Eruptive Xanthomas Masquerading as Molluscum Contagiosum

abstract

Eruptive xanthomas are cutaneous manifestations of hyperlipidemias in which lipids accumulate in large foam cells within the skin. They classically present as crops of 1- to 4-mm yellow-orange papules and are often associated with extreme hypertriglyceridemia. We describe a 12-year-old boy with autism who was thought to have widespread molluscum contagiosum for a year before dermatologic consultation was obtained. Recognition of eruptive xanthomas led to the discovery of massive hypertriglyceridemia (serum triglycerides 6853 mg/dL) and diabetes mellitus. Through medical intervention, including insulin and fenofibrate therapy, and dietary modification with weight loss, the xanthomas cleared during the subsequent months, and his serum triglyceride levels nearly normalized. Pediatrics 2014;134:e1–e4

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KEY WORDS
behavior eating, BMI, dermatology, autism

ABBREVIATION
HbA1c—hemoglobin A1C

Drs Sorrell and Paller drafted the initial manuscript and reviewed and revised the manuscript; Dr Salvaggio drafted the initial manuscript; Dr Garg reviewed and revised the manuscript; Ms Guo drafted the initial manuscript; Dr Duck critically reviewed the manuscript; and all authors approved the final manuscript as submitted.

www.pediatrics.org/cgi/doi/10.1542/peds.2013-2108
doi:10.1542/peds.2013-2108
Accepted for publication Dec 30, 2013

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).
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FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.
Eruptive xanthomas are classically crops of 1- to 4-mm yellow-orange papules, commonly located on the hands, buttocks, and extensor portions of the extremities. They may koebnerize and often have an erythematous base early in the eruption. Eruptive xanthomas are most commonly associated with primary and secondary hypertriglyceridemia, with triglyceride levels often >2000 mg/dL. Evaluation for familial hyperlipoproteinemia and successful lowering of triglyceride levels are critical for resolution of eruptive xanthomas.

PRESENTATION
A 12-year-old boy with autism and a history of hypertension was referred to the dermatology clinic for evaluation of presumed molluscum contagiosum that had been present for a year. The eruption initially involved the upper extremities and had since spread to involve the trunk, buttocks, thighs, and neck. He occasionally scratched the lesions, but the eruption was otherwise asymptomatic. Among his behavioral difficulties was an aversion to all foods except bananas, applesauce, sugar-free JELL-O, yogurt, cream cheese, cookies, and occasional watermelon, but his hyperphagia led to being overweight. Almost 2 years before his cutaneous eruption developed, he had a BMI of 27.95 (>95th percentile) and markedly elevated serum triglyceride levels (3463 mg/dL; normal: 24–145 mg/dL), cholesterol (329 mg/dL; normal: <189 mg/dL) and hemoglobin A1C (HbA1c; 6.2%; normal: 4.5%–5.6%), with low high-density lipoprotein cholesterol (<5 mg/dL; and HbA1c 11.2% (normal: 4.5%–5.6%). He was also noted to have a fasting serum glucose of 313 mg/dL (normal: 60–100 mg/dL) and an insulin level of 55.5 µU/mL (normal: 2–17 µU/mL), which suggested that he had type 2 diabetes. His serum chemistry panel was remarkable for a bilirubin of 1.2 mg/dL (normal, 0.2–1.0 mg/dL), alanine aminotransferase 161 IU/L (normal, 2–30 IU/L), and aspartate aminotransferase 72 IU/L (normal: 16–52 IU/L). Serum amylase, lipase, blood urea nitrogen, creatinine, and thyroid function studies were normal.

The patient was admitted to the hospital for acute management of hyperglycemia and was treated with insulin, metformin 500 mg twice daily, and daily enalapril 20 mg, clonidine 0.2 mg, sertraline 100 mg, and fenofibrate 54 mg. Dietary modification was also instituted at this time. Within 1 month of this regimen, his triglycerides had decreased to 396 mg/dL, and serum aspartate aminotransferase and alanine aminotransferase had normalized. During the next several months, his xanthomas flattened and became less opalescent. By 5 months after initiation of therapy, his xanthomas had virtually disappeared, his BMI (25.8 kg/m²) and triglycerides (253 mg/dL) had improved, and his blood pressure (115/51 mm Hg) and HbA1c (5.1%) had normalized.

DISCUSSION
The patient was referred with a presumed diagnosis of molluscum contagiosum by his primary medical provider. Eruptive xanthomas and molluscum contagiosum papules (example in Fig 2) have distinctive clinical features that allow differentiation (Table 1); dermatologic consultation can aid in the diagnosis. Molluscum is a self-limited infection, which is cleared by immunologic response after ~6 to 24 months.1 Squash preparation, in which the contents of the molluscum central dell are extruded and stained with Giemsa stain, and biopsy will show characteristic microscopic round inclusion bodies (Henderson-Patterson bodies; Fig 3A). In contrast, eruptive xanthomas on histology show lipid-filled macrophages (Fig 3B).

