



ERUPTIVE XANTHOMA: A CASE REPORT

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1. INTRODUCTION

Xanthomas are well-circumscribed lesions in the connective tissue of the skin, tendons, or fasciae that predominantly consist of foam cells; these specific cells are formed from macrophages as a result of an excessive uptake of low-density lipoprotein (LDL) particles and their oxidative modification¹. The clinical variants of cutaneous xanthomas include eruptive xanthomas, tuberous xanthomas, tendinous xanthomas, plane xanthomas (including xanthelasma), and verruciform xanthomas. Xanthomas can present as early manifestations of systemic disorders and uncommonly as sole manifestations. Early recognition and treatment of the underlying condition decrease morbidity and mortality. Eruptive xanthomas are highly suggestive of hypertriglyceridemia and are often associated with serum triglyceride levels exceeding 1500 to 2000 mg/dL. Occasionally, eruptive xanthomas are the initial sign of diabetes. Eruptive xanthomas have also occurred in association with hypertriglyceridemia-induced pancreatitis².

Here, we report a case of eruptive xanthoma in a Vietnamese man based on the physical findings, biochemistry tests, and confirmed with a skin biopsy.

2. CASE REPORT

A 37-year-old obese man presented with multiple asymptomatic skin-colored and yellowish papules on his trunk and extremities for 6 months. Initially, these papules focused mainly on his elbows and knees on both sides. Lesions are asymptomatic,

slowly increase in size, and some lesions regressed spontaneously leaving hyperpigmented macules. 2 months before the examination, the patient appeared with many lesions spreading to his limbs and trunk, which were concentrated on the extensor surface of both arms, thighs with some involvement of the abdomen and back.



Figure 1. Yellowish papules on the buttock and legs



Figure 2. Yellowish papules on the extensor surface of the patient's arms

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Our patient was overweight (BMI 32.3 kg/m²), casual drinking, and smoked regularly. His past medical history included gastroesophageal reflux and steatosis. No food or drug allergy history was detected. Personal or family history of similar lesions was lacking. He did not report any family history of diabetes mellitus or familial hypertriglyceridemia.

Laboratory tests revealed hyperlipidemia with total cholesterol 20.86 mmol/L (807 mg/dL), triglycerides 35.6 mmol/L (3153 mg/dL), HDL-C 0.52 mmol/L (20 mg/dL), LDL-C can't be measured due to milky appearance of plasma, AST/ALT 41/49 U/L, biopsy and H.E stain demonstrated foamy macrophages in the dermis.

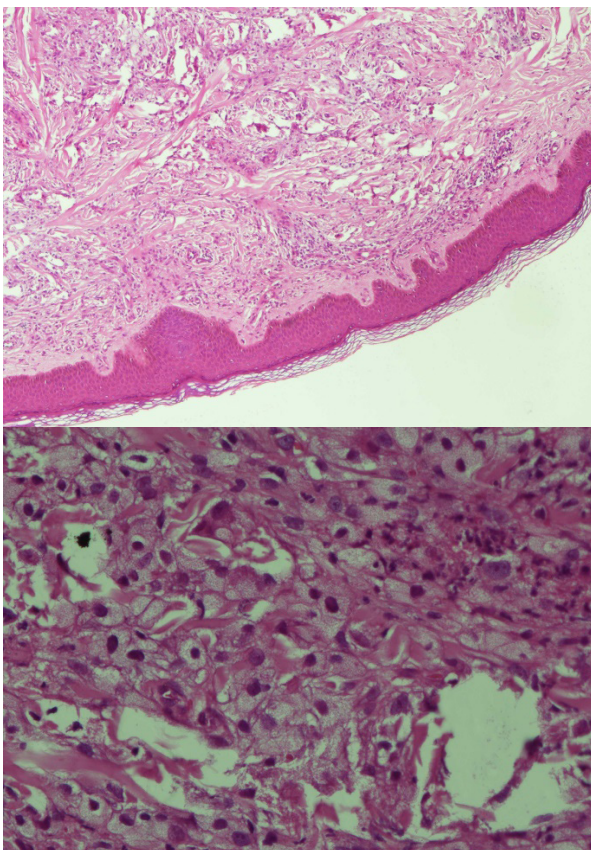


Figure 3. H.E stain with foamy macrophages in the dermis

Our patient was then started on statins and fibrates.

