Eruptive Xanthoma: A Case Report and Review of the Literature

Dermatologists can play a key role in disease prevention and management as cutaneous lesions are often the initial finding in systemic disease.

BY DOUG RICHLEY, DO, STEPHEN J PLUMB, DO, JONATHAN CLEAVER, DO, FAOCD, and LLOYD CLEAVER, DO, FAOCD

CASE REPORT

A 44-year-old obese Caucasian male presented for initial evaluation of a generalized, pruritic eruption. The eruption had been present for approximately three weeks, beginning on his elbows and subsequently spread to involve his back, abdomen, knees, and posterior thighs. The patient denied recent illness or changes in medications and also admitted to having frequent bouts of blurry vision over the past couple of weeks. His medical history included diabetes mellitus type II (unknown control), COPD, anxiety, arthritis, obesity (BMI – 38), alcohol abuse (admitting to consuming one half gallon of whiskey per day), and GERD. Interestingly, the patient’s father was recently given the diagnosis of hyperlipidemia.

On physical examination there were multiple excoriated, orange-red firm papules on an erythematous base. Lesions were distributed on the abdomen, back, bilateral elbows, knees, and posterior thighs (Fig. 1). The remainder of the dermatologic exam was normal. A scabies prep was performed which showed no mites, ova, or scybala. A 4mm punch biopsy of one of the papules was performed (Fig. 2). The lesion was sent for histologic examination with a differential diagnosis that included contact dermatitis, dermatitis herpetiformis, lichen planus, granuloma annulare, xan-thomas, