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Case Report

A rare case of hypercholesterolemia in a young girl

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Introduction

Familial hypercholesterolemia though recognized in children is rarely reported with severe manifestations in early childhood. We report a child who presented with xanthomas with hypercholesterolemia at age of 7 years. She was put on statin therapy but in next 3 years had rapid progression of disease with development of severe valvular and supravalvular aortic stenosis, coronary artery disease and diffuse narrowing of descending thoracic aorta.

Case report

A 7-year-old female patient presented with multiple raised, firm, cutaneous swellings of 5–8 mm size over elbow and

buttocks when she was recognized to be having tuberous xanthomas and dyslipidemia. She had raised total cholesterol to 600 mg/dl and LDL 430 mg/dl while triglycerides were 160 mg/dl, HDL 70 mg/dl and VLDL was 25 mg/dl. She was prescribed Atorvastatin 10 mg a day along with dietary restrictions and exercise regimen but she was lost to follow up though as per parents they followed the given advice.

At age of 10 years she reported with us with complaints of progressive dyspnea on exertion for last 2 months which had now progressed to New York Heart Association (NYHA) class IV. On examination she was thin built, had blood pressure of 90/60 mmHg in both upper limbs while lower limb BP was 100/60 mmHg. She had multiple xanthomas over wrist, hands, knees, elbows and buttocks (Figs. 1–4). Cardiovascular system examination revealed apical impulse shifted to 7th intercostal space in left anterior axillary line, normal S1, soft S2, Grade IV/VI ejection systolic murmur over left parasternal region and right 2nd intercostal space. The murmur was radiating over the carotids into neck. Chest radiograph demonstrated cardiomegaly with CT ratio 0.65:1 and electrocardiogram revealed sinus rhythm with features of left ventricular hypertrophy. There was no evidence of myocardial ischemia. Transthoracic echocardiography showed bicuspid aortic valve which was doming. Trivial aortic regurgitation was also present. There was severe aortic stenosis with gradient of 80 mmHg. Aortic annulus diameter was 10 mm with associated narrowing of supravalvular region of aorta with diameter of 11 mm while ascending aorta with post-stenotic dilatation was of 17 mm (Fig. 5). Left ventricle had concentric hypertrophy with ejection fraction of 60%. Lipid profile demonstrated total

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Fig. 1 – Xanthomas over fingers.

Fig. 3 – Xanthomas over elbow.

cholesterol 583 mg%, LDL 423 mg% with normal triglycerides, HDL and VLDL levels.

In view of her NYHA class IV status patient was not considered fit for any anesthesia and surgery. As a palliative measure balloon dilatation of aortic valve was attempted.

Gradient across aortic valve was recorded as 76 mm while catheter pull back recorded additional gradient of 30 mm in supra-ventricular region thus proving presence of both valvular and supra-ventricular aortic stenosis. Balloon dilatation was

Fig. 2 – Xanthomas over knee joint.

Fig. 4 – Xanthomas over buttocks.

Fig. 5 – Aortic root angiogram showing narrowing of aortic root with post-stenotic dilatation of ascending aorta and ostial stenosis of coronary arteries.

Fig. 6 – Aortogram showing diffuse narrowing of descending thoracic aorta.

performed with a 9 mm balloon which brought down the gradient across aortic valve to 45 mm. Incidentally aortic root angiogram also demonstrated presence of left main coronary artery stenosis with diameter narrowing to 50%. Right coronary artery was also stenosed at origin in diameter by approximately 40%. Patient had symptomatic improvement and became NYHA class II. She was offered surgery for supravulvular aortic stenosis with coronary artery bypass grafting. In view of explained risks, parents opted for medical management only. Patient remained in NYHA class II for next 4 months but progressively deteriorated.

She was brought to hospital again when she was found to be in NYHA class IV and now parents gave consent for surgical management. Echocardiography revealed left ventricular ejection fraction 60% with gradient of 80 mm across supra-aortic region. Electrocardiogram revealed no features of ischemia. During induction of anesthesia femoral arteries were found to be weak with radio femoral delay. Blood pressure in lower limbs was 70/60 mm as compared to upper limb blood pressure of 100/60 mm. Repeat echocardiogram did not demonstrate any narrowing till level of isthmus. A check angiogram was performed in catheterization laboratory located close to operation theater. Descending aorta had diffuse long segment narrowing from isthmus to origin of celiac arteries (Fig. 6). Surgery was abandoned and patient succumbed to her illness in next 4 days.

She was the only child, a product of non-consanguineous marriage and both parents had normal lipid profile.

Discussion

Familial hypercholesterolemia (FH) is an autosomal dominantly inherited disorder. FH is caused by mutations in the LDL receptor, which prevents its synthesis, reduces its appearance on cell surface or impairs its ability to bind and internalize LDL. Heterozygous FH occurs in approximately 1 in 500 people and is characterized by elevated total & LDL cholesterol levels with normal triglycerides and a family history of hypercholesterolemia or premature cardiovascular disease.¹ Consensus paper released in 2011 recommends that screening for children suspected to be having familial hypercholesterolemia should be performed.²

Homozygous FH is rare and occurs in approximately 1 in 1 million persons worldwide and is a much more severe clinical disorder than heterozygous FH. These patients are further classified into two groups based on the LDL cholesterol level and the amount of LDL receptor activity measured in their skin fibroblasts. Receptor negative patients are the one who have less than 2% of normal LDL receptor activity and higher LDL cholesterol levels. They present in childhood with cutaneous xanthomas on hands, wrists, elbows, knees, heels or buttocks. The serious complications of homozygous FH is accelerated atherosclerosis, which can result in clinical sequelae even in childhood. Premature coronary artery disease and atheromatous involvement of aortic valve and

aortic root are almost always present in homozygotes.³ Though several reports with patients of hypercholesterolemia are reported in literature,^{4,5} patient with such severe disease and rapid progression inspite of adequate dietary management and drug therapy must be rare. Rigorous low fat diet containing more grain products, fruits, vegetables, low fat milk substitutes, beans, poultry, fish and other protein rich foods should be given to child. These dietary recommendations provide adequate calories for optimal growth & development without promoting obesity. Compliance about following strict dietary regimen by children is difficult to follow hence if the same menu should be followed by all members of the family rather than strictness being applied to the affected child only. As per 1992 NCEP guidelines pharmacological treatment of hyperlipidemia in children should be started after age of 8 years and that also when adequate period of dietary restriction has not achieved the desired therapeutic goals. In patients with homozygous FH and when LDL cholesterol exceeds 500 mg/dl pharmacological treatment should be started even in children younger than 8 years. HMG-CoA reductase inhibitors also called statins are capable of lowering LDL cholesterol levels by half. They also have modest effect in reducing triglycerides. Children on statin therapy should have regular monitoring of liver enzymes and creatinine phosphokinase (CPK). Liver enzymes may be allowed to rise threefold before discontinuing statin therapy. Experience with other cholesterol lowering drugs like nicotinic acid and fibrates is not available in children and are less often used.

The disease per se involves aortic valve, aortic sinuses and aortic root in both heterozygous and homozygous hypercholesterolemia with extensive atheromatous deposition^{6,7} and vascular calcification,⁸ but the extent of involvement of descending aorta is not reported in literature. This patient had severe diffuse long segment involvement of descending thoracic aorta which was well demonstrated by angiography. We recommend that all cases of hypercholesterolemia where aortic valve or aortic root surgery is being contemplated,

should have detailed assessment of descending aorta also as associated diffuse disease may alter the management strategy and effect on prognosis.

Conflicts of interest

All authors have none to declare.

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