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Case Report

Hypercholesterolemia Associated Eruptive Xanthoma - A Rare Case Report

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ABSTRACT

A 40 year old female presented to our medicine OPD with a severe cutaneous manifestations over the arm, forearm, back of the chest and both the legs. She is a known case of diabetes mellitus on irregular treatment. Her fasting and post prandial blood sugar values were 254 & 386 mg/dl respectively. Not a hypertensive. The fasting lipid profile picture showed a very high increase in the total cholesterol (>1000 mg/dl) and the triglycerides (>2000 mg/dl) levels along with an increase in LDL and VLDL levels. The HPE report of the skin biopsy along with the clinical examination confirmed the diagnosis as eruptive xanthomas due to hypertriglyceridemia. The patient was started on Atorvastatin 40 mg/day and Fenofibrate 200 mg/day and the patient was also advised on a fat restricted diet. She was treated with Human Mixtard Insulin (30/70), 40 units in the morning and 20 units in the night. Her diabetic state came to near normal sugar values. On follow-up at the end of 3 months the skin lesions had started to reduce and the patient's lipid profile reduced considerably.

Keywords: hypercholesterolemia, eruptive xanthoma, skin biopsy.

INTRODUCTION

Xanthomas occur as clusters of foam cells in the connective tissue of the skin, tendons and fasciae and rarely in the periosteum. Foam cells are formed from macrophages as a consequence of gradual intracellular accumulation of lipids taken up by specific receptors or by the mechanism of phagocytosis. [1] The clinical picture of xanthomas is variable, from soft to semisolid skin macules or papules to large nodules, usually of a yellow colour (Greek xanthos = yellow), due to the presence of carotene contained in lipids. [2]

The mechanisms involved in the development of these pathological lesions appear to be almost similar to the development of early stages of atherosclerotic plaques. The high plasma concentration of lipoproteins facilitates its permeation through dermal capillaries. [3] However, any conditions that increase the relative vascular permeability to lipoproteins such as local injury, oedema, altered lipoprotein structure or paraproteins in the plasma, can also lead to lipoprotein leakage into the dermis. Direct phagocytosis of lipoproteins by dermal histiocytes or a reactive process involving in-situ lipid synthesis in the histiocytes will then evolve into foam cells. [4]

From the clinical point of view, xanthomas are usually associated with inborn or acquired dyslipidemias. Of the various types of inborn errors of lipid metabolism, autosomal dominant hypercholesterolemias found to be relatively common. [5] This broad group consists of

familial hypercholesterolemia caused by mutations in the genes encoding the LDL receptor (LDLR), familial defective apolipoprotein B-100 with mutations in the gene APOB, and non-FH/ non-FDB hypercholesterolemia with mutations in the gene PCSK9. Other types of xanthomas are helpful diagnostic markers of severe hypertriglyceridemia and primary dysbetalipoproteinemia. [6]

Eruptive xanthomas may occur suddenly and at any site, but most commonly favour the buttocks, flexors of arms, thighs, knees or may be localized to pressure points. So with this current background we are presenting a case of eruptive xanthomas with increased levels of triglycerides.

CASE REPORT

A 40 year old diabetic female presented to our medicine OPD with a severe cutaneous manifestations over the arm, forearm, back of the chest and both the legs, which the patient mentioned it a wart. She said that initially it started in the arms and slowly spread to the back and the legs. The lesions were present for almost 4 months. The lesions began as a small red bumps that grew in size and became more yellow in colour. The lumps were non-pruritic. She had no prior history of similar cutaneous lesions earlier and could not recall anyone else in his family having a similar condition. She is a diabetic on treatment with irregular treatment. Not a hypertensive. She was initially seen by a primary care provider and was diagnosed with molluscum contagiosum. She was treated with 0.5% triamcinolone ointment. The patient's spouse was very upset by the diagnosis and was afraid of the supposed infection spreading to him or their children. Patient also had a complaint of blurring of vision, for which ophthalmologist's opinion was obtained.

The patient's entire blood examination report was shown in table 1. The serum of the patient was found to be milky white (fig 1). It is seen from the table that the complete hemogram picture of the patient was found to be normal with a slight elevation in ESR. The fasting blood sugar, urea and creatinine were within the normal limits. The fasting lipid profile picture showed a very high increase in the total cholesterol (>1000 mg/dl) and the triglycerides (>2000 mg/dl) levels along with an increase in LDL and VLDL levels.

