An unusual presentation of eruptive xanthoma  
A case report and literature review

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Abstract
Background: Eruptive xanthomas are benign skin lesions caused by localized deposition of lipids in the dermis. The lesions are generally caused by elevated levels of serum triglycerides that leak through the capillaries and are phagocytosed by macrophages in the dermis. Clinical manifestation varies from asymptomatic skin lesions to intense pruritus and tenderness.

Methods: We present a case of a middle-aged man admitted with diabetic ketoacidosis secondary to noncompliance with insulin. He was found to have skin lesions as multiple crusted papules on the extremities. Further evaluation revealed elevated serum triglycerides. A diagnosis of eruptive xanthomas was made on skin biopsy, and after starting treatment with lipid lowering agents his cutaneous lesions gradually subsided.

Conclusion: Appearance of eruptive xanthomas can signify the onset of serious complications. Prompt recognition of such skin manifestations is warranted to prevent development of fatal medical condition like coronary artery disease and pancreatitis.

Abbreviation: VLDL = very low-density lipoprotein.

Keywords: benign skin lesion, case report eruptive xanthoma, diabetic ketoacidosis, unusual presentation

1. Introduction
Cutaneous manifestations are often an early warning sign of a systemic disease. Practitioners should be familiar with common dermatological symptoms of medical conditions so that they may recognize such symptoms early and prevent complications with timely evaluation and therapy. Eruptive xanthomas are benign skin lesions that are caused by localized deposition of lipids in the dermis, which are typically caused by elevated levels of serum triglycerides and uncontrolled diabetes. Xanthomas can present as early manifestations of systemic disorders and uncommonly as sole manifestations. Early recognition and treatment of the underlying condition decreases morbidity and mortality. We present a patient with multiple yellowish, erythematous papules on the extremities suggestive of eruptive xanthomas admitted to our hospital with diabetic ketoacidosis.

2. Case presentation
We present a case of 44-year-old man who presented to the emergency department with nausea, vomiting, and epigastric discomfort of 1-day duration. Epigastric pain was dull, intermittent, nonradiating with no specific aggravating factors and relieved with pain medications and antacids. He did not have chest pain, fever or diarrhea, or urinary symptoms. He never had similar symptoms in the past. His past medical history was significant for poorly controlled diabetes mellitus. He had never smoked tobacco and had no toxic habits. He had no reported allergies. His medications included low-dose aspirin, atorvastatin, and insulin. However, he was not compliant with medications. He had a sedentary lifestyle and was not adherent to diabetic dietary regimen. He was diagnosed to have severe diabetic ketoacidosis during the initial investigations and was admitted to the intensive care unit for further management.

Physical examination in intensive care unit revealed a middle-aged man of average built. Vitals showed temperature of 98.6°F, pulse rate 88/minute, respiratory rate of 16/minute, blood pressure 120/80 mmHg, and body mass index of 28 kg/m². He was saturating 98% on ambient air. He was found to have multiple skin-colored to yellowish nontender, nonfollicular papules of variable sizes (5–7 mm) flecked with collarettes of scale. Lesions were concentrated on extensor surface of both arms, thighs with some involvement of the abdomen (Fig. 1). On further evaluation, patient had these lesions for 2-weeks and they were asymptomatic. He did not complain of any joint pain. He had no known history of food- or drug-allergy. Personal or family history of similar lesions was lacking. He did not report any family history of diabetes mellitus or familial hypertriglyceridemia. Fasting lipid profile showed a triglyceride level of 1389 mg/dL, total cholesterol of 599 mg/dL, and low-density lipoprotein level of 278 mg/dL (Table 1). His lipoprotein lipase level was 25 mg/dL and was also found to have HbA1c level of 13.4, elevated fasting, postprandial blood glucose levels, glycosuria, and ketonuria. Punch biopsy from an elbow lesion was consistent...
with eruptive xanthoma (Fig. 2). The patient was started on a treatment with gemfibrozil and atorvastatin in addition to dietary and lifestyle modification. He was subsequently followed in the clinic and had a complete resolution of the skin lesions (Fig. 3), with an associated decrease in his serum triglyceride, cholesterol levels, and hemoglobin A1c.

3. Discussion
Xanthomas are fatty deposits in the skin, and 5 different forms have been described, including eruptive xanthomas, tuberous/tendinous xanthoma, flat xanthomas, verrucous xanthomas, and xanthelasma.[1]

Eruptive xanthoma most commonly involves the extensor surfaces of the extremities, buttocks, and back.[2] The disease is a characteristic manifestation of extreme hypertriglyceridemia.[3] Exact epidemiological data on the prevalence of various types of xanthoma are lacking, eruptive xanthomas are retrospectively reported in 10% of patients with severe hypertriglyceridemia.[4]

High-fasting triglyceride concentrations invariably are related to high chylomicron, very low-density lipoprotein (VLDL) levels, and familial lipoprotein lipase deficiency. Elevated VLDL and chylomicron levels can result from increased hepatic VLDL production or decreased lipolysis of VLDL and chylomicrons. Increased hepatic VLDL production can be either familial in origin or secondary to obesity, diabetes, alcohol, or estrogen administration. Decreased lipolysis of VLDL and chylomicrons can also be genetic or acquired, such as resulting from hypothyroidism, β blockade, or diabetes mellitus. Secondary hypertriglyceridemia can sometimes be seen with end-stage renal disease, human immunodeficiency virus infection, and treatment with several medications (isotretinoin, sodium valproate, protease inhibitors, sertraline, thiazide diuretics, cyclosporine, and tacrolimus).[5] Eruptive xanthoma presents as crops of small, pinkish-yellow, shiny papules, nodules, or plaques.[6] The lesions usually vary in size from 1- to 4-mm.[7] Patients usually present due to itchiness or for cosmetic reasons. Acutely, variable amounts of pruritus and pain can occur. In this case however patient did not report any symptoms related to the skin lesions. Koebner phenomenon has been reported with eruptive xanthomas.[8]

