



Case Report

Eruptive xanthomas secondary to severe hypertriglyceridemia

Wade Hopper¹, Spiro Veria², Logan Glosser^{2*}, Anu Garg³,
Mohammed T Awad³, Justin Smith² and Shahab Ud Din³

¹Edward via College of Osteopathic Medicine, 350 Howard St, Spartanburg, SC, 29307, USA

²University of Toledo College of Medicine and Life Sciences, 3000 Arlington Ave, Toledo, OH, 43614, USA

³Department of Internal Medicine, University of Toledo Medical Center, Toledo, OH, 43614, USA

Received: 29 September, 2021

Accepted: 16 October, 2021

Published: 18 October, 2021

***Corresponding author:** Logan D Glosser, University of Toledo College of Medicine and Life Sciences, 3000 Arlington Ave, Toledo, OH, 43614, USA, Tel: 419-705-6757; E-mail: Logan.glosser@rockets.utoledo.edu

ORCID: <https://orcid.org/0000-0003-0978-7930>

Keywords: Hypertriglyceridemia; Xanthoma; Hyperlipidemia; Lipid-reducing therapy; Statins

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Abstract

Xanthomas are benign cutaneous manifestations of extracellular lipid accumulation. Eruptive xanthoma is characterized by the acute, widespread presentation of a papular rash and usually involves the back, buttocks, and extremities. Eruptive xanthoma is associated with hyperlipidemia, hypertriglyceridemia, and an increased long-term risk of atherosclerotic cardiovascular disease. We present a case of eruptive xanthoma accompanied by severe hypertriglyceridemia (10,164 mg/dL) in which the course of the disease was reversed following implementation of lipid-lowering pharmacotherapy.

Abbreviations

BMI: Body Mass Index; PCP: Primary Care Physician; CBC: Complete Blood Count; CMP: Complete Metabolic Panel

Introduction

One of the manifestations of hypertriglyceridemia is xanthomas which are defined as skin lesions that develop secondary to extracellular lipid accumulation. Eruptive xanthoma is one of the uncommon presentations of severe hypertriglyceridemia. It is a sudden eruption of small yellowish skin papules rounded by an erythematous halo. It usually appears on the buttocks, thighs, elbows, and lumbar region. It also can appear within three weeks after a significant increase in triglyceride level [1]. The lesions can be tender but tend to be asymptomatic. Eruptive xanthomas are herald signs of hypertriglyceridemia, which itself is associated with acute pancreatitis [2-4]. There is a 5-10% risk of acute pancreatitis in patients with serum triglycerides >1000 mg/dL, and that risk rises to 20% in patients with blood triglycerides >2000 mg/dL [5]. Other associations with eruptive xanthomas are diabetes mellitus, hepatosteatorosis, and lipemia retinalis [6]. Here, we

are reporting a rare case of eruptive xanthomas which was secondary to severe hypertriglyceridemia.

Case presentation

A 21-year-old Caucasian male presented to a Primary Care Physician (PCP) to establish care, as he had not been to a doctor in "a while." He reported a 3-week history of progressively worsening skin bumps. The patient reported having similar bumps about 1 year prior, however he did not seek medical care as it resolved on its own. The patient denied itching, fever/chills, abdominal pain, joint pain, or neurologic disturbances. His reported prior medical history only included obesity (BMI of 33 kg/m²), dyslipidemia, and repair of a left arm fracture. He was not taking any medications and had no allergies. He was a non-drinker, non-smoker, did not use marijuana or other illicit drugs. His family history was significant for type 2 diabetes in his father, and hypertension in his mother.

On physical exam, the patient had skin lesions diffusely covering the body, with the most concentrated lesions over the face, trunk, and bilateral upper/lower extremities (Figure 1). His vital signs were significant for elevated blood pressure



Figure 1: Initial presentation of patient with Xanthomas with clear eruptive papules.

2 months after the initial presentation, the patient returned to his PCP for a follow-up visit. Results from the daily morning glucose checks showed his blood sugars were still uncontrolled ranging from 188-300 with a fasting average of ~200. At this point the patient was started on insulin glargine (Lantus) 12 units daily.

4 months after the initial presentation, the patient returned to the PCP for follow-up. He again reported no adverse effects to the medications, however he did not schedule a visit to see the ophthalmologist, stating again it was related to insurance issues. Physical exam showed drastic improvement in the size and number of the lesions (Figure 2). Laboratory analysis coincided with the improvement, as his triglyceride levels reduced to 256 mg/dL with total cholesterol 144 mg/dL (normal), HDL 28 mg/dL (normal), VLDL 51 mg/dL (elevated), and LDL 65 mg/dL (normal). Hemoglobin A1c had normalized to 6.2%. Despite the improvement in laboratory values and lesions, the patient had gained 7 pounds since the prior visit.

