CASE REPORT

# Familial dysbetalipoproteinaemia presenting with cauliflower xanthoma

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## ABSTRACT

Familial dysbetalipoproteinaemia (FDL) is an inherited disorder in which both cholesterol and triglycerides are elevated in the plasma, pre-disposing the people to coronary artery disease and peripheral vascular disease. The disease is mostly manifested by xanthomas, which have variable forms according to lipid amounts in the plasma of the blood. Hereby, we report a 43-year-old man with FDL, presenting with a rare form of xanthomas calling "Cauliflower xanthoma" all over the body.

**Key words:** Cauliflower xanthoma, familial dysbetalipoproteinaemia, hyperlipidaemia, metabolism disorders

## INTRODUCTION

Type III dysbetalipoproteinaemia is a kind of lipid metabolism disorders, caused by apo-E deficiency, which leads to accumulation of chylomicrons and very low density lipoprotein remnants in the plasma.[1-3]

Lipid metabolism disorders are mostly manifested by xanthomas, which are known as yellowish cholesterol-rich material in large foam cells accumulating in the skins and tendons.[1,4] These yellowish lesions may appear all over the body, on the palm of the hands, sole of the foot, tendons, and even on the eyelids.[5]

These lesions firstly described with or without hyperlipidaemia in association with monoclonal immunoglobulin. Based on this fact, there are three forms of xanthoma: Hyperlipaemic xanthoma, normolipaemic xanthoma and necrobiotic xanthogranuloma.[6] Xanthomatosis is usually associated with hyperlipidaemia, and morbidity and mortality of this condition are related to atherosclerosis and pancreatitis.[7] Hyperlipaemic xanthoma lesions are more polymorphic and can include tuberous, tendinous, palmar or eruptive xanthoma. Verruciform xanthoma usually presents as a hyperkeratotic, cauliflower like, verrucous or papillomatous lesion.[6] It initially was described as a unique clinicopathologic lesion of the oral mucosa and was subsequently reported in the skin. Mucosal and cutaneous lesions are histologically very similar. The epidermal-mucosal changes of hyperparakeratosis, neutrophilic infiltrate and dermal-submucosal foam cell reaction are distinctive features of these xanthomas.[8] Hereby, we present a rare type of xanthomas calling "Cauliflower xanthoma" in a 43-year-old man with dysbetalipoproteinaemia.

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## CASE REPORT

A 43-year-old man was presented to outpatient endocrine clinic of Tabriz University of Medical Sciences, Tabriz, Iran, by his sister for evaluation of skin lesions. He had multiple lesions on shoulders and back, lateral and medial part of dorsal surface of the foot, medial and lateral malleus of both feet, and dorsal and palmar surface of both hands. Siblings of the patient have been followed up in that clinic for clinically diagnosed type-III dysbetalipoproteinaemia. This diagnosis was based on characteristic palmar, eruptive, tuberous and trauma site xanthomas with typical high levels of both total cholesterol and triglycerides in the plasma. Both parents had normal serum lipid levels. History of coronary artery or other atherosclerotic disorders were negative in index case and siblings. There were not any other complaint, and as a greengrocer, he had an active lifestyle. He had a pathology report of skin lesion biopsy that was performed by a dermatologist few months ago, with presence of lipid laden macrophages consistent with diagnosis of xanthoma. Fasting serum lipid levels reported as: Total cholesterol = 507 mg/dl, Triglycerides = 470 mg/dl

and High Density Lipoprotein (HDL) cholesterol = 41 mg/dl. He had normal fasting blood sugar, and normal thyroid, renal and liver function tests. Complete blood counts and urine analysis was also normal. Physical examinations revealed numerous xanthomas resembling cauliflower on both knees [Figure 1], unusual eruptive, tuberous xanthomas same as previous lesions, on the lateral malleus of both feet [Figure 2].

There were lots of smaller xanthomas on the right shoulder [Figure 3], and cauliflower like xanthomas on the extensor side of the left upper extremity, especially on the elbow [Figure 4]. Based on available information, the patient diagnosed as familial dysbetalipoproteinaemia (FDL) and the unique lesions on the lower limb called "Cauliflower xanthoma". Although siblings of this case had the same disorder, they didn't develop such lesions.

By searching in the medical data bases, we cannot find a previous such a lesion. Therefore, we decided to present this case without revealing patient's name, after taking his consent.

Considering the fact that the treatment with high dose Statin was effective in correction of lipid abnormality and regression of skin lesions in his three siblings, we wanted to try the treatment procedure in this patient but he refused any intervention.

## DISCUSSION

FDL, also known as hyperlipoproteinemia type-III or broad beta disease, is a rare inherited disorder characterised by improper metabolism of certain lipids, specially plasma cholesterol, triglyceride rich chylomicron and very low density lipoproteins (VLDL) remnants.[1] Presence or absence of the symptoms of this disease depends on two major risk factors: Genetic and diet.[9,10] Mutations in the gene for apolipoprotein E (Apo E) are the main cause of this disease. Replacement of an arginine by a cysteine in position 158 of the 299-amino acid chain of apo E5 is responsible for the defective binding of chylomicron and VLDL remnants to cell receptors. Thereafter, slower plasma clearance of these particles occurs, and results in the abnormal accumulation of lipids in the body.[9] On the other side, diet has an essential role in the development of the disease. This means that with standard cholesterol diet, symptoms of FDL will not appear, even in the genetically susceptible person.[10]

