



Eruptive Xanthomas in a Patient with Metabolic Syndrome

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ABSTRACT

Eruptive xanthomas are characterized by large numbers of yellow papules, typically 1-4 mm in size, sometimes with an erythematous halo, sometimes pruritic, of sudden onset and generally observed on the extensor surfaces of the extremities. These are seen in less than 0.1% of diabetic patients. Diabetes mellitus is the most common secondary cause of type 5 hyperlipoproteinemia, a form of chylomicronemia. Eruptive xanthomas generally emerge at triglyceride levels above 2000 mg/dL proceeding with chylomicronemia. This case report of a 36-year-old woman diagnosed with eruptive xanthoma on the basis of clinical and histopathological findings is presented in order to emphasize that these are an important finding of diseases associated with metabolic syndrome, such as diabetes mellitus and hypertriglyceridemia.

Keywords : Eruptive xanthoma, diabetes mellitus, hypertriglyceridemia, metabolic syndrome

INTRODUCTION

Eruptive xanthomas are seen in fewer than 0.1% of diabetic patients. Diabetes mellitus is the most common secondary cause of type 5 hyperlipoproteinemia, a form of chylomicronemia. Eruptive xanthomas generally appear at a triglyceride level above 2000 mg/dL proceeding with chylomicronemia. They are generally characterized by yellow papules of sudden onset, typically 1-4 mm in diameter, sometimes surrounded by an erythematous halo, that are usually observed in large numbers on the extensor surfaces of the extremities. Eruptive xanthomas improve with carbohydrate restriction and lipid metabolism control (1,2).

We describe a case of eruptive xanthomas in a 36-year-old female patient in order to emphasize an important finding of diseases associated with metabolic syndrome, such as diabetes mellitus and hypertriglyceridemia, capable of causing severe complications such as atherosclerosis and acute pancreatitis.

CASE REPORT

A 36-year-old woman presented to our clinic with large numbers of yellow eruptions on the outer surfaces of the extremities and the hips over the previous 15-20 days previously. There were no other symptoms, and her history was unremarkable. Systemic examination revealed no finding suggestive of hepato-splenomegaly or cardiovascular involvement. Waist circumference was 90 cm and body mass index (BMI) 33.2 kg/m².

Dermatological examination revealed large numbers of widespread, asymptomatic yellow papules on the extremity extensor surfaces, approximately 4-6 mm in size (Figure 1). Histopathological examination of lesion biopsy revealed cutaneous deposition of lipid-containing macrophages with an abundant, often vacuolated cytoplasm (Figure 2, 3).

Laboratory investigations were performed after 12-h fasting. These revealed levels of total triglyceride 1980 (normal 0-200) mg/dL, total cholesterol 719 (normal 0-200) mg/dL, high-density lipoprotein (HDL) cholesterol 14 (normal 40-60) mg/dL, alanine aminotransferase (ALT) 43 (normal 0-35) U/L, glucose 147 (74-106) mg/dL, and 6.7% glycosylated hemoglobin (HbA1C) (normal 4.1-5.4%). Kidney and liver function tests were normal except for ALT. Test results for thyroid stimulating hormone, amylase and lipase were also normal. It was impossible to assess levels of low-density lipoprotein (LDL) cholesterol and very-low-density lipoprotein (VLDL) cholesterol since the specimens were grossly lipemic.

Grade 3 hepatosteatosis and an enlarged vertical dimension of the right hepatic lobe were determined at abdominal ultrasound. No finding was present at ocular examination.

Eruptive xanthoma was diagnosed on the basis of significant high hypertriglyceridemia and hyperglycemia. Dietary restriction was introduced, triglyceride-lowering therapy with fenofibrate and antidiabetic therapy were initiated and follow-up was advised. The patient failed to attend check-ups, however.

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Figure 1: Asymptomatic yellow papules on the extremity extensor surfaces

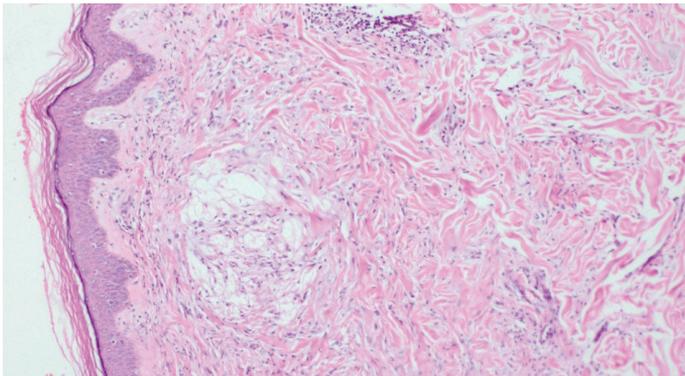


Figure 2: Microscopic appearance of mass of xanthomatous cells in the superficial dermis (HE, X100).

