International Journal of Health Sciences and Research
Vol.11; Issue: 3; March 2021
Website: www.ijhsr.org
Case Report *ISSN: 2249-9571*

Familial Hypercholesterolemia with Coronary Artery Disease in a Nine Year Old Girl

Setu P. Dagli[1], Arpita Thakker Adhikari[2], Mona P. Gajre[3]

[1]MBBS, Intern, Lokmanya Tilak Municipal Medical College and General Hospital, Mumbai
[2]MD, Professor, Department of Pediatrics, Lokmanya Tilak Municipal Medical College and General Hospital, Mumbai
[3]MD, Professor, Department of Pediatrics, Lokmanya Tilak Municipal Medical College and General Hospital, Mumbai

Corresponding Author: Arpita Thakker Adhikari

ABSTRACT

Familial Hypercholesterolemia is an inherited disorder of lipid metabolism. We present case of a nine year old girl with chest pain and multiple xanthomas. Her lipid profile showed increased levels low density and very low density lipoproteins and triglycerides. Her ECG had ST abnormalities. Major arteries had luminal narrowing and her Angiography revealed Triple Vessel Disease. Angioplasty with stent placement was done and she was advised aggressive diet modification and medical management.

Keywords: Familial hypercholesterolemia, Xanthoma, low density lipoprotein, cholesterol

INTRODUCTION

Familial hypercholesterolemia (FH) is a hereditary dyslipidemia characterized primarily by high levels of plasma cholesterol and low density lipoprotein (LDL) along with xanthomas, xanthelasma and premature coronary artery disease. It is caused by a mutation of the LDL receptor gene on Chromosome 19. This disease continues to be gravely underdiagnosed and therefore early diagnosis, aggressive treatment and screening of first degree relatives is of paramount importance to decrease morbidity and mortality.

CASE REPORT

A 9 year old girl, 2nd by birth order, born out of a 3rd degree consanguineous marriage, presented with chief complaints of multiple nodules on the joints of the body since 2.5 years and chest pain since 4-5 hours. The nodules first appeared on her knee joint. They were of insidious onset and gradually increased in size. They gradually spread to the wrist, elbow, ankle and the interphalangeal joints of both upper limbs and lower limbs. They were not associated with pain, itching or discharge.

5 hours ago, she was admitted with chest pain which was retrosternal, squeezing in nature, was aggravated on exertional activities such as running or climbing stairs and was relieved by rest. It was associated with dyspnea, Grade II progressing to Grade III. She had multiple episodes of similar pain in the last 1.5 months. She had no history of congenital heart disorders. Her father had been diagnosed with hypercholesterolemia 4 years ago.

Upon examination, she was alert, cooperative and well oriented to time place and person and averagely built and nourished. Her pulse was 112/min in the right radial artery in sitting position, regular in rate, rhythm, volume, force and tension, bilaterally equal with no radio-radio or radio-femoral delay, and all peripheral pulses were felt. Her blood pressure was 102/68mm of Hg in right brachial artery in sitting position. No Pallor, icterus, cyanosis,

clubbing, edema or lymphadenopathy was found. Her anthropometrical parameters were adequate for her age.

Her skull and spine appeared normal. Multiple xanthomas, about 2*3 cm were seen on the elbow, wrist, metacarpophalangeal, knee, metatarsophalangeal and interphalangeal joints and Achilles tendon. *(Figures1, 2, 3)* They were spherical, firm, smooth and non tender. There were no scars, sinuses or dilated veins surrounding the swellings and the overlying skin appeared normal.

Her cardiovascular and other systemic examination was unremarkable.