FIGURE 1
Eruptive xanthomas. Discrete pink to yellow, smooth-surfaced, firm, monomorphic papules on the buttocks at presentation to our clinic.
Eruptive xanthomas are a cutaneous sign of excessive serum levels of triglyceride-rich, very low-density lipoproteins and chylomicrons. Although rare in children, eruptive xanthomas occur as a manifestation of primary genetic or secondary hyperlipidemias, a variety of systemic disorders, and as a complication of drug administration (Table 2). Recognition of eruptive xanthomas in patients with extreme hypertriglyceridemia is critical because of potentially life-threatening complications such as acute pancreatitis. Uncontrolled diabetes mellitus (both type I and type II) and metabolic syndrome have been associated with eruptive xanthomas as a result of insulin resistance and impaired clearance of triglycerides by lipoprotein lipase. In adults, heavy alcohol intake and medications that increase endogenous triglycerides have been associated with eruptive xanthomas, most commonly estrogens, isotretinoin, glucocorticoids, olanzapine, and anti-retroviral agents. The selective serotonin reuptake inhibitor medications sertraline and citalopram may increase triglyceride levels, and eruptive xanthomas have been described in patients taking sertraline. Although our patient's hypertriglyceridemia was evident before starting either sertraline or citalopram, we speculate that these medications may have exacerbated the hypertriglyceridemia. Laboratory evaluation for lipid levels should be obtained after a 12-hour or overnight fast. To elucidate the underlying cause of the hyperlipoproteinemia, our patient underwent further testing, but analysis was complicated by his significant clinical and laboratory improvement from previous intervention by the time of this diagnostic testing. His original presentation showed extreme elevation of triglycerides and elevation in chylomicron levels, which could have reflected an underlying unidentified genetic predisposition, in addition to newly developed metabolic syndrome and his SSRI medication use. Although the family has been offered gene testing, they have not expressed interest in further elucidating an underlying genetic cause.

Treatment of eruptive xanthomas is focused on lowering triglycerides with medications such as fibrates, omega-3 fatty acids, and nicotinic acid. Nutritional support with dietary modification and optimizing treatment of diabetes mellitus, as appropriate, usually leads to resolution of xanthomas within several weeks to months. Because chylomicrons are formed in the small intestine after absorption of fat, reduction or near total elimination of dietary fat should be advised.

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**TABLE 1 Clinical and Histologic Characteristics of Eruptive Xanthoma Versus Molluscum Contagiosum**

<table>
<thead>
<tr>
<th>Cause</th>
<th>Eruptive Xanthoma</th>
<th>Molluscum Contagiosum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphology</td>
<td>Hypertriglyceridemia</td>
<td>Poxirus</td>
</tr>
<tr>
<td>Usual size</td>
<td>1–4 mm</td>
<td>1–8 mm</td>
</tr>
<tr>
<td>Central core or umbilication</td>
<td>Occasional</td>
<td>Often</td>
</tr>
<tr>
<td>Confluence of papules</td>
<td>Occasional</td>
<td>Occasional</td>
</tr>
<tr>
<td>Color</td>
<td>Skin-colored to yellow-orange</td>
<td>Skin-colored to pink</td>
</tr>
<tr>
<td>Koebnerization</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Inflammation</td>
<td>None</td>
<td>Often, including surrounding dermatitis</td>
</tr>
<tr>
<td>Histopathology</td>
<td>Lipidized dermal macrophages</td>
<td>Epidermal intracellular invasion with Henderson-Patterson bodies</td>
</tr>
</tbody>
</table>

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**TABLE 2 Causes of Eruptive Xanthomas Described in Children**

<table>
<thead>
<tr>
<th>Type I hyperlipoproteinemia</th>
</tr>
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<tbody>
<tr>
<td>Type Ia: lipoprotein lipase deficiency</td>
</tr>
<tr>
<td>Type Ib: apolipoprotein C-II deficiency</td>
</tr>
<tr>
<td>Type Ic: GPHB1 deficiency</td>
</tr>
<tr>
<td>Type Id: Apolipoprotein A-5 mutations</td>
</tr>
<tr>
<td>Type Ie: lipase maturation factor 1 deficiency</td>
</tr>
<tr>
<td>Type II hyperlipoproteinemia (eruptive xanthomas rare)</td>
</tr>
<tr>
<td>Hypercholesterolemia, homozygous familial</td>
</tr>
<tr>
<td>Sitosterolemia</td>
</tr>
<tr>
<td>Type III hyperlipoproteinemia</td>
</tr>
<tr>
<td>Apolipoprotein E2 variants (or mutations)</td>
</tr>
<tr>
<td>Type V hyperlipoproteinemia</td>
</tr>
<tr>
<td>Secondary to poorly controlled diabetes mellitus and drugs such as estrogens, isotretinoin, HIV-1 protease inhibitors for HIV infection, Sirolimus for organ transplantation, Other genetic or acquired lipodystrophies, Other secondary hyperlipidemias, Alagille syndrome</td>
</tr>
<tr>
<td>Biliary cirrhosis, primary</td>
</tr>
<tr>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>Nephrotic syndrome</td>
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</tbody>
</table>
REFERENCES


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*Pediatrics* originally published online June 2, 2014;

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Pediatrics originally published online June 2, 2014;

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