

CASE REPORT

Mixed Hypercholesterolemic and Hypertriglyceridemic Xanthomatosis: Four classic types of Xanthomas in one patient at the same time

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Abstract:

Xanthomas are localized infiltrates of lipid-containing cells found within the dermis. Cutaneous xanthomas are mostly cosmetic disorders but xanthomas can indicate the presence of an underlying generalized disturbance in lipid metabolism possibly associated with coronary artery disease. Because hyperlipidemia may present as xanthomatosis, a dermatologist might be the first to diagnose these associated lipid abnormalities,

We report a 36-year-old male who presented with four classic types of xanthomas (Xanthelasma, Tuberous, Eruptive and Plane xanthomas) at the same time. Laboratory tests confirmed hypercholesterolemia and hypertriglyceridemia of dysbetalipoprotein Type III of the Fredrickson classification. The occurrence of four clinical types of xanthomas simultaneously in the same patient is rarely reported in the literature.

The clinical, histopathology, laboratory investigation and management of hyperlipidemia and cutaneous lesions is fully discussed together with a review of the literature.

Keywords: Xanthomatosis; Cosmetic disorder; Hypercholesterolemia; Hypertriglyceridemia; Anti-hyperlipidemic drugs

Case Report:

A slightly overweight 36-year-old male in good general condition, blood pressure 120/80 mmHg, presented with a six-month history of widespread, asymptomatic papules, plaques and flat yellowish lesions affecting different sites on his body. His medical history was unremarkable and he reported no current local or systemic symptoms. There was no family history of a similar condition.

He had bilateral, symmetrical soft, velvety yellow flat patches near the inner canths of the upper eye lids (Xanthelasma) (Figure 1). Firm, painless. Yellowish nodules affect both knee and elbows joints (Tuberous Xanthoma) (Figure 2). Numerous yellowish papules on the extensor surface of both arms, legs, fingers and gluteal region (Eruptive Xanthoma) (Figure 3-5). Diffuse yellowish macules lesions spread over the palms, soles and finger creases including the creases of both forearms (Plane Xanthoma) (Figure 6,7).



Figure 1:



Figure 2:

Laboratory results were as follows: cholesterol 22.55 mmol/L, grossly lipemic (normal range 3.37-5.70 mmol/L); triglyceride 23.35 mmol/L, chylomicrons present (normal range 0.56-2.03 mmol/L); Low-density lipoprotein (LDL-C) 7.95 mmol/L

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Figure 3:



Figure 4:



Figure 5:



Figure 6:



Figure 7:

L (normal range 3.36mmol/L), High density lipoprotein (HDL-C) 2.7 mmol/L (normal range <1.0 mmol/L). His complete blood cell count, serum glucose, thyroid-stimulating hormone, liver function tests, kidney function tests, amylase and electrolyte panel were within normal limits. The blood specimen showed lipemic plasma (Figure 8).

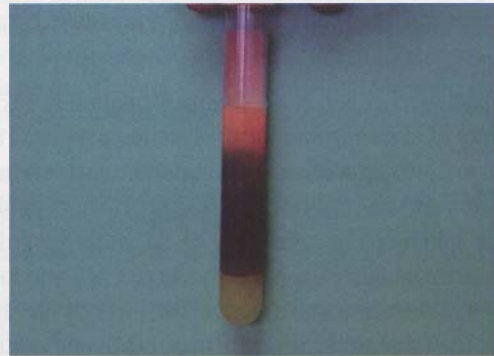


Figure 8:

Bunch biopsy specimens obtained from the different types of skin lesions all showed foamy histiocytes between the collagen bundles throughout the dermis with infiltrates of lymphocytes and neutrophils around the venules (Figure 9).

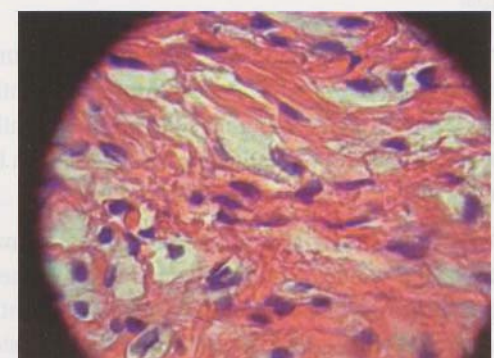


Figure 9:

He was referred to the internal medicine department where he was started on a low-calorie, low-fat diet and lipid lowering drugs: gemfibrozil (Lopid; Pfizer Ltd.) 600 mg. twice daily 30 minutes before the morning and evening meals and Omega-3 marine triglycerides (Maxepa; Seven Seas) five 1000 mg. capsules twice daily.

The cutaneous xanthelasma lesions were treated with topical 25% trichloro-acetic acid (TCA) and other types were treated with 50% TCA. The drugs were well tolerated. After nine weeks the lipoprotein levels were markedly reduced with the lipid profile being cholesterol 4.12 mmol/L; triglyceride: 2.24 mmol/L. The skin lesions, especially the eruptive type, gradually resolved.

Discussion:

Xanthomas are cutaneous lesions characterized by accumulations of lipid laden macrophages. They may result from lipid metabolism alteration or local cell dysfunction to complexes of lipoproteins⁽¹⁾. Cutaneous xanthomas are mostly cosmetic disorders the presence of which might suggest an underlying disorder of lipid metabolism, preceding a diagnosis of hyperlipidemia. Morbidity and mortality are related to atherosclerosis, coronary artery disease and pancreatitis⁽²⁾.

