Xanthomas heralding pediatric coronary artery disease

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INTRODUCTION

Familial hypercholesterolemia is a form of genetic or primary dyslipidemia, which affects 0.2% of the population.[1] Children with familial hypercholesterolemia are subject to early atherosclerosis, leading to greater risk of coronary events. The presence of xanthomas should thus prompt a thorough evaluation for an underlying lipid abnormality because early detection and aggressive treatment are key. We report a case of a pediatric patient with xanthomas misdiagnosed as keloids who presented with premature coronary artery disease.

CASE REPORT

A previously healthy 14-year-old boy presented to the hospital after sudden cardiac arrest while playing basketball at school. On cardiac catheterization, the patient was found to have significant stenosis of the left main coronary artery, which required urgent coronary artery bypass grafting with implantable cardioverter-defibrillator placement. Inpatient dermatology was consulted for evaluation of asymptomatic lesions overlying the buttocks, hands, elbows, and knees. These lesions had been present for approximately 5 years and had previously been diagnosed as keloids. No previous biopsy or other diagnostic evaluation was performed before admission. Neither the patient nor his mother recalled preceding trauma to the affected areas. Family history was notable for "elevated cholesterol" in the patient's mother.

Physical examination revealed erythematous to yellow, large, firm, nontender, mobile nodules on his elbows (Fig 1), flesh-colored to yellow nodules on the buttocks (Fig 2), and hyperpigmented papules on the dorsal aspect of his hands (Fig 3), his knees, and the dorsal aspect of his feet. Laboratory evaluation revealed a serum cholesterol level of 517 mg/dL, low-density lipoprotein level of 480 mg/dL, high-density lipoprotein level of 21 mg/dL, and triglyceride level of 82 mg/dL. Skin biopsy demonstrated collections of foam cells and lipid-laden macrophages consistent with a xanthoma. On evaluation of medical genetics, the patient was found to be a heterozygous carrier of 2 different low-density lipoprotein receptor defects (*LDLR* c. 1201C>G [p.Leu401Val]; *LDLR* c. 352G>A [p.Asp118Asn]). The patient received a diagnosis of type 2 familial hypercholesterolemia. Medical therapy with atorvastatin, lisinopril, and daily aspirin was initiated. He was recommended a low-fat and high-fiber diet. Four weeks after these lipid-decreasing agents were initiated, some of the xanthomas flattened and decreased in size.

DISCUSSION

Xanthomas are characterized by yellowish papules, plaques, or nodules and occur because of alteration in the lipid metabolism. The characteristic histologic feature of xanthomas is lipid-laden macrophages, also known as foam cells.[2] As demonstrated by this case, xanthomas can be the only presentation of a serious underlying lipid abnormality such as familial hypercholesterolemia. Patients with familial hypercholesterolemia have an increased risk of premature coronary artery disease and eventual heart failure because of elevated levels of low-density lipoprotein cholesterol present from early childhood.[1,3] Familial hypercholesterolemia type 2 is characterized by tendinous xanthomas, tuberous xanthomas, and premature cardiovascular disease.[2] The presence of interdigital planar xanthomas (Fig 3) is presumed to be a pathognomonic feature of homozygous or compound heterozygous

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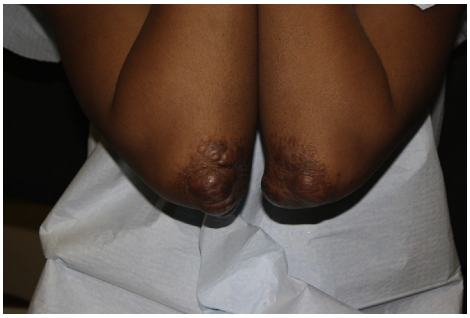

Fig 1. Tuberous xanthomas on the elbows.

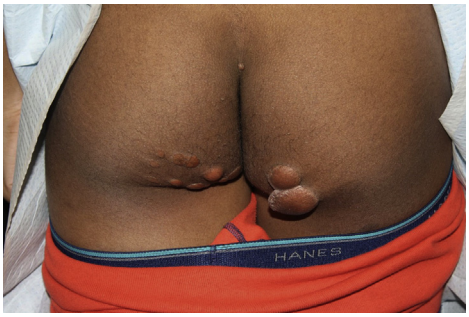

Fig 2. Tuberous xanthomas on the buttocks.

type 2 hypercholesterolemia. As demonstrated in our patient, xanthomas associated with familial hypercholesterolemia often begin to develop before aged 10 years.[4] Our patient was found to be a compound heterozygote, inheriting 2 different mutations of the same gene. Risk stratification of compound heterozygotes is similar to that of true homozygotes, with concern for rapid progression of atherosclerotic cardiovascular disease with early mortality.[4] The pathogenesis of hypercholesterolemia in this patient was likely related to a reduced low-density lipoprotein cholesterol clearance.[5]

Xanthomas are frequently indicators of underlying lipid abnormality. This case highlights the importance of a prompt and thorough evaluation by the clinician to prevent potentially fatal complications. Furthermore, genetic counseling of the family is important. Management typically involves a healthy lifestyle and medications such as statins in combination with bile acid sequestrants, fibrates, ezetimibe, or other lipid-modifying therapy.[6] Pharmacologic treatment of dyslipidemia often leads to concomitant improvement in xanthomas.[6]

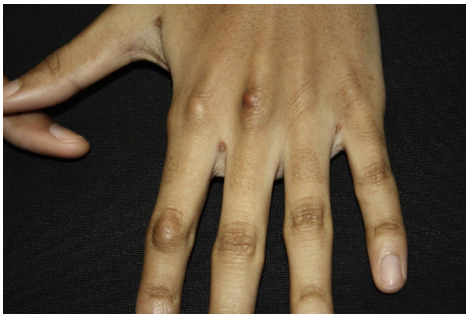

Fig 3. Interdigital xanthomas on the hands.

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