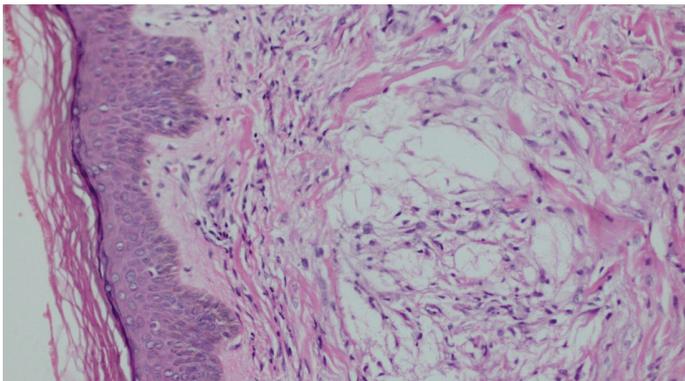


Figure 3: Close-up image of xanthomatous cells (HE, X200).

DISCUSSION

Eruptive xanthomas are generally associated with chylomicronemia and hypertriglyceridemia resulting from primary or secondary dyslipidemia (3). Primary forms are associated with familial chylomicronemia (previously known as

Fredrickson type 1) with familial lipoprotein lipase deficiency and primary combined hyperlipidemia (type 5). Pathological presence of chylomicrons following 12-14-h fasting and a creamy supernatant in lipemic plasma following overnight refrigeration are characteristic in both types (3-5). Clinical features of chylomicronemia other than eruptive xanthoma include lipemia retinalis, hepato-splenomegaly, focal neurological symptoms, epigastric discomfort and pancreatitis. Xanthomas have also been reported to be associated with familial dysbetalipoproteinemia (type 3) homozygous for binding-defective apolipoprotein isoform ApoE2. However, such xanthomas generally consist of the tuberous type located over major tendons. Secondary hypertriglyceridemia is commonly associated with obesity, alcohol abuse and poorly controlled type 2 diabetes. This leads to excessive production of large, triglyceride-rich, VLDLs (4-6). When metabolic syndrome accompanies type 2 diabetes mellitus, insulin resistance results in acquired lipoprotein lipase deficiency. This in turn compromises chylomicron and VLDL clearance. Various drugs, including systemic glucocorticosteroids, retinoids, thiazide diuretics and antiretrovirals can also trigger metabolic stress (7). Our patient had no history of drug use, and there was no such family history. Metabolic syndrome diabetes mellitus, hypertriglyceridemia and obesity components were identified as a result of physical examination and laboratory tests.

Eruptive xanthomas typically evolve very quickly, generally in a matter of days or weeks. Pruritus is not inevitable. If it does occur, however, it can be severe and lead to scratching, in which case the xanthomas exhibit a linear appearance due to Köebner's isomorphic reaction (8). Our patient's skin finding had been present for 2-3 weeks, and there was no accompanying pruritus.

Clinical presentation and laboratory findings are generally highly indicative of eruptive xanthomas. Histological evidence of macrophages with high lipid contents is still required however, particularly in early lesions, in order to exclude other causes of papular rashes such as lichen planus (LP) or similar drug eruptions, non-Langerhans cell histiocytosis, xanthomatous lesions of Langerhans cell histiocytosis or disseminated granuloma annulare (1,3). Diagnosis of eruptive xanthomas based on clinical findings was confirmed by laboratory tests and histopathology in our case.

Xanthomas usually resolve completely in a matter of weeks with a combination of intensive triglyceride-reducing therapy consisting of fibrates, omega-3 fatty acids and nicotinic acids and cessation of accompanying factors such as alcohol consumption and a high-fat diet (1,9).

In conclusion, eruptive xanthomas play a significant role in the diagnosis of diseases associated with metabolic syndrome, such as diabetes mellitus and hypertriglyceridemia, which can lead to severe complications such as atherosclerosis and acute pancreatitis.

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