Blood Examination:

Table 1: Blood investigation report of the patient

Hb : 13.5 gm /dl ; **TC :** 10,300 cells/cumm ; **DC :** P49, L49, E02 **ESR :** 26 & 54 mm
Blood Urea : 27 mg/dl
Blood sugar (fasting) : 254 mg/dl ; **Post Prandial :** 386 mg ; **Acetone :** Negative
Serum Creatinine : 1.1 mg/dl
Serum Sodium : 145 mEq /L
Serum Potassium : 4.8 mEq / L
LIPID PROFILE :
Total Cholesterol : More than 1000 mg / dl
Sr. Triglycerides : More than 2000 mg / dl
HDL-Cholesterol : 32 mg / dl
LDL-Cholesterol : 440 mg / dl
VLDL- Cholesterol :195 mg / dl
Serum Chylomicrons : Positive
Liver Function Test
Serum Bilirubin :
Total : 1.0 mg / dl
Direct : 0.52
SGOT : 37 iu / ml ; **SGPT :** 29 iu / ml
Alkaline Phosphatase : 57 iu / ml
Total Proteins : 6.9 gm/dl
Albumin : 3.5 gm/dl
Globulin : 3.4 gm/dl
Serum Amylase & Lipase : Normal

Figure 1: Serum sample of the patient found to be milky white

The dermatological examination of the patient revealed 3 to 6 mm yellowish papules with erythematous borders and central lobulation with more in number. The papules were distributed across the elbows,

forearm, right knee and upper back (Fig 1). The face, hands, flexor surfaces, and genitals were spared. Her diagnosis initially made by a primary care physician as molluscum contagiosum was unlikely due to the morphology and the distribution of the papules. Molluscum is usually a sexually transmitted infection in adults and therefore most commonly found in the genital area.

To make a confirmatory diagnosis a skin biopsy was obtained and was sent for histopathological examination. The HPE report showed dermal histolytic inflammation with extracellular lipid deposition (Fig 2). Ophthalmology department conducted a fundus examination and the fundus photograph suggested features of lipemiaretinalis (Fig 3). The information from the biopsy combined with the clinical presentation and the history we arrived to a final diagnosis as eruptive xanthoma.

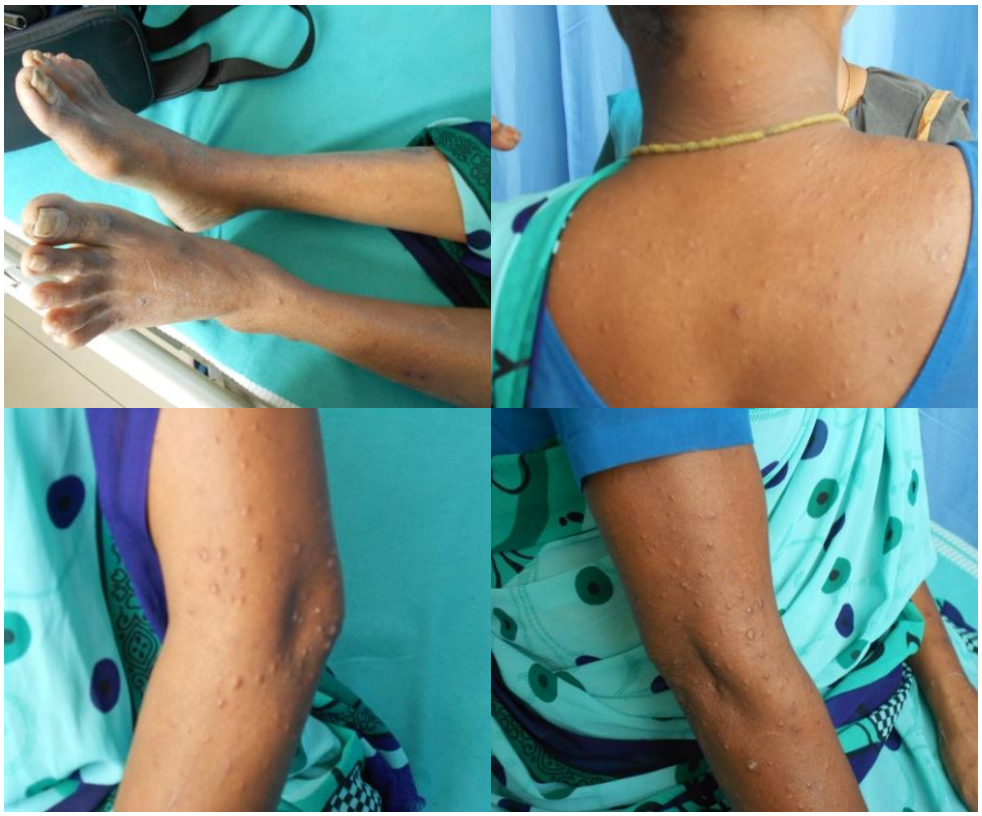

Figure 2: Eruptive xanthomas distributed over upper back, legs, elbows and forearm