3. DISCUSSION

Xanthomas are localized lipid deposits within organs that may manifest as papules, plaques, or nodules in the skin. The clinical picture of xanthomas is variable, from soft to semisolid skin macules or papules to large nodules, usually of a yellow color (Greek *xanthos* = yellow), due to the presence of carotene contained in lipids.

The clinical variants of cutaneous xanthomas include plane xanthomas (including xanthelasma), eruptive xanthomas, tuberous xanthomas, tendinous xanthomas, and verruciform xanthomas. Except for xanthelasma, the most common subtype, cutaneous xanthomas are uncommon².

Eruptive xanthomas consist of yellow papules 2 - 5 mm in diameter arising on an erythematous base. They usually appear in large numbers over extensor surfaces, particularly the buttocks, back, legs, and arms. In extreme cases, they are pruritic and are more widely distributed. Their foamy macrophages contain triglycerides as well as cholesterol. Resulting from hypertriglyceridemia, they are almost always accompanied by lipaemia retinalis, a creamy yellow discoloration of the retinal blood vessels, and a lipaemic appearance of blood or serum samples³. The Koebner phenomenon has been reported to occur with eruptive xanthomas⁴.

Eruptive xanthomas can be seen in the setting of primary or secondary hypertriglyceridemia. Approximately 8.5% of patients with severe hypertriglyceridemia will present with these cutaneous findings⁵. Triglyceride levels in patients with eruptive xanthomas often exceed 3000 to 4000 mg/dl. In the Frederickson classification of hyperlipidemias, hypertriglyceridemia can be seen in type I (elevated chylomicrons), type IV (elevated VLDLs) and type V (elevated chylomicrons and VLDLs).



One reason for elevated triglyceride levels is failure to remove such lipids from the circulation. Deficient activity of lipoprotein lipase will lead to the accumulation of triglyceride-rich chylomicrons and VLDLs. This can be related to abnormalities in the enzyme itself, as in *lipoprotein lipase deficiency (chylomicronemia syndrome)*, or in other controlling factors such as *dysfunctional apoprotein C-II* or *impaired insulin activity*.

Another reason for increased triglyceride levels is the hepatic overproduction of triglyceride-rich lipoproteins via the endogenous pathway. In endogenous familial hypertriglyceridemia, a genetic defect exists that causes the liver to respond abnormally to dietary carbohydrates and insulin, with overproduction of hepatic VLDLs. The result is a Frederickson type IV pattern of hypertriglyceridemia. Secondary acquired defects in lipoprotein lipase activity, such as those due to diabetes mellitus, are not uncommon in these patients. With this second insult, the lipoprotein lipase system can become saturated and, as a result, no longer handles dietary lipids, leading

to chylomicron elevations as well. This pattern is classified as a Frederickson type V phenotype.

Environmental factors and underlying diseases commonly exacerbate genetic defects of triglyceride metabolism, leading to worsening of hypertriglyceridemia with eruptive xanthoma formation. Such factors include obesity, high caloric intake, diabetes mellitus, alcohol abuse, oral estrogen replacement, and systemic medications that can lead to hypertriglyceridemia (e.g. retinoids, protease inhibitors, olanzapine). The resultant pattern usually leads to a Frederickson type IV phenotype.

Oral retinoid therapy (especially bexarotene) can elevate triglyceride levels through the elevation of hepatic VLDL secretion. With isotretinoin, this finding seems to be more prevalent in genetically predisposed individuals and may signal an increased risk for future metabolic syndrome. Two of the five criteria for the clinical diagnosis of metabolic syndrome are lipid abnormalities - elevated triglycerides and reduced HDLs⁶.