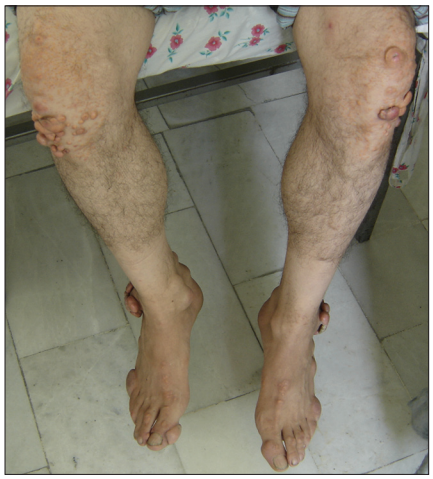

**Figure 1:** Cauliflower xanthomas on the knees and lateral malleus of both lower extremities

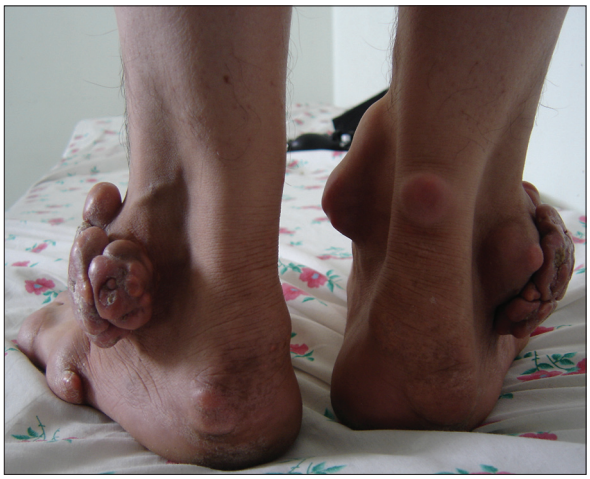

**Figure 2:** Cauliflower xanthomas on the lateral malleus of lower extremities

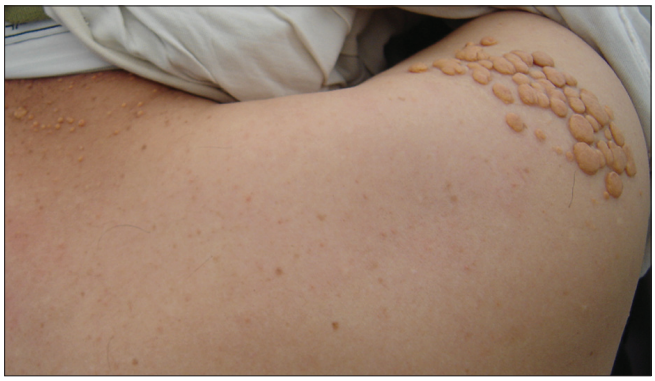

**Figure 3:** Xanthomas on the shoulder and back of the neck

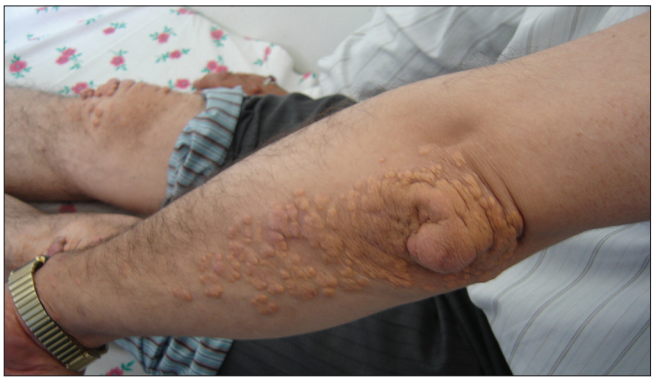

**Figure 4:** Xanthomas on the extensor side of the hand

Xanthomas can be a symptom of FDL. Xanthomas may also be the symptoms of a generalised histiocytosis, or a local fat phagocytosing storage process.[11] They are yellowish lesions on the skins and tendons, macroscopically. On microscopy, xanthomas are characterised by the presence of vacuolated macrophages in dermis. These macrophages are filled with lipid droplets, which are dissolved and removed from tissue during histologic processing.[8]

FDL is mostly diagnosed by combination of clinical and laboratory findings.[12] Most cases are inherited as autosomal recessive trait. Men are more susceptible for FDL probably because of protective impact of estrogen in women. Most of the diagnosed patients were typically young males, with strong family history, characteristic skin lesions, high serum levels of cholesterol and triglycerides and confirming skin histology.[1,13] Most of these cases have premature atherosclerosis and other signs of ischaemic disorders.[9] The patient in this article was a middle aged man with family history of dysbetalipoproteinaemia and high levels of serum lipids as follows: Total cholesterol = 507 mg/dl and Triglycerides = 470 mg/dl. He had a rare form of xanthoma all over his body, causing social problems for him.

Nicotinic acid, Clofibrate, Statins or Gemfibrozil properly reduce cholesterol and triglycerides in people affected with dysbetalipoproteinaemia.[1] The patient mentioned in this article refused receiving any medical intervention. He has just been advised to have low lipid diet, fish oil and regular moderate exercise in order to reducing serum lipid levels.

There should be distinctive monitoring of FDL patients including regular checking of their serum lipids. Controlling underlying disorders, and reducing excess calories, saturated fat and cholesterol, is the main aim of treating these patients. According to this article, Cauliflower xanthomas could be a symptom of FDL, and it should be considered as a differential diagnosis while approaching to these lesions.

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