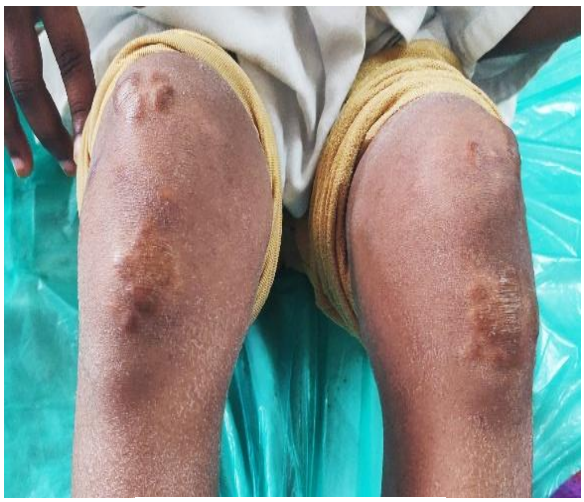

Figure 1: Xanthomas on knee joint

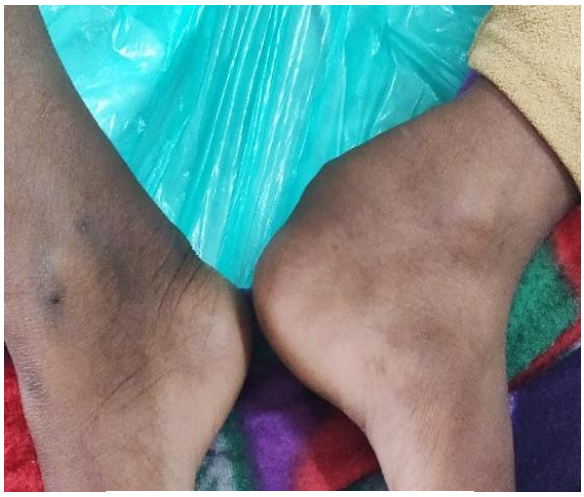

Figure 2: Xanthomas on Achilles Tendon

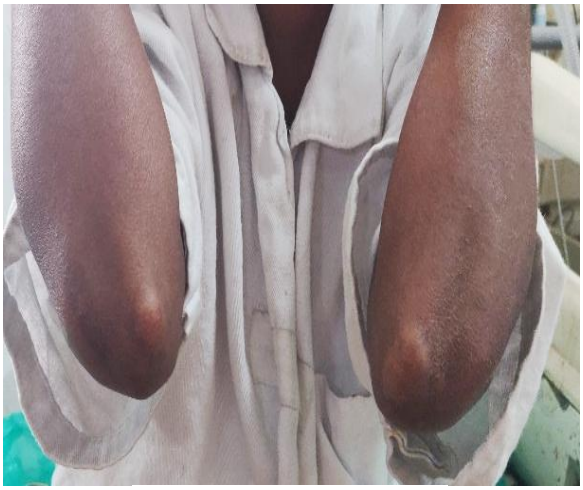

Figure 3: Xanthoma on Elbow joint

Investigations

Lipid profile

TEST NAME	RESULT	REFERENCE
Total Cholesterol	**1010**	150-250mg/dl
HDL	62	35-80mg/dl
LDL	**898**	90-160mg/dl
VLDL	**50**	10-30mg/dl
Triglycerides	**250**	50-150mg/dl

ECG showed widespread ST-T abnormality.

Hemogram and other blood reports were normal.

Echocardiography showed a moderate MR with posteriorly directed flow and calcification of the ostium of the left main Coronary artery.

Screening of major arteries showed extensive, diffuse, concentric intimomedial thickening involving bilateral Carotid, Subclavian and Brachiocephalic Arteries, mid luminal narrowing of bilateral radial arteries and elevated peak systolic velocity in left Renal Artery.

Angiography showed Triple Vessel Disease

The Left Main Coronary artery showed 50-55% stenosis in the middle part. The Left Descending Artery (LAD) showed 60-70% stenosis followed by a plaque proximally, 60% discreet stenosis in mid LAD and 70-75% stenosis at the D1 ostium. The Left circumflex artery (LCx) showed 90-95% stenosis at the origin with mid LCx showing 50% stenosis.

Right Coronary artery showed 50% stenosis at the ostium, a plaque proximally and Rentrop Grade III intracardiac collaterals arising from the RCA and filling LCx retrogradely.