Xanthomatous lesions result from uptake and storage of cholesterol, triglycerides, and phospholipids by macrophages (formation of “foam cells”) with their subsequent deposition in the dermis. A skin biopsy reveals inflammatory cells and extracellular deposition of lipids between the collagen fibers. In the papillary and upper reticular dermis, affected patients typically possess a nodular infiltrate of histiocytes with abundant, finely vacuolated cytoplasm that is indicative of lipidized macrophages, the so-called foam cells. There is an accompanying mild perivascular and lymphocytic infiltrate.[9]

Diagnosis is often clinical, but a biopsy is indicated for confirmation. The differential diagnosis includes Langerhans cell histiocytosis, disseminated granuloma annulare, non-Langerhans cell histiocytosis (xanthoma disseminatum, the micronodular form of juvenile xanthogranuloma), and generalized eruptive histiocytoma. Langerhans cell histiocytosis manifests histologically as numerous histiocytes cells with an abundant pale cytoplasm and an eccentric, indented, kidney-shaped nucleus, but few clear cells and no touton giant cells.[10] Eruptive xanthoma is differentiated from disseminated granuloma annulare by the abundance of perivascular histiocytes and xanthomized histiocytes, the presence of lipid deposits, and the deposition of hyaluronic acid on the edges.[11] Xanthoma disseminatum consists of numerous, small, reddish-brown papules that are evenly spread over the face, skin-folds, trunk, and proximal extremities. Juvenile xanthogranuloma occurs primarily in

| Laboratory parameters. | Levels at presentation | Levels 1 month later | Levels at 3 months |
|------------------------|------------------------|----------------------|-------------------|
| Triglycerides, mg/dL   | 1389                   | 165                  | 98                |
| LDL, mg/dL             | 279                    | 120                  | 96                |
| Total cholesterol, mg/dL | 599                  | 310                  | 163               |
| HDL, mg/dL             | 32                     | 40                   | 54                |
| Hba1c                  | 13.4                   | 8                    |                   |

Hba1c = hemoglobin A1c, HDL = high-density lipoprotein, LDL = low-density lipoprotein.
children and is characterized by discrete yellowish-orange nodules, which commonly appear on the scalp, face, and upper trunk. This disease is in most cases a solitary lesion, but multiple lesions may occur. Generalized eruptive histiocytoma lesions are firm, erythematous, or brownish papules that appear in successive crops over the face, trunk, and proximal surfaces of the limbs. Apolipoprotein testing can be used to determine if the xanthomas are a manifestation of an inherited condition, but could not be performed in this case due to the patient’s insurance issues.

Appearance of eruptive xanthomas should lead to evaluation for severe hypertriglyceridemia, especially in patients with newly diagnosed or poorly controlled diabetes mellitus. An elevated risk of acute pancreatitis and coronary artery disease occurs if the condition is unrecognized. Adequate treatment involves controlling the underlying hyperlipidemia with strict dietary therapy and HMG-CoA reductase inhibitors. Weight reduction and carbohydrate intake restriction are helpful in cases associated with insulin resistance. Once lipid levels normalize, gradual resolution of cutaneous lesions is typically observed. In cases in which medical management does not resolve the lesions surgery, laser, or cryosurgery are therapeutic alternatives.

4. Conclusion

Appearance of eruptive xanthoma can herald the onset of serious complications related to severe hypertriglyceridemia. Prompt recognition of eruptive xanthomas and awareness of its association with hypertriglyceridemia, newly diagnosed or decompensated diabetes mellitus can help to decrease any lag between a patient being seen by a physician and initiating treatment for a serious medical condition.

References

[1] Streit E, Helmbold P. 65-year-old man with yellow-orange papules on both forearms. Eruptive xanthomas. Hautarzt 2009;60:834–7.
[2] Abdelghany M, Massoud S. Eruptive xanthoma. Cleve Clin J Med 2015;82:209–10.
[3] Durrington P. Dyslipidaemia. Lancet 2003;362:717–31.
[4] Zak A, Zeman M, Slaby A, et al. Xanthomas: clinical and pathophysiological relations. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 2014;158:181–8.
[5] Brunzell JD. Clinical practice. Hypertriglyceridemia. N Engl J Med 2007;357:1009–17.
[6] Green WL, Benitez F, Velez L, et al. Man with a rash. Eruptive xanthoma. Ann Emerg Med 2013;61:595-603.
[7] Zaremba J, Zaczkiewicz A, Placek W. Eruptive xanthomas. Postepy Dermatol Alergol 2013;30:399–402.
[8] Naik NS. Eruptive xanthomas. Dermatol Online J 2001;7:11.
[9] Merola JF, Mengden SJ, Soldano A, et al. Eruptive xanthomas. Dermatol Online J 2008;14:10.
[10] Chi DH, Sung KJ, Koh JK. Eruptive xanthoma-like cutaneous Langerhans cell histiocytosis in an adult. J Am Acad Dermatol 1996;34:688–9.
[11] Cooper PH. Eruptive xanthoma: a microscopic simulant of granuloma annulare. J Cutan Pathol 1986;13:207–15.
[12] Roller E, Schulte KW, Hengge U, et al. Eruptive xanthomas. Hautarzt 2004;55:978–80.