After 7 months of treatment, the patient visited the PCP with remarkable improvement in his skin lesions (Figure 3). The patient had gained an additional 10 pounds over the 2 months since the prior visit, and his home fasting blood glucose monitoring were still consistently elevated. Lantus

of 142/88 mmHg, but otherwise within normal limits. A skin biopsy of one of the lesions on the left upper arm was taken, and the patient was sent to the lab for immediate workup with a lipid profile, CBC, and CMP. These returned with severe abnormalities including hypercholesterolemia (1251 mg/dL), hypertriglyceridemia (9603 mg/dL), HDL (16 mg/dL). The patient was started on fenofibrate 130 mg capsule daily and atorvastatin (Lipitor) 40 mg tablet daily.

The patient returned 1 week later to review the results. The lipid profile revealed severely elevated fasting total cholesterol at 1308 mg/dL, elevated triglycerides at 10,164 mg/dL. HDL 16 (low), VLDL and LDL were unable to be calculated. Random blood glucose was elevated at 320 mg/dL, and hemoglobin A1c was elevated at 9.1%. Skin biopsy result showed a grossly pale tan papular lesion at the epidermal surface and foamy histiocytes were identified on microscopic evaluation, consistent with eruptive xanthoma. The patient was diagnosed with mixed hypercholesterolemia and hypertriglyceridemia, type 2 diabetes mellitus, and eruptive xanthoma. For the hypertriglyceridemia, fenofibrate was discontinued, and gemfibrozil 600 mg tablet twice daily was started. For diabetes management, metformin 500 mg tablet twice daily was started, and a lengthy discussion was held to emphasize the importance of weight loss and lifestyle improvement. The patient also received verbal and printed guidance for dietary and exercise counseling. The patient was referred to endocrinology to achieve optimal management of the diabetes.

1 month later, the patient returned to the PCP. The patient stated that he was unable to obtain the metformin or schedule the visit with endocrinology due to lack of insurance coverage. The patient reported mild improvement of his skin lesions and no side effects from the medications initiated at the prior visit. The patient had lost 7 pounds since the last visit, reporting "regular walking for exercise" and "watching what he ate". Urinalysis showed albuminuria, with a microalbumin/creatinine ratio of 548.4 mg/g. For the albuminuria the patient was started on lisinopril 2.5 mg tablet once daily and referred to ophthalmology to evaluate for diabetic changes. The patient was also prescribed a glucometer with OneTouch delica lancets for daily morning blood sugar checks.



Figure 2: After 4-months on anti-lipid therapy, the papules have reduced in size and quantity.



Figure 3: Image of the patient's right arm with significant improvement in lesions size and density, and the left arm with most of the lesions resolved with a well-healing scar from the initial biopsy.

was increased to 14 units daily for the hyperglycemia, and gemfibrozil was discontinued with the normalizing triglycerides.

At the 8 months follow-up, the patients continued to improve with the home monitoring average fasting blood glucose of 120 and office blood pressure recorded at 102/65. During this visit, the patient reported years of anxiety episodes lasting weeks at a time, scoring a 10 on the GAD-7 in the office. The patient was initiated on escitalopram 10 mg tablet once daily. A TSH₃ with reflex and FT₄ were ordered to rule-out thyroid related disease.

10 months after initial presentation, the patient again returned to the PCP. The patient reported improvement in his anxiety with the escitalopram, however he had been non-compliant with taking gemfibrozil on a regular basis, although he did not report any specific reason or adverse effects. This was evident as his triglyceride level had spiked to 330 mg/dL, with a total cholesterol of 159 mg/dL (normal), VLDL 66 mg/dL (elevated), LDL 58 mg/dL, HDL 4.5 mg/dL. The gemfibrozil was discontinued, and omega-3 fatty acid 1000 mg capsule once daily was initiated. Fortunately, the skin lesions had completely resolved. The patient remains on medical management for the diabetes and hypertriglyceridemia.

