

YU-CHUN HSUEH, MD

Division of Endocrinology and Metabolism,
Department of Internal Medicine,
Wan Fang Hospital, Taipei Medical
University, Taipei, Taiwan

CHUAN-LIANG CHOU, MD

Division of Endocrinology and Metabolism,
Department of Internal Medicine,
Wan Fang Hospital, Taipei Medical
University, Taipei, Taiwan

TING-I. LEE, MD, PhD

Division of Endocrinology and Metabolism,
Department of Internal Medicine,
Wan Fang Hospital, Taipei Medical
University, Taipei, Taiwan

Diabetic dyslipidemia with eruptive xanthoma

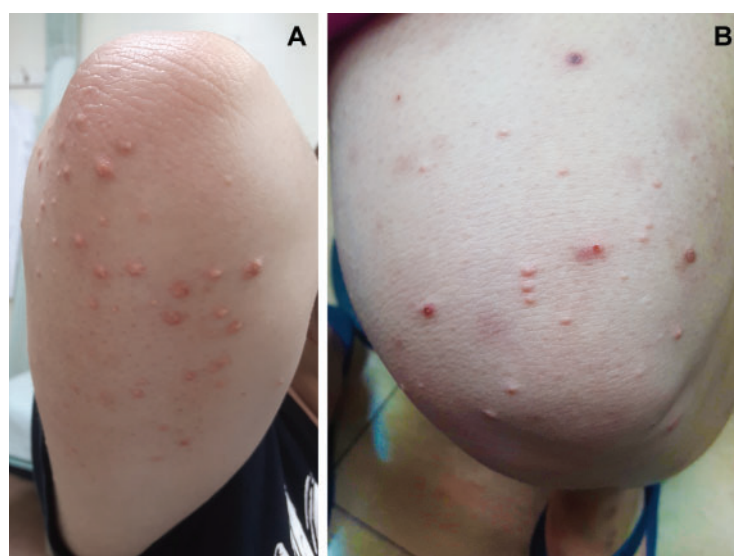


Figure 1. The patient had multiple pink to yellowish papules 2 to 5 mm in diameter over the extensor surface of the right upper arm (A) and left thigh (B).

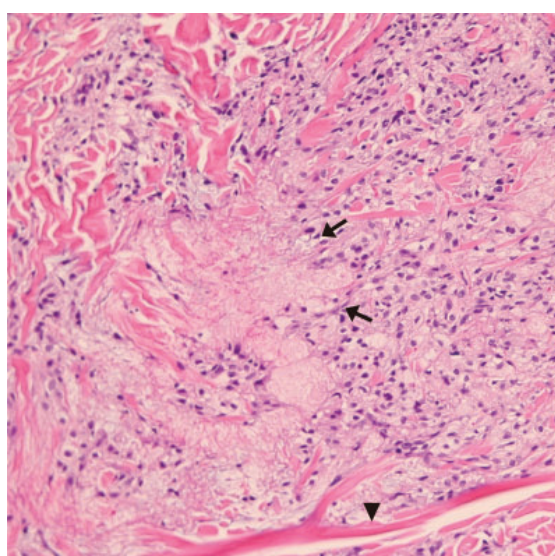


Figure 2. Biopsy study showed foamy histiocytes (arrows) mixed with streaks of connective tissue (arrowhead) in the dermis, features typical of eruptive xanthoma (hematoxylin and eosin, $\times 200$).

A 21-YEAR-OLD WOMAN with obesity, type 2 diabetes mellitus, and dyslipidemia presented with eruptive lesions on her extremities that first appeared 2 weeks earlier. Yellowish erythematous papules were noted on the extensor surfaces of both arms and thighs (**Figure 1**).

Skin biopsy study showed foamy histiocytes mixed with streaks of connective tissue in the dermis (**Figure 2**). Her fasting serum triglyceride level was 10,250 mg/dL (reference range < 150) and her hemoglobin A_{1c} level was 12.4% (reference range 4%–5.6%). On further questioning, the patient said that she had stopped taking her prescribed antidiabetic medications and fenofibrate a year previously.

A workup for secondary causes of hypertriglyceridemia was negative for hypothyroidism and nephrotic syndrome. She was currently taking no medications. She had no family history of dyslipidemia, and she denied alcohol consumption.

Based on the patient's presentation, history, and the results of laboratory testing and skin biopsy, the diagnosis was eruptive xanthoma.