Left Subclavian Artery showed 50% stenosis and Right Subclavian Artery showed a plaque

Left Renal Artery showed 50% stenosis at the ostium.

She was diagnosed with Familial hypercholesterolemia type IIA with Diffuse Multiversal Atherosclerosis and Moderate MR and underwent Percutaneous Transluminal Coronary Angioplasty with stent placement at LAD and LCx. She was treated with a 3-hydroxy-3-methyl-glutaryl-coenzyme inhibitor (Rosuvastatin 40 mg), Ezetimibe 10mg, Aspirin 75 mg and Clopidogrel 37.5 mg once a day. She was advised aggressive diet and lifestyle management.

The xanthomas softened upon treatment with Rosuvastatin and her angina was relieved. However her lipid profile continued to be deranged. She was advised LDL apheresis but it could not be done due to financial constraints.

DISCUSSION

Hyperlipidemia is caused by increased concentration of plasma lipoproteins. It can be primary or secondary. Secondary hyperlipidemia occurs due to alterations in lipoprotein metabolism commonly caused due to Diabetes mellitus, hypothyroidism, nephrotic syndrome, etc. Primary Hyperlipidemia is caused due to genetic defects. Mutations have been found in four genes. The most common ones include LDL receptor and Apo lipoprotein B. Proprotein convertase subtilin/kexin 9 and LDL receptor adaptor protein mutations are less common[1].The triad of Hypercholesterolemia, xanthomas and angina has been described as a dominantly inherited syndrome.[2] Our patient had triple vessel disease, multiple xanthomas and angina. Over 400 genetic mutations causing this triad have been identified[3]. Classically, lipid levels are deranged at birth and continue to be throughout life.

Familial hypercholesterolemia is a autosomal dominant disorder. The incidence of the heterozygous form is approximately 1 in 500-550 individuals. Homozygotes (like in our case) are found approximately 1 in a million[4.] Heterozygotes manifest with asymptomatic hypercholesterolemia at birth and present with symptoms of varying severities only in adulthood[5.] Homozygotes typically present with xanthomas in early childhood and cardiovascular abnormalities in their twenties and thirties. There have, however been reports of Homozygotes succumbing to Myocardial infarctions as early as 18 months of age. [6] Our patient had cardiovascular anomalies at the age of 9.

FH is characterized by atheroma and xanthomas. Tendon xanthomas are found in 40% of the patients and are pathognomonic for the condition.[7] It can be diagnosed both clinically, on the basis of history, examination and lipid levels and genetically by detecting a pathological mutation. The International panel on Management of Familial Hypercholesterolemia has recommended 3 sets of criteria: "The Simon Broome criteria, The Dutch Lipid Network and The Make Early Diagnosis to Prevent Early Death criteria" to reach a diagnosis. [7] Patients of FH are often young and thin and do not possess any comorbidities or risk factors for cardiovascular disease.[7] Our patient was also diagnosed with Mitral Regurgitation which is rather uncommon in patients of Homozygous FH as compared to Aortic valve lesions[8]

Treatment is primarily lifestyle and diet modifications along with high dose multidrug therapy. Statins along with Ezetimibe and Bile acid sequestrants are known to decline the LDL cholesterol levels.[7] The American Heart Association suggests the initiation of pharmacotherapy at age 10 years in boys and after the onset of puberty in girls with high-risk lipid abnormalities.[7] However in our case the patient was homozygous and developed cardiovascular abnormalities earlier than

most patients, prompting the initiation of statins. If they do not show satisfactory results they can be combined with LDL apheresis on a biweekly basis. This has been shown to reduce the cholesterol levels by almost 60%[9]. It is however extremely expensive and out of reach of several patients. Gene therapy is still undergoing clinical trials.[10] Lomitapide and Mipomersen sodium have been tried successfully in patients of FH[11,12,13]. Liver transplants and partial ileal bypass have also been tried to treat FH with some success.