Discussion

We reported a case of eruptive xanthomas which are commonly found in the extremities and trunk. The patient presented to his primary care provider with skin lesions. The differential diagnosis for eruptive xanthoma includes molluscum contagiosum, histiocytosis, and generalized granuloma annulare, all of which would be confirmed via pathology in the absence of remarkably elevated triglycerides. The patient was found to have severe hypertriglyceridemia (more than 10000 mg/dl) and type II diabetes mellitus, both of which play a causative role in the formation of xanthomas: lipids form the core of such lesions, while vascular injury associated with high blood glucose encourages the diffusion of lipids into tissues [1]. Histologic examination of the lesions is necessary to confirm the diagnosis of eruptive xanthoma and typically demonstrates foamy macrophages, as in this case.

There are currently no professional guidelines specific to the medical treatment of cutaneous xanthomas. The treatment of eruptive xanthomas is dependent upon correcting underlying blood lipid imbalances through lifestyle modification and pharmacological therapy. Normalizing lipid profiles generally leads to the progressive resolution of cutaneous xanthomas over the course of months to years. The mechanism by which this happens is unclear, but medical literature does show a few examples of xanthomas resolving following the treatment of high blood lipids [7-11]. Lipid-lowering therapies are also important in reducing the long-term risk for serious cardiovascular disease that is associated with high blood triglycerides [12]. We report a case of eruptive xanthoma with papules which receded following initiation of therapy with fenofibrate, atorvastatin, and insulin. We present evidence that these therapeutic steps can slow and reverse the cutaneous

course of eruptive xanthoma by treating the underlying cause of the rash.

The patient had a baseline serum triglyceride level of 9603 mg/dL and a baseline total cholesterol of 1251 mg/dL. A high-intensity statin was paired with a fibrate to normalize this patient's blood lipid profile. Statins and fibrates reduce the long-term risk of cardiovascular events in patients with high LDL cholesterol and hypertriglyceridemia, respectively [13]. Per American guidelines, statins are first-line therapy for lowering LDL [14]. After 4 months of treatment with atorvastatin, this patient showed a total cholesterol of 144 mg/dL (88% reduction) with normal fractions of HDL and LDL. Whereas statins are well-proven, the role of fibrates in the treatment of cardiovascular disease is still being explored by the medical community [15]. Currently, many professional medical organizations view both fibrates and high-dose omega-3 fatty acids as first-line therapies for attempting to lower very high triglyceride levels [16]. After 4 months of treatment with fibrates, this patient showed a serum triglyceride level of 256 mg/dL (97% reduction). In this case, when the patient reported poor compliance with gemfibrozil, the fibrate was discontinued and replaced with a once-daily 1000mg capsule of omega-3 fatty acids. Supplementary omega-3 fatty acids have a minimal risk profile and can be easily taken with meals.

The patient had a baseline HbA_{1c} of 9.1%. The American Diabetes Association (ADA) endorses a HbA_{1c} goal of 7.0% as being appropriate for most adults with diabetes [17]. The ADA also endorses metformin as the preferred initial pharmacotherapy in the treatment of adults with type II diabetes [18]. Due to a lack of insurance coverage, this patient could not afford metformin and could not follow up with endocrinology. Upon this revelation, the treatment strategy shifted towards nonpharmaceutical blood glucose management. However, daily fasting blood glucose checks revealed the patient had difficulty controlling his sugars. Basal insulin was covered by the patient's insurance and therefore was started at the 2-month follow-up. By the 4-month follow-up, the patient had achieved satisfactory glycemic control with an A_{1c} of 6.2%.

Conclusion

This case demonstrates that lipid-lowering pharmacotherapy can reverse the cutaneous course of eruptive xanthoma. The severely elevated triglyceride level accompanying the typical skin lesions made our case unique. It is important for health care providers to know that eruptive xanthomas are usually herald signs of metabolic imbalance that can lead to severe and potentially fatal consequences. Future research should focus on establishing guidelines for the proper pharmacologic treatment of xanthomas given the growing case literature on the topic.

Contributions

All authors read and approved the final version to be published.

