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Case Report

Polyuria, Polydipsia and Papules in a 9-Year-Old Girl: A Case Report

Busch H[1]*, Nashed LM[1], Neacsu O[2] and Silverman RA[3]

[1]Department of Pediatrics, Inova L. J. Murphy Children's Hospital, USA

[2]Pediatric Specialists of Virginia, Department of Endocrinology, USA

[3]Department of Pediatrics, Medstar Georgetown, USA

***Corresponding author:** Busch Hayley, Department of Pediatrics, Inova L. J. Murphy Children's Hospital, 3300 Gallows Rd, Falls Church, VA 22042, USA

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Abstract

Eruptive xanthomas can be cutaneous manifestations of hypertriglyceridemia but are commonly misdiagnosed as molluscum contagiosum. They appear as yellow papules without an umbilicated surface and have a broad differential. One benign etiology is papular acrodermatitis of childhood (Gianotti-Crosti syndrome) that may develop after several different viral illnesses and may be of similar size, number and location as eruptive xanthomas. Juvenile xanthogranulomas are another diagnostic differential but are more often a single lesion. When multiple xanthogranulomas are present, the clinician should look for NF-1 associated with hematologic malignancy. Pruritus is not a typical feature and, if present, should prompt further investigations, specifically to rule out cholestasis. Finally, xanthomas may also present with newly diagnosed diabetes mellitus as insulin is a key component of lipid metabolism. In such cases, eruptive xanthomas should be expected to resolve with adequate diabetic control, when presenting concomitantly; however, adult patients may require medical therapy.

Keywords: Case Report; Xanthomas; Hypertriglyceridemia; Diabetes Mellitus

Case Presentation

A 9-year-old girl presents to the emergency department with several weeks of fatigue, polyuria, polydipsia and a 40-pound weight loss. She is previously healthy, not taking any medications or supplements. She has markedly decreased in her percentage of weight for age from the 91st to the 3rd percentiles despite reporting an increased appetite. The patient is alert and oriented, but she appears exhausted; her physical exam is notable for dry mucous membranes, capillary refill about 2 seconds, and tachycardia. She is subsequently found to have laboratory values consistent with new onset Type 1 Diabetes Mellitus: blood glucose of 665mg/dL [36.91mmol/L] (reference range, 71-99mg/dL [3.94 -5.49 mmol/L]), blood pH of 7.4 (reference range, 7.35-7.45), and bicarbonate of 24.7mEq/L [24.7mmol/L] (reference range, 20.0-29.0 mmol/L [20.0-29.0 mmol/L]). The patient is admitted to the acute pediatric medical and surgical unit. Upon further examination, she is noted to have a multitude of painless, mildly pruritic papules on the upper and lower extremities that are primarily present on the extensor surfaces. The monomorphous eruption was first observed about two weeks prior to hospitalization and had improved slightly with topical steroid cream prescribed by the pediatrician. These rounds, yellow papules are surrounded by a rim of erythema and initially diagnosed as molluscum contagiosum, although lacking an umbilicated surface.

The patient is admitted for rehydration, initiation of insulin therapy, diabetes education and stabilization of the patient's hyperglycemia. Investigation reveals an extensive history of familial hypertriglyceridemia and multiple family members with myocardial infarctions at a young age. The patient's mother denies any family history of diabetes, celiac disease, thyroid disease, or other autoimmune diseases. When serological tests are drawn, the blood appears chylous and milky white. The triglyceride level is 2,672mg/dL [30.19mmol/L] (reference range, 34-149 mg/dL [0.38-1.68 mmol/L]), cholesterol is 735mg/dL [19.04mmol/L] (reference range, 0-199 mg/dL [0-5.15 mmol/L]), and HDL is 27mg/dL [0.70mmol/L] (reference range, 0-80 mg/dL [0-2.07 mmol/L). The LDL and VLDL are not calculated, as the patient's triglyceride level is greater than 400mg/dl [4.52mmol/L].

Diagnosis

The cutaneous findings are characteristic of eruptive xanthomas, which typically indicate systemic hyperlipidemia. Xanthomas appear as yellow papules with a faint erythematous ring, they range from 1 to 4 mm in diameter and are rarely pruritic or painful.