The importance of early identification of patients and prompt initiation of treatment is reiterated by the fact that approximately 85% of the males and 50% of females with FH will suffer a coronary event before the age of 65 if appropriate interventions are not implemented.[7] Adequate diagnosis, meticulous treatment, strict compliance to lifestyle changes and appropriate screening and genetic counselling of first degree relatives with drastically improve the quality of life of these patients.

ACKNOWLEDGEMENT

We would like to Acknowledge D.A. Mahajan, Professor and head of Unit, Department of Cardiology, Lokmanya Tilak Municipal Medical College and General Hospital, Mumbai.

REFERENCES

1. Singh S, Bittner V. Familial hypercholesterolemia-epidemiology, diagnosis, and screening. Current atherosclerosis reports. 2015 Feb 1;17(2):3.
2. Müller C. Xanthomata, hypercholesterolemia, angina pectoris. Acta Medica Scandinavica. 1938 Jan 12;95(S89):75-84.
3. Brown MS, Herz J, Goldstein JL. Calcium cages, acid baths and recycling receptors. Nature. 1997 Aug;388(6643):629-30.
4. Lavin N. Manual of endocrinology and metabolism. Lippincott Williams & Wilkins; 2012 Mar 28.
5. Goldstein JL. Familial hypercholesterolemia.
6. Fredrickson, D.S., and Levy, R.I.: Familial hyperlipoproteinemia, in Stanbury, J.B., Wyngaarden, J.B., and Fredrickson, D.S. (eds.) The Metabolic Basis of Inherited Disease, 3rd ed. (New York: McGraw-Hill Book Co., 1972), pp. 545-614.
7. Civeira F, International Panel on Management of Familial Hypercholesterolemia. Guidelines for the diagnosis and management of heterozygous familial hypercholesterolemia. Atherosclerosis. 2004 Mar 1;173(1):55-68.
8. Fahed AC, Shibbani K, Andary RR, Arabi MT, Habib RH, Nguyen DD, Haddad FF, Moubarak E, Nemer G, Azar ST, Bitar FF. Premature valvular heart disease in homozygous familial hypercholesterolemia. Cholesterol. 2017;2017.
9. Mabuchi H, Koizumi J, Shimizu M, Kajinami K, Miyamoto S, Ueda K, Takegoshi T. Long-term efficacy of low-density lipoprotein apheresis on coronary heart disease in familial hypercholesterolemia. The American journal of cardiology. 1998 Dec 15;82(12): 1489-95.
10. Oka K, Pastore L, Kim IH, Merched A, Nomura S, Lee HJ, Merched-Sauvage M, Arden-Riley C, Lee B, Finegold M, Beaudet A. Long-Term Stable Correction of Low-Density Lipoprotein Receptor–Deficient Mice With a Helper-Dependent Adenoviral Vector Expressing the Very Low-Density Lipoprotein Receptor. Circulation. 2001 Mar 6;103(9):1274-81.
11. Rader DJ, Kastelein JJ. Lomitapide and mipomersen: two first-in-class drugs for reducing low-density lipoprotein cholesterol in patients with homozygous familial hypercholesterolemia. Circulation. 2014 Mar 4;129(9):1022-32.
12. Cuchel M, Blom DJ, Averna MR. Clinical experience of lomitapide therapy in patients with homozygous familial hypercholesterolaemia. Atherosclerosis Supplements. 2014 Sep 1;15(2):33-45.
13. Raal FJ, Santos RD, Blom DJ, Marais AD, Charng MJ, Cromwell WC, Lachmann RH, Gaudet D, Tan JL, Chasan-Taber S, Tribble DL.

Mipomersen, an apolipoprotein B synthesis inhibitor, for lowering of LDL cholesterol concentrations in patients with homozygous familial hypercholestero-laemia: a randomised, double-blind, placebo-controlled trial. The Lancet. 2010 Mar 20;375(9719):998-1006.

How to cite this article: Dagli SP, Adhikari AT, Gajre MP. Familial hypercholesterolemia with coronary artery disease in a nine year old girl. *Int J Health Sci Res.* 2021; 11(3):78-82.

******