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CASE REPORT / OLGU SUNUMU

Aortic valve involvement and premature coronary artery disease in Heterozygous Familial Hypercholesterolemia

Heterozigot Ailevi Hiperkolesterolemide aort kapağı tutulumu ve erken koroner arter hastalığı

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ABSTRACT

Familial hypercholesterolemia (FH) is an autosomal dominant disorder characterized by an elevation of LDL cholesterol concentration in plasma leading to deposition of excess LDL-derived cholesterol in tendons, skin and arteries. We studied a 34 year old woman who applied to dermatology department due to multiple xanthomas. Cardiac consulting was demanded by dermatology department to determine development of atherosclerosis. Patient had no risk factor and symptom related to cardiac problem, except family history included premature coronary artery disease (CAD). On examination systolic murmur was present in aortic area. Echocardiography showed valvular severe aortic stenosis with a good left ventricle systolic function and severe left ventricular hypertrophy. The coronary arteriogram showed widespread CAD involving 3 coronary vessels. We report a case of heterozygous FH type II a with premature CAD and aortic valve involvement. *J Clin Exp Invest 2011; 2 (3): 308-311.*

Key words: Aortic stenosis, Coronary artery disease, Heterozygous familial hypercholesterolemia

ÖZET

Ailesel hiperkolesterolemi (AH) arterlerde, ciltte ve tendonlarda aşırı kolesterol birikimine yol açan plazma kolesterol yüksekliği ile karakterize otozomal dominant bir hastalıktır. Multipl ksantomlar nedeniyle cildiye polikliniğine başvuran 34 yaşında bayan hasta için aterosklerotik hastalık açısından kardiyoloji konsültasyonu istendi. Hastanın herhangi bir kardiyak şikayeti yoktu. Koroner arter hastalığı (KAH) açısından risk faktörü olarak ailede erken KAH öyküsü mevcuttu. Fizik muayenede aort odakta 3/6 sistolik üfürüm saptandı. Yapılan ekokardiyografide ciddi aort darlığı saptandı. Yapılan koroner anjiografide 3 koroner damarın etkilendiği yaygın KAH saptandı. Biz bu yazıda aort kapak tutulumu ve erken yaşta KAH nın eşlik ettiği heterozigos AH vakasını sunduk. *Klin Deney Ar Derg 2011; 2 (3): 308-311.*

Anahtar kelimeler: Aort stenozu, koroner arter hastalığı, heterozigoz ailesel hiperlipidemi

INTRODUCTION

Familial hypercholesterolemia (FH) is a common autosomal dominant disorder caused by a mutation of the gene for the low-density lipoprotein (LDL) receptor.[1] FH is usually a manifestation of increased levels of LDL cholesterol. Triglyceride levels are usually normal (type II a) or may be elevated (type IIb). Heterozygous FH (HeFH) (1:500) more frequent than homozygous FH (HoFH) (1:1 000 000) in general population.[2] FH is characterized by a high level of dominantly inherited hypercholesterolemia, early appearance of cutaneous and tendon xanthomata, and increased risk of premature coronary artery disease (CAD). Approximately 85% of males and 50% females of suffer from coronary events before 65 years old if they are not treated.[3] The rate of death from CAD among HeFH patients is several times higher than that among the general population.[4] Hyper cholesterolemi affects not only the coronary artery, but also cardiac valve especially aortic valve and aortic root. Hyperlipidemia is associated with degenerative aortic valve stenosis, and the disease resembles the inflammatory process of atherosclerosis.[5] Hypercholesterolemia constitute

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an important factor for etyologies of aortic stenosis in adult patients. We report a case of HeFH type II a with concomitant aortic stenosis and coronary artery disease involving three vessels.

CASE

A 34 year old female patient applied to dermatology department due to xanthomata. Cutaneous examination of the case revealed multiple eruptive yellowish papules on the eyelids, trunk, and limbs. There were a few nodules covering the ankle joints and feet of patient. Yellowish papules were detected on the interdigital web space of the fingers (Figure 1). Mucosa, hair and nails were normal. Although the patient had no symptom related to cardiac problem cardiac consulting was demanded by dermatology department to determine development of atherosclerosis. The patient had no risk factors for cardiovascular disease except family history including death of her brother due to cardiac problem at the age of 30 during operation making for removal of multiple xanthomas and her father and uncle had coronary arter disease. However, her mother and other siblings didn't have hyperlipidemia, thereby indicating HeFH in this patient. The patient's blood pressure was 120/70 and pulse rate was regular (96 beats/min). On cardiac examination, a systolic ejection murmur was heard in aortic area. Electrocardiography (ECG) revealed normal sinus rhythm. Total cholesterol, triglyceride, HDL and LDL values were 493, 121, 24, and 442 mg/dL, respectively. Echocardiography demonstrated left ventricle hypertrophy with normal systolic function, calcified and degenerative aortic valve with limited opening and 44 mm Hg mean gradient across the aortic valve (Figure 2). Aortic valve area was 1.2 cm^2. The mitral valve was looked high-echogenic and thickened but gradient was not obtained. Coronary anjiography detected 60% occlusion at the proximal to Left Anterior Desending (LAD) before D1 branch, 40% occlusion at LAD mid-portion, 40% occlusion at Circumflex artery (Cx) mid-portion, and 100% occlusion proximal to Right Coronary Artery (RCA). Retrograde flow of RCA was also present from Cx artery. Medical therapy was initiated for prevention of secondary coronary arter dissease and progretion of aortic stenosis.. Hypercholesterolemia was managed with atorvastatin 80 mg per day. Because the patient had no symptom related to cardiac problem routine follow-up was advised.

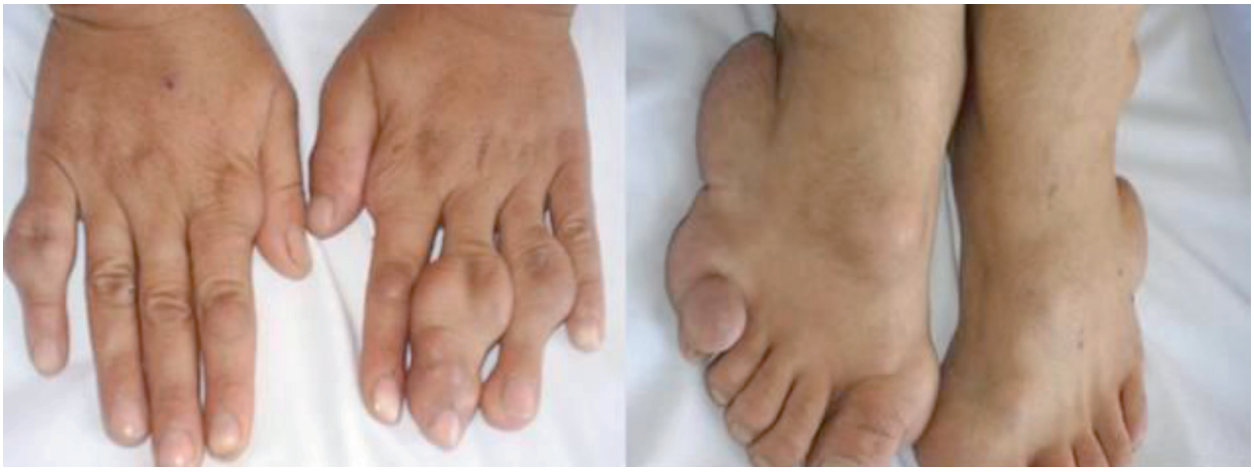

Figure 1. Multiple xanthomata showed on fingers of hand and foot.

