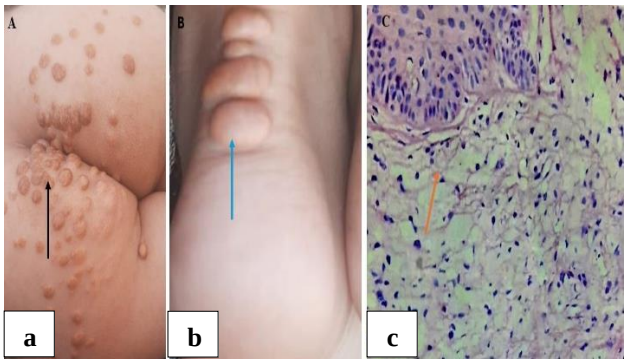

Figure 1: (a) Diffuse flat xanthomas over buttocks, (b) large tuberous xanthomas over ankle, and (c) at 40x magnification, histopathological examination (haematoxylin and eosin staining) of the skin from the right elbow showed sheets of foamy histiocytes admixed with fibroblasts and lymphocytes.

DISCUSSION

FH is an autosomal dominant genetic disorder caused by a mutation in the gene encoding the receptor for LDL located on chromosome 19.[2] FH most commonly presents as heterozygous form, becomes symptomatic in the third and sixth decades, and responds well to treatment. Whereas homozygous state is rare and presents in early childhood with poor response to therapy.[3] Xanthomas are the characteristics lesion which is lipid-containing papules, plaques, nodules, or tumors that may be found anywhere on the skin and mucous membranes. Although the mechanism of their formation is not completely understood, it appears that serum lipids infiltrate the tissues where they are phagocytized by macrophages to form lipid-laden foam cells.[4,5]

Children with this condition are at risk of early-onset atherosclerosis, aortic valve disease, metabolic syndrome, cardiovascular accident, and premature coronary death. A very aggressive dietary restriction of saturated fat, cholesterol-lowering drugs should be initiated as soon as possible to prevent or delay the development of coronary heart disease.[6] The diagnosis is usually made by biochemical and clinical evaluation.[7,8] However, LDL receptor activity and genetic mutational analysis can also be done for further confirmation.[9,10] Treatment with a statin and ezetimibe must be started at diagnosis.

CONCLUSION

Detection of xanthomas in a child should raise suspicion for underlying hyperlipidemia and screening of parents and other siblings should be done for FH. Early diagnosis and treatment can reduce the morbidity and mortality rate associated with the condition.

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REFERENCES

1. Singh S, Bittner V. Familial hypercholesterolemia epidemiology, diagnosis, and screening. Curr Atheroscler Rep. 2015;17:482.
2. Paller AS, Mancini AJ. Inborn errors of metabolism. In: Hurwitz Clinical Pediatric Dermatology: A Textbook of Skin Disorders of Childhood and Adolescence. 5th edition. Canada: Elsevier Saunders. 2016;564.
3. Van Aalst Cohen ES, Jansen AC, de Jongh S, de Sauvage Nolting PR, Kastelein JJ. Clinical, diagnostic, and therapeutic aspects of familial hypercholesterolemia. Semin Vasc Med. 2004;4:31-41.
4. Mabuchi H. Half a century tales of familial hypercholesterolemia (FH) in Japan. J Atheroscler Thromb. 2017;24:189 207.
5. Davidson MH. A systematic review of bile acid sequestrant therapy in children with familial hypercholesterolemia. J Clin Lipidol. 2011;5:76 81.
6. Brown MS, Goldstein JL. A receptor mediated pathway for cholesterol homeostasis. Science. 1986;232:34 47.
7. Wiegman A, Gidding SS, Watts GF, Chapman MJ, Ginsberg HN, Cuchel M, et al. Familial hypercholesterolaemia in children and adolescents: Gaining decades of life by optimizing detection and treatment. Eur Heart J. 2015;36:2425 37.
8. Kolansky DM, Cuchel M, Clark BJ, Paridon S, McCrindle BW, Wiegers SE, et al. Longitudinal evaluation and assessment of cardiovascular disease in patients with homozygous familial hypercholesterolemia. Am J Cardiol. 2008;102:1438 43.
9. Holzer G, Volc-Platzer B. Skin Manifestations of Paediatric Metabolic Syndrome. In: Hoeger PH, Kinsler VA, Yan AC, Harper J, Oranje AP, Bodemer C, et al. Harper's Textbook of Paediatric Dermatology, 4th edition. Hoboken, New Jersey: Wiley-Blackwell. 2019;841-58.
10. Widhalm K, Binder CB, Kreissl A, Aldover Macasaet E, Fritsch M, Kroisboeck S, et al. Sudden death in a 4 year old boy: A near complete occlusion

of the coronary artery caused by an aggressive low density lipoprotein receptor mutation (W556R) in homozygous familial hypercholesterolemia. J Pediatr. 2011;158:167.

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