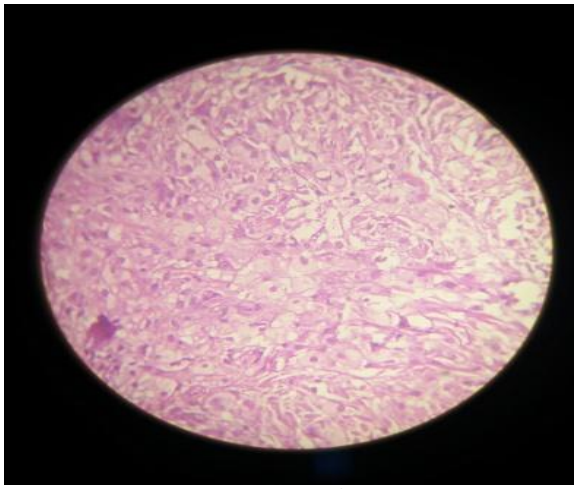

Figure 3: HPE report of Skin Biopsy

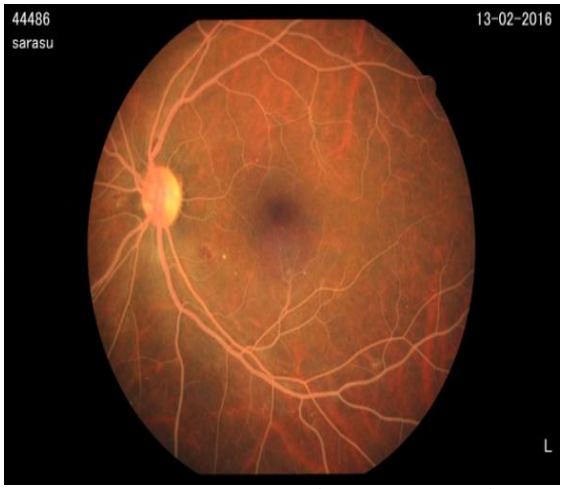

Figure 4: Fundus picture of the patient featuring Lipemiaretinalis

The patient was prescribed with statins 40 mg/day and fenofibrate 200 mg/day for period of 3 months and the patient was also advised on a fat free diet. Injection Human Mixtard (30/70) 40 units in the morning and 20 units in the evening was given. On follow-up at the end of 3 months the skin lesions had started to reduce and the patient felt satisfied.

DISCUSSIONS

Dermic eruptive xanthomatosis is a typical but rare sign of acute hypertriglyceridemia. It manifests itself with sudden appearance of yellowish papules surrounded by a 1-4 mm wide erythematous halo. These are firm and they are normally located on the buttocks and extensor areas of extremities. Histologically, xanthomas are identified by the presence of froth-like histiocytes, containing mainly triglycerides. [7,8] With regard to lipid metabolism, they can be associated with high levels of chylomicrons or with high levels of very low density lipoproteins in serum. Eruptive xanthomas are typical of type-I hyperlipoproteinemia (HLP) (congenital lipoprotein lipase deficit) and type-V HLP (familial combined hyperlipidaemia). They are also known to be associated with type-IV HLP (familial endogenous hypertriglyceridemia) and type-III HLP (serum remnant lipoproteins disease). [9]

Cutaneous xanthomas can be divided into subgroups, including eruptive xanthomas, tuberous xanthomas, tendon xanthomas, xanthelasma, and plane xanthomas. [2] Eruptive xanthomas can be associated with hypertriglyceridemia (Type I, IV, or V hypercholesterolemia), particularly when diabetes is poorly controlled. [10,11] Eruptive xanthomas contain more triglycerides and fewer cholesteryl esters than other types of xanthomas, and lipids present in xanthomas are derived from circulating plasma lipoproteins. Triglyceride is mobilized more rapidly than cholesterol, so resolving eruptive xanthomas are rich in cholesterol.

Clinically eruptive xanthoma may sometimes be confused with other xanthomatosis or non-Langerhans' cell histiocytosis. Rarely the cutaneous lesions may mimic Sweet's syndrome. [12] Most of the time a skin biopsy can reliably differentiate eruptive xanthoma from other xanthomatoses and non- Langerhans' cell histiocytosis, similarly in our case the HPE report of the skin biopsy helped us to derive the diagnosis as eruptive xanthomas. [13]

Treatment of eruptive xanthoma is directed to the underlying causes. Since eruptive xanthoma secondary to hypertriglyceridemia typically responds well to dietary control, a dietician's advice should be sought first. In general, a low carbohydrates and saturated fat diet is the first treatment of choice. Anti-hyperlipidaemic agents should be considered when dietary control fails. As quoted in the literature our case also had shown a dramatic improvement with fat free diet and antilipidemic drugs.

CONCLUSIONS

Patients presenting with diffuse cutaneous papules eruptive xanthomas should be one of the important differential diagnosis and also being aware of hypertriglyceridemia as one of its important feature. A thorough and a proper investigation including a skin biopsy and clinical examination would help us to diagnose the condition earlier and so that proper interventions could be planned. Patients should be reassured that these cutaneous lesions would revert to normal in a span of few weeks with proper antilipidemic drugs and low fat diet.

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