

Eruptive Xanthomas – Two Case Reports With Distinct Features

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Abstract

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BACKGROUND: Eruptive xanthomas are rare and often asymptomatic. On the other hand, these cutaneous lesions are a red flag for serious underlying metabolic disorders that demand an early diagnosis to prevent morbidity and mortality.

CASE REPORT: We report on two male patients, aged 23 and 27 years, who presented with eruptive xanthomas. Clinical, histological and laboratory investigations disclosed a metabolic syndrome in the younger patient and an alcohol-induced chylomicronemia in the elder one. Two types of macromorphology of cutaneous lesions were observed. Treatment was tailored according to underlying pathologies and resulted in significant improvement of the metabolic parameters and improvement of skin lesions.

CONCLUSION: Dermatologists should be aware of the diagnostic importance of eruptive xanthomas for serious metabolic disorders.

Introduction

Xanthomas are cutaneous lesions developing as a result of local storage of lipids. Xanthomas can be classified according to the clinical presentation of the individual lesion or by the mode of appearance. Eruptive xanthomas are uncommon and represent an important clinical sign for serious metabolic disorders. Low-density lipoprotein particles are preferably stored in foam cells and giant cells [1]. A particular subtype is neutrophilic eruptive xanthomas, mostly but not exclusively seen in cases of immunosuppression or immunodeficiency [2].

Clinically, the lesions appear as rapidly evolving papules with a red-to-yellowish hue and are about 1-5 mm in diameter. They generally form across the extensor surfaces of the arms and legs, as well as across the buttocks, and may involve palmoplantar skin along the creases. The lesions can be tender, often they remain asymptomatic, but early lesions may be pruritic. Eruptive xanthomas may be associated with diabetes mellitus,

hypercholesterolemia, hypertriglyceridemia, lipemia retinalis, or hepatosteatorosis [3], [4]. Another but unusual cause is tattooing that causes a Koebner phenomenon [5], [6]. The recognition of underlying metabolic disorders is necessary to prevent conceivable fatal medical conditions such as coronary artery disease or pancreatitis [7].

Case reports

Case 1: A 23-year-old male presented with multiple non-pruriginous papules, that developed during five years. He was a heavy cigarette smoker without alcohol abuse. His medical history was remarkable for acute pancreatitis one year before of unknown cause. His father died from myocardial infarction.

On examination, we found an obese male patient with a body-mass-index of 35.9. He had

disseminated reddish to yellowish papules of variable diameter (from several millimetres to 1 cm) arranged in stripes on his trunk and the extremities (Figure 1). Predominant sites were the neck, lower back, buttocks, palmar area, and the extension sites of the arms.



Figure 1: Eruptive xanthomas with unrecognised metabolic syndrome; a) Multiple papules on the buttocks and lower back; b) extension sites of the arms and c) palms

We took a biopsy for histopathological examination. The investigations revealed foam cells and some Touton giant cells in the upper dermis. The foam cells were CD68 positive, while stains for S100 and CD1a remained negative (Figure 2). The diagnosis of xanthomas was made.

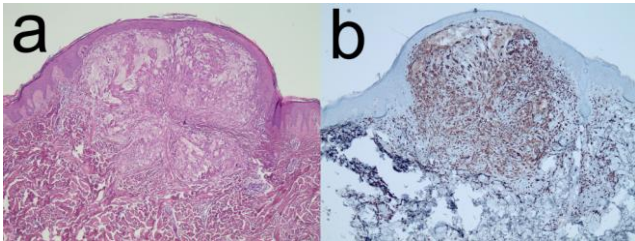


Figure 2: Histology of eruptive xanthomas; a) Hematoxylin-eosin stain with foam cells of the upper dermis; b) Positive staining for CD68 (Original magnification x 4)

Laboratory investigations: Blood glucose 16.7 mmol/l; HbA1c 11.6 % (normal range 4-6); cholesterol 16.5 mmol/l (normal range < 5.2); triglycerides 4.66 mmol/l (< 2.3), very low-density lipoprotein (VLDL) was extremely increased. Blood cell counts, liver enzymes, lipoprotein (a), and clotting parameters were in the normal range. Blood serum was lipemic (Figure 3).

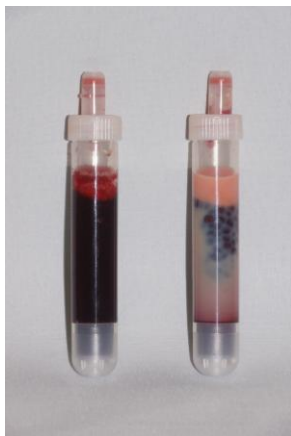


Figure 3: Lipemic serum (right) versus normal serum (left)

Imaging: X-ray of the chest and ultrasound of the abdomen were unremarkable. Repeated blood pressure measurements revealed hypertension. The patient was treated by an interdisciplinary approach for diabetes mellitus type II and hyperlipidemia. We started with subcutaneous insulin and certoparin injections to stimulate the lipoprotein lipase. After significant improvement of the glucose metabolism, the treatment was switched to combined oral medication of metformin and sitagliptin. The hypertension was treated with oral ramipril. We also recommended a low-lipid diet. At the end of his hospital stay, blood glucose was 5.7 mmol/l and cholesterol 3.67 mmol/l. The cutaneous lesion started to diminish.