Discussion

The case at hand describes a 9-year-old female with hypertriglyceridemia secondary to uncontrolled T1DM due to new diagnosis, with subsequent eruptive xanthomas. Physiologically, T1DM is characterized by insulinopenia. Lack of insulin activates lipolysis in adipose tissue releasing increased free fatty acids, which accelerates formation of very-low-density lipoprotein (VLDL) in the liver. Insulin is necessary to activate lipoprotein lipase, a key step in the catabolism of triglycerides. Reduced activity of lipoprotein lipase in peripheral tissue decreases removal of VLDL from the plasma, resulting in hypertriglyceridemia [1,2].

Xanthomas usually emerge on the extensor surfaces of the arms, legs, hands and buttocks but also can develop in tendinous regions, fasciae, and bone [3]. Histologically, xanthomas are composed of a dermal infiltrate of foamy macrophages with surrounding inflammatory cells [4,5]. The literature reports self-resolution of these cutaneous findings within weeks to months of adequate diabetic control; however, adult patients are often initiated on triglyceride lowering medications as the risk of pancreatitis and coronary artery

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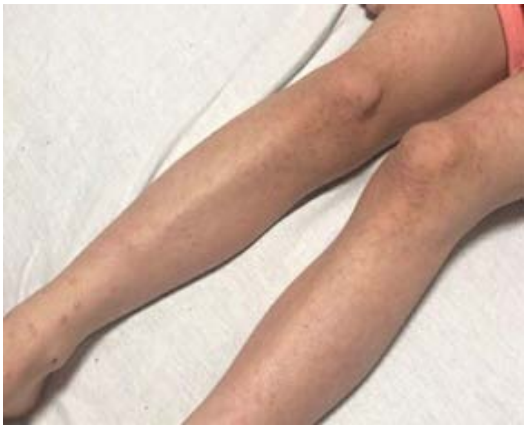

Figure 1A: Lower extremities with a multitude of round, raised lesions seen bilaterally.

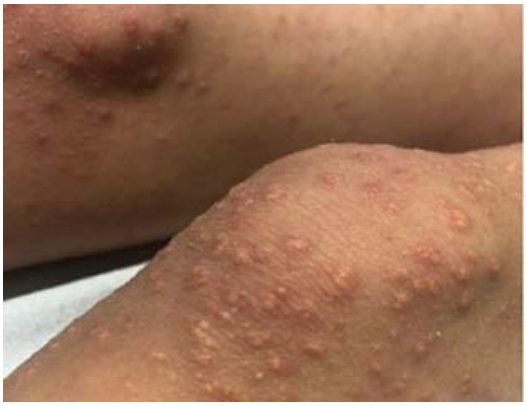

Figure 1B: Lesions visualized on the left knee.

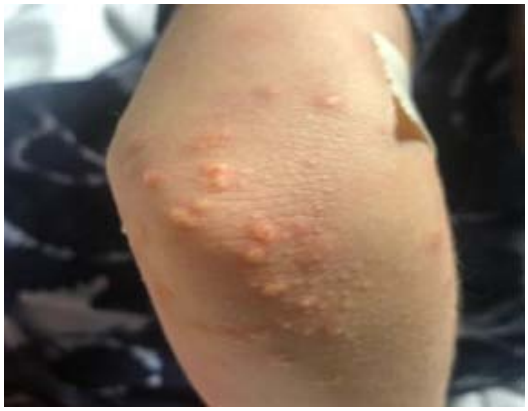

Figure 1C: Lesions visualized on the right elbow.

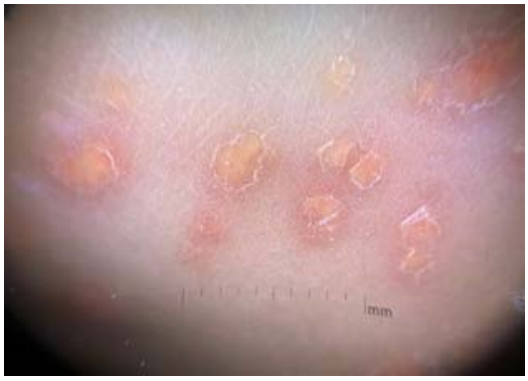

Figure 1D: Dermatoscopic view, lesions each a few millimeters in size.

disease is greater in this population [4,6]. In cases where the size or location is bothersome, xanthomas can be surgically excised; however, vigilant surgical management is essential, as recurrence is more likely with incomplete excision [7].