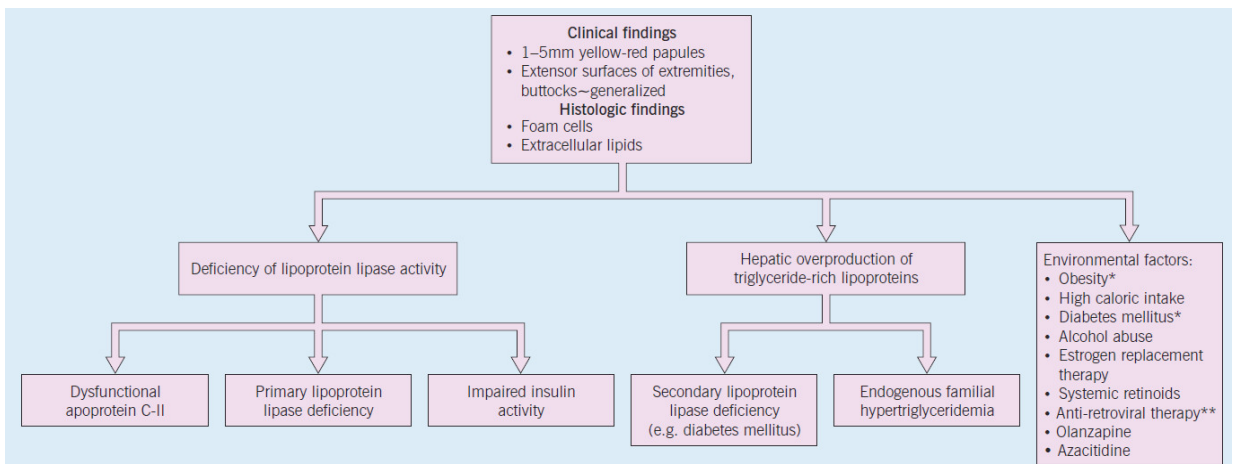


Figure 4 . Underlying disorders in patients with eruptive xanthomas⁶

Histopathology of eruptive xanthomas demonstrates foam cells, a mixed inflammatory cell infiltrate with lymphocytes, neutrophils, and histiocytes, and extracellular lipid deposits. Foam cells may be few in number in early eruptive xanthomas².

The treatment of eruptive xanthomas involves identifying and treating the underlying causes of hypertriglyceridemia. Failure to recognize and treat the patient with hypertriglyceridemia could lead to complications such as acute pancreatitis and other serious medical conditions such as coronary artery disease⁷. Pharmacologic and dietary lowering of the circulating triglycerides to reasonable levels will result in the prompt resolution of the eruptive lesions. If the xanthomas do not resolve spontaneously or following

treatment of the underlying condition, surgery, laser or cryosurgery may be an option.

4. CONCLUSION

Appearance of eruptive xanthoma can herald the onset of serious complications related to severe hypertriglyceridemia. Failure to diagnose and treat hyperlipidemia leads to an increased risk of atherosclerosis, cardiovascular disease, and pancreatitis. The present case shows how important the role of a dermatologist is in the process of metabolic disease diagnosis.

REFERENCES

1. Zak A, Zeman M, Slaby A, Vecka M. Xanthomas: clinical and pathophysiological relations. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub.* 2014;158(2):181-188. doi:10.5507/bp.2014.016.
2. Cutaneous xanthomas - UpToDate. Accessed July 10, 2022. https://www.uptodate.com/contents/cutaneous-xanthomas?search=eruptive%20xanthoma&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1.
3. Christopher E. M. Griffiths, Jonathan Barker, Tanya Bleiker, Robert Chalmers, Daniel Creamer. *Rook's Text Book of Dermatology.*
4. Scavo S, Magro G, Gurrera A, Gozzo E, Ignaccolo L, Neri S. Isomorphic response in eruptive xanthomas. *Dermatology.* 2004;209(1):66-68. doi:10.1159/000078592.
5. Roga G, Jithendriya M. Eruptive xanthoma: Warning sign of systemic disease. *Cleve Clin J Med.* 2016;83(10):715-716. doi:10.3949/ccjm.83a.15126.
6. Jeffrey P. Callen, Lorenzo Cerroni. Bologna, Dermatology. In: 3th edition.
7. Inoue-Nishimoto T, Hanafusa T, Hirohata A, et al. Eruptive Xanthoma with Acute Pancreatitis in a Patient with Hypertriglyceridemia and Diabetes. *Annals of Dermatology.* 2016;28(1):136-137. doi:10.5021/ad.2016.28.1.136.