Case 2: A 27-year-old male presented with multiple, moderate pruritic cutaneous plane yellowish plaques which developed throughout 2 weeks. His medical history was positive for pollinosis and nodular struma. The family history disclosed no risk factors for cardiovascular or cutaneous disorders. He had regular alcohol consume.

On examination, we observed an otherwise healthy non-obese male patient with disseminated yellowish plane cutaneous lesions on trunk and flexion sites of extremities (Figure 4). Palms, soles and face were spared.

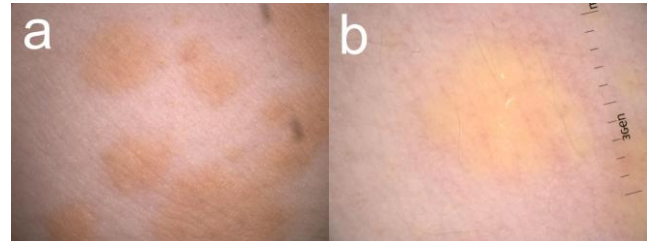


Figure 4: Eruptive xanthomas with chylomicronemia; a) Flat yellowish plaques; b) Dermoscopy with polarised light (Dermogenius) demonstrating structureless plaque without erythema or vascular proliferation

We took a skin biopsy. Histopathologic examination revealed lipid storing macrophages in the upper and mid-dermis, foam cells were absent. Infiltrates composed of lymphocytes and mast cells with some intermingled neutrophils and eosinophils were localised perivascular. The macrophages were CD 68-positive but lacked S-100 or CD1a. The diagnosis of eruptive xanthomas was confirmed.

Laboratory investigations: Triglycerides 9.84 mmol/l (normal range < 2.3); cholesterol 15.94 mmol/l (normal range < 5.2); lipoprotein (a) 0.74 g/l (normal range < 0.3); triglyceride/ cholesterol ratio 12.62 (normal range < 1.5); gamma-glutamyl transferase 6.66 μ kat/l (normal range < 1). Liver transaminases and eosinophil count were slightly increased. Blood glucose levels and pancreatic lipase were in the normal range. Imaging: Chest-X-ray and abdominal

ultrasound unremarkable. The diagnosis of an alcohol-induced chylomicronemia with eruptive xanthomas was made. A reduction of alcohol consumption was recommended what significantly reduced hyperlipidemia. In the interdisciplinary consultation, medical drug therapy was not recommended since the reduction or avoidance of substance abuse leads to normalisation. There was no clue for familial chylomicronemia syndrome.

Discussion

Eruptive xanthomas may be the result of a variety of metabolic disorders, medical drugs (glucocorticoids, retinoids, estrogens), secondary insulin resistance, and alcohol abuse. The most common causes represent chylomicronemia and hypertriglyceridemia either due to lipoprotein lipase deficiency (Type I hyperlipoproteinemia) or familial hyperlipoproteinemia (Type V hyperlipoproteinemia). In diabetic patients unresponsive to insulin, an acquired lipoprotein lipase deficiency may develop [8]. Rare syndromes associated with eruptive xanthomas are the Berardinelli-Seip syndrome [9], the von Gierke syndrome (glycogen storage disease type I) [10], or the primary lipoprotein-lipase deficiency [11].

LDL is one of the major carriers of cholesterol. Circulating LDL particles in the blood stream realise the cholesterol transport to those cells that are requiring lipids. These cells express higher levels of the LDL-receptor (LDLR) that mediates uptake of LDL particles by receptor-mediated endocytosis. For plane xanthomas, development of foam cells is associated with the uptake of LDL particles that are modified due to increased residence time in plasma by over-expressed macrophage scavenger receptor (SR) [12]. Sortilin, a transmembrane receptor expressed by macrophages that binds LDL and support intracellular LDL uptake, is another driver for their transformation into foam cell [13]. In eruptive xanthomas, foam cells may develop due to inflammatory stress. Thereby, LDL receptor negative feedback regulation induced by intracellular cholesterol becomes disrupted [14].

We presented two young male patients with eruptive xanthomas with a slightly different clinical appearance of the cutaneous lesions. In case # 1 the lesions were reddish to yellowish papules with a preference of the extension sites of the arms. The underlying pathology was an unrecognised metabolic syndrome. In case # 2, the lesions were flat, moderate pruritic, yellowish without an erythematous note and preferred the flexion sites of the arms. The underlying pathology was alcohol-induced chylomicronemia. The treatment was tailored according to the individual needs. Diagnosis of underlying metabolic disorders and their correction by treatment is an appropriate method to improve eruptive xanthomas.

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