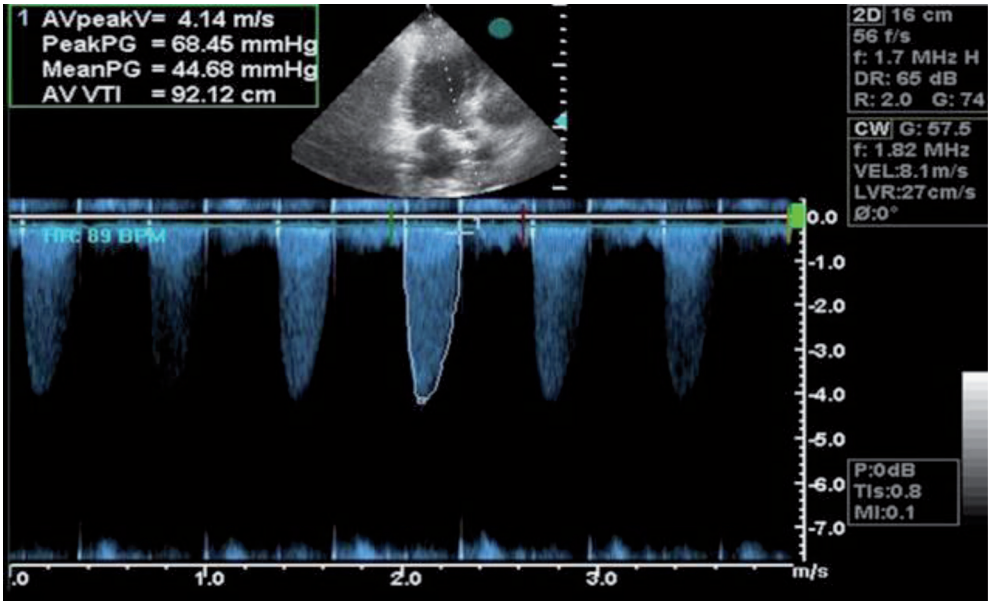

Figure2. Gradient was obtained on the aortic valve

DISCUSSION

HeFH, with incidence of 1 in 500, is the most common known monogenic form of inherited metabolic disease.[2] It is characterized by markedly elevated plasma concentrations of LDL cholesterol. HeFH patients usually have a twofold increase in total cholesterol and LDL-derived cholesterol and typically present with cardiovascular disease in their 30s and 40s as in our patient. If undiagnosed and untreated, the cumulative risk of CAD by age 60 years is more than 60% among men and more than 30% among women with FH.[6] CAD is the major cause of death in HeFH.[7] Excess rates of death from CAD in people with HeFH were highest between the ages of 20 and 39 years. Thus, HeFH was associated with a markedly increased risk of death, especially among young adults.[8] In view of the markedly high LDL and total cholesterol levels, normal triglyceride level, presence of tendon xanthomata, premature coronary lesions and propable autosomal dominant inheritance (since father and brother are involved), FH would be the most propable type of hyperlipidemia in our case. Although aortic valve involvement is rarely seen in heterozygotes our patient propably heterozygous since the mother and other siblings are not hyperlipidemic and the patient present with cardiovascular disease at the age of 34 year. Atherosclerosis affects the aortic valve as well as the aorta and coronary vessels, resulting in life threatening aortic stenosis. Aortic stenosis is critical to the prognosis for most homoFH and some HeFH patients.[9] HeFH patients who require surgical replacement, show additional risk factors suh as high blood pressure, smoking, and / or diabetes mellitus which all contribute to the aggravation of aortic valvular dysfunction result from underlying hypercholesterolemia.[10] Our patient did not have additional risk factory and severe aortic stenosis. The most common cause of AS is slow progressive calcific degeneration, with an asymptomatic period which can last decade's 10; therefore, it was thought that calcific AS resulted from aging and 'wear and tear' of the aortic valve.. Currently, this perception has been changing and some similarities have been found between the lesions of AS and atheromatous coronary artery disease 10 and calcific AS is being increasingly recognized as an inflammatory, atheromatous and potentially modifiable disease. The young age of the patient indicates etiologic factors other than wear and tear due to ageing processes. In conclusion HeFH is a treatable and important cause of early CAD and valvular lesions, thus it is important that this condition be recognized, diagnosed and treated in affected patients.

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