■ A RESULT OF ELEVATED TRIGLYCERIDES

Eruptive xanthoma is associated with elevation of chylomicrons and triglycerides.¹ Hyperlipidemia that causes eruptive xanthoma may be familial (ie, due to a primary genetic

doi:10.3949/ccjm.86a.18104

defect) or secondary to another disease, or both.

Types of primary hypertriglyceridemia include elevated chylomicrons (Frederickson classification type I), elevated very-low-density lipoprotein (VLDL) (Frederickson type IV), and elevation of both chylomicrons and VLDL (Frederickson type V).^{2,3} Hypertriglyceridemia may also be secondary to obesity, diabetes mellitus, hypothyroidism, nephrotic syndrome, liver cirrhosis, excess ethanol ingestion, and medicines such as retinoids and estrogens.^{2,3}

Lesions of eruptive xanthoma are yellowish papules 2 to 5 mm in diameter surrounded by an erythematous border. They are formed by clusters of foamy cells caused by phagocytosis of macrophages as a consequence of increased accumulations of intracellular lipids. The most common sites are the buttocks, extensor surfaces of the arms, and the back.⁴

Eruptive xanthoma occurs with markedly elevated triglyceride levels (ie, > 1,000 mg/dL),⁵ with an estimated prevalence of 18 cases per 100,000 people (< 0.02%).⁶ Diagnosis is usually established through the clinical history, physical examination, and prompt laboratory confirmation of hypertriglyceridemia. Skin biopsy is rarely if ever needed.

RECOGNIZE AND TREAT PROMPTLY TO AVOID FURTHER COMPLICATIONS

Severe hypertriglyceridemia poses an increased risk of acute pancreatitis. Early recognition and medical treatment in our patient prevented serious complications.

Treatment of eruptive xanthoma includes identifying the underlying cause of hypertriglyceridemia and commencing lifestyle modifications that include weight reduction, aerobic exercise, a strict low-fat diet with avoidance of simple carbohydrates and alcohol,⁷ and drug therapy.

The patient's treatment plan

Although HMG-CoA reductase inhibitors (statins) have a modest triglyceride-lowering effect and are useful to modify cardiovascular risk, fibric acid derivatives (eg, gemfibrozil, fenofibrate) are the first-line therapy.⁸ Omega-3 fatty acids, statins, or niacin may be added if necessary.⁸

Our patient's uncontrolled glycemia caused marked hypertriglyceridemia, perhaps from a decrease in lipoprotein lipase activity in adipose tissue and muscle. Lifestyle modifications, glucose-lowering agents (metformin, glimepiride), and fenofibrate were prescribed. She was also advised to seek medical attention if she developed upper-abdominal pain, which could be a symptom of pancreatitis.

REFERENCES

1. Flynn PD, Burns T, Breathnach S, Cox N, Griffiths C. Xanthomas and abnormalities of lipid metabolism and storage. In: Rook's Textbook of Dermatology. 8th ed. Oxford: Blackwell Science; 2010.
2. Breckenridge WC, Alaupovic P, Cox DW, Little JA. Apolipoprotein and lipoprotein concentrations in familial apolipoprotein C-II deficiency. *Atherosclerosis* 1982; 44(2):223–235. PMID:7138621
3. Santamarina-Fojo S. The familial chylomicronemia syndrome. *Endocrinol Metab Clin North Am* 1998; 27(3):551–567. PMID:9785052
4. Melmed S, Polonsky KS, Larsen PR, Kronenberg H. *Williams Textbook of Endocrinology*. 13th ed. Philadelphia: Elsevier; 2016.
5. 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
6. Leaf DA. Chylomicronemia and the chylomicronemia syndrome: a practical approach to management. *Am J Med* 2008; 121(1):10–12. doi:10.1016/j.amjmed.2007.10.004
7. Hegele RA, Ginsberg HN, Chapman MJ, et al; European Atherosclerosis Society Consensus Panel. The polygenic nature of hypertriglyceridaemia: implications for definition, diagnosis, and management. *Lancet Diabetes Endocrinol* 2014; 2(8):655–666. doi:10.1016/S2213-8587(13)70191-8
8. Berglund L, Brunzell JD, Goldberg AC, et al; Endocrine Society. Evaluation and treatment of hypertriglyceridemia: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2012; 97(9):2969–2989. doi:10.1210/jc.2011-3213

ADDRESS: Ting-I Lee, MD, PhD, Wan Fang Hospital, Taipei Medical University, 111 Shin Lung Road Section 3, Taipei, Taiwan; agleems29@gmail.com