Consent

Written informed consent was obtained from the patient



for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Provenance and peer review

Not commissioned, externally peer-reviewed

References

- Zak A, Zeman M, Slaby A, Vecka M (2014) Xanthomas: clinical and pathophysiological relations. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 158: 181-188. [Link: https://bit.ly/3DS5lv4](https://bit.ly/3DS5lv4)
- Roga G, Jithendriya M (2016) Eruptive xanthoma: Warning sign of systemic disease. Cleve Clin J Med 83: 715-716. [Link: https://bit.ly/3jdJCvn](https://bit.ly/3jdJCvn)
- Martínez DP, Díaz JO, Bobes CM (2008) Eruptive xanthomas and acute pancreatitis in a patient with hypertriglyceridemia. Int Arch Med 1: 6. [Link: https://bit.ly/3FSE6YG](https://bit.ly/3FSE6YG)
- Duzayak S, Sayiner ZA, Erkiç S, Inaloz HS (2017) Acute pancreatitis with eruptive xanthoma. BMJ Case Rep 2017: bcr2017221543. [Link: https://bit.ly/3FY51Cw](https://bit.ly/3FY51Cw)
- Scherer J, Singh VP, Pitchumoni CS, Yadav D (2014) Issues in hypertriglyceridemic pancreatitis: an update. J Clin Gastroenterol 48: 195-203. [Link: https://bit.ly/3j9WAKq](https://bit.ly/3j9WAKq)
- Santiago L, Pinho A, Cardoso JC (2018) Eruptive Xanthomas: A Cardinal Manifestation of Serious Metabolic Disease. Acta Med Port 31: 219-222. [Link: https://bit.ly/2Xn831J](https://bit.ly/2Xn831J)
- Kashif M, Kumar H, Khaja M (2016) An unusual presentation of eruptive xanthoma: a case report and literature review. Medicine 95: e4866. [Link: https://bit.ly/3BQsjb2](https://bit.ly/3BQsjb2)
- Solak B, Kara RO, Acikgoz SB, Kosem M (2015) First and only symptom of undiagnosed diabetes mellitus: eruptive xanthoma. BMJ Case Rep bcr2015212160. [Link: https://bit.ly/3BN58OG](https://bit.ly/3BN58OG)
- Lee SY, Sheth CA (2019) Eruptive xanthoma associated with severe hypertriglyceridemia and poorly controlled type 1 diabetes mellitus. J Community Hosp Intern Med Perspect 9: 344-346. [Link: https://bit.ly/3n6C261](https://bit.ly/3n6C261)
- Kim WJ, Ko HC, Kim BS, Kim MB (2012) Successful treatment of xanthoma disseminatum with combined lipid lowering agents. Ann Dermatol 24: 380-382. [Link: https://bit.ly/3AQG7AW](https://bit.ly/3AQG7AW)
- Wu NG, Guo YL, Zhu CG, Gao Y, Liu G, et al. (2019) Rapid Regression of Multiple-Site Xanthomas in an Adult with Homozygous Familial Hypercholesterolemia by Triple Lipid-Lowering Drugs. Am J Ther 26: e775- e777. [Link: https://bit.ly/3IQamUv](https://bit.ly/3IQamUv)
- Peng J, Luo F, Ruan G, Peng R, Li X, et al. (2017) Hypertriglyceridemia and atherosclerosis. Lipids Health Dis 16: 233. [Link: https://bit.ly/3BTTOQK](https://bit.ly/3BTTOQK)
- Bruckert E, Labreuche J, Deplanque D, Touboul PJ, Amarencio P (2011) Fibrates effect on cardiovascular risk is greater in patients with high triglyceride levels or atherogenic dyslipidemia profile: a systematic review and meta-analysis. J Cardiovasc Pharmacol 57: 267-272. [Link: https://bit.ly/3DH06XE](https://bit.ly/3DH06XE)
- Ridker PM, Cook NR (2013) Statins: new American guidelines for prevention of cardiovascular disease. Lancet 382: 1762-1765. [Link: https://bit.ly/3aMHuGo](https://bit.ly/3aMHuGo)
- Hussain A, Ballantyne CM, Saeed A, Virani SS (2020) Triglycerides and ASCVD risk reduction: recent insights and future directions. Curr Atheroscler Rep 22: 25. [Link: https://bit.ly/3BWSbqo](https://bit.ly/3BWSbqo)
- Karalis DG (2017) A review of clinical practice guidelines for the management of hypertriglyceridemia: a focus on high dose omega-3 fatty acids. Adv Ther 34: 300-323. [Link: https://bit.ly/2Xppj6s](https://bit.ly/2Xppj6s)
- American Diabetes Association 6 (2021) Glycemic targets: standards of medical care in diabetes—2021. Diabetes Care 44: S73-84. [Link: https://bit.ly/2Z3OkF4](https://bit.ly/2Z3OkF4)
- American Diabetes Association 9 (2021) Pharmacologic approaches to glycemic treatment: Standards of Medical Care in Diabetes—2021. Diabetes Care 44: S111- S124. [Link: https://bit.ly/3pcLHLG](https://bit.ly/3pcLHLG)

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