The exact mechanism of xanthoma formation is unknown, but a variety of systemic and local tissue factors play a role⁽³⁾. Alteration in lipid metabolism is an important factor in xanthoma formation and this can be classified as primary (familial or genetically inherited) or secondary to an underlying disease such as diabetes mellitus, nephrotic syndrome, hypothyroidism, pancreatitis, hemochromatosis, myeloma, lipodystrophy and cholestatic liver disease⁽⁴⁾. Several drugs, estrogens, corticosteroids, isotretinoin and ethanol have been implicated also in causing hyperlipoproteinemia⁽⁵⁾.

There is considerable biochemical and ultra-structural evidence to suggest that low density lipoprotein (LDL) and very low density lipoprotein (VLDL) when found in high plasma concentrations permeate the walls of the dermal capillaries and are then phagocytosed by dermal histiocytes that evolve into foam cells⁽⁶⁾.

Cutaneous xanthomas associated with hyperlipidemia can be subdivided clinically into xanthelasma, tuberous xanthoma, tendinous xanthoma, plane xanthoma and eruptive xanthoma. Xanthoma disseminatum is not usually associated with hyperlipidemia.

The most common type of xanthoma is xanthelasma; the lesions are asymptomatic, usually bilateral and symmetrical, occurring near the inner canthus of the eyelids. In twenty-five percent of patients with xanthelasma, the plasma cholesterol is elevated especially in young patients; in patients over forty years of age there is often no underlying lipid abnormality⁽⁷⁾.

Tuberous xanthoma consist of firm, painless, red-yellow nodules that appear early as small papules (and can be confused with eruptive xanthoma) which coalesce to form multi-lobulated tumors in pressure areas such as the extensor surfaces of the knees, elbows, and buttocks. These are seen typically in remnant disease (Type III) especially in association with xanthoma palmer⁽⁸⁾ as in our patient.

Tendinous xanthoma appear as slowly enlarging subcutaneous nodules related to the tendons or ligaments especially the extensor tendons of the hands, feet and the Achilles' tendons. Tendinous xanthomas almost always indicate an underlying hypercholesteremia and elevation of low density lipoprotein as occurs in Type IIa and Type IIb primary disease⁽⁹⁾.

Eruptive xanthomas appear suddenly as crops of small yellow papules especially on extensor surfaces and buttocks and may arise around hair follicles. The lesions may also koebnerize⁽¹⁰⁾. Eruptive xanthomas are commonly seen when serum triglyceride levels exceed 2000 mg/dl. and they result from the phagocytosis of triglyceride-rich lipoprotein by macrophages in the skin as in Type I, IV and V primary disease⁽¹¹⁾.

Plane xanthomas can occur in any site, are mostly macular and rarely form elevated lesions. Involvement of the palmer creases and volar finger creases is characteristic. Generalized plane xanthomas may cover large areas of the face, neck and flexures and are commonly associated with hyperlipidemia as well as biliary cirrhosis^(12,13).

Xanthomatosis should be differentiated from macular lichen and nodular amyloidosis, erythema elevatum diutinum, juvenile xanthogranuloma, lipoid proteinosis, necrobiosis lipoidica and sarcoidosis⁽¹⁴⁾.

Treatment of xanthomatosis is important not because of problems posed by superficial xanthomas but to reduce the risk of atherosclerosis and coronary artery disease as well as effects upon other vital organs of the body which can result in hepatosplenomegaly, lipemia retinalis and pancreatitis.

Diet, exercise and drug therapy are equally effective in preventing pancreatitis and the disabling abdominal pain occasionally encountered in hyperlipemic conditions. Dietary manipulations should always be tried first but if the elevated lipoprotein fails to respond within two to three months appropriate drugs should be added; modern day treatment with statins is highly effective and well tolerated⁽¹⁵⁾.

The course and ultimate prognosis of patients with xanthomatosis depend upon the underlying disease process. Specific treatment of underlying disease may cause resolution of secondary xanthoma. Therapeutic options in the treatment of cutaneous xanthomatosis are based on mechanical removal by dermabrasion, excision, trichloro acetic acid (TCA), electrodesiccation and ablative laser therapy⁽¹⁶⁾. Erbium YAG laser

therapy is an effective ablative treatment that shows acceptable rates of adverse effects and fast re-epithelization⁽¹⁷⁾. Basar et al studied 24 patients with 40 xanthelasma treated with an argon laser; complete removal of all lesions occurred with 1-4 sessions at intervals of 2-3 weeks⁽¹⁸⁾.

The most significant threat to health is peripheral vascular, cerebro-vascular and coronary artery disease. In addition, patients with diabetes, myxedema and nephrosis are susceptible to atherosclerosis. Those with primary biliary cirrhosis have less tendency to develop cardio-vascular disease. Patients with normolipidemic xanthomas have a more favorable outlook. Xanthoma disseminatum is usually a benign disease except where lesions involve vital regions in the upper respiratory tract

or pituitary-hypothalamic area⁽¹⁹⁾.

We have reported here a dysbetalipoprotein Type III patient with a combination of four classic types of xanthomatosis: Xanthelasma, Tuberosus, Plane and Eruptive xanthomatosis.

This combination of xanthoma lesions in our patient was probably due to a combination of hypercholesterolemia and hypertriglyceridemia. To our knowledge there are few reports in the literature of hyperlipidemic cases with a combination of more than one type of xanthoma. In our patient reducing the hyperlipoproteinemia by diet, exercise and anti-hyperlipidemic therapy led to gradual resolution of the skin lesions, especially those of eruptive xanthoma.

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