Common misdiagnoses include molluscum contagiosum, juvenile xanthogranulomas, papular acrodermatitis, or a viral exanthem. Molluscum contagiosum, the initial diagnosis for this case, is a viral infection of papules with central umbilication that appear on friction-prone surfaces (axillae, genitalia). In contrast, our patient's papules lacked central umbilication and were found on extensor surfaces. A rare finding but also confused with eruptive xanthoma is juvenile xanthogranuloma. These red, yellow, or brown papules are benign, non-Langerhans cell histiocytosis that appear as solitary lesions of the upper body; multiple juvenile xanthogranulomas are rare but observed in Neurofibromatosis Type 1 (NF-1) patients that have and increased risk of hematologic cancer [8]. The presence of multiple papules on the lower extremities in the setting of hypertriglyceridemia make the diagnosis of juvenile xanthogranulomas less likely. Another differential diagnosis to consider is papular acrodermatitis of childhood, otherwise known as Gianotti-Crosti syndrome. Typically present in young children, papular acrodermatitis manifests as skin colored vesiculopapular lesions sometimes in conjunction with viral symptoms. These self-limited lesions arise on the face, buttocks, or acral regions and may last up to several months [9]. Given the patient's historical paucity of any viral symptoms or vesicular findings, papular acrodermatitis or viral exanthem are less likely to be the correct diagnosis.

Xanthomas can occur in a normolipemic patient or a patient with underlying hypertriglyceridemia [5]. In normolipemic patients, eruptive xanthomas form due to increased vascular permeability to chylomicron particles. Thus, the pathogenesis for eruptive xanthomas in normolipemic patients can be secondary to trauma, histiocytosis, juvenile xanthogranuloma, xanthoma disseminatum or papular xanthoma. These patients lack laboratory hyperlipidemia but have lipid-laden reactive cells or undergo spilling of lipoproteins into the dermis which are then phagocytosed by dermal histiocytes [5,10]. In patients with underlying hypertriglyceridemia, eruptive xanthomas develop secondary to familial dyslipidemia or an acquired disease. Eruptive xanthomas most commonly emerge in type V hyperlipoproteinemia, but can also be present in Type 1 hyperlipoproteinemia, Type 1a lipoprotein lipase deficiency, and other familial dyslipidemias [4,5]. Uncontrolled type one and two diabetes, metabolic syndrome, hypothyroidism, and nephrotic syndrome have all been reported to cause eruptive xanthomas. In addition, other factors such as alcohol abuse, retinoid therapy, estrogen supplementation, and metabolic syndrome have been associated with eruptive xanthomas [1,8,11]. Rarely, a child with xanthomas may report pruritus, which should prompt the practitioner to rule

out cholestasis; this specific constellation of xanthomas, pruritus, and cholestasis should raise suspicion for Alagille syndrome, primary biliary cholangitis, biliary atresia, or other obstructive biliary processes [12]. Xanthomas present on the palm, flexural surfaces of the fingers and within the skin, folds are typically associated with biliary cirrhosis; in contrast, xanthomas on the palmar crease alone are more specific for familial dysbetalipoproteinemia type III [7].

Patient Course

After discharge, the patient followed regularly with her endocrinologist for continuing management of type one diabetes mellitus, confirmed by positive specific T1DM antibodies. She achieved excellent metabolic control with 71% time-in-range based on her Continuous Glucose Monitoring System; she maintained a low-fat diet on subcutaneous insulin. A second lipid panel was drawn four months later revealing triglycerides 88mg/dL [0.99mmol/L] (reference range 0 - 89 mg/dL [0-1.02 mmol/L]), cholesterol 195mg/dL [5.05mmol/L] (reference rage 100-169 mg/dL [2.59-4.38 mmol/L]), and HDL 47mg/dL [1.22mmol/L] (reference range, >39mg/dL [>1.01mmol/L]). The patient's cutaneous manifestations had improved at four weeks and completely resolved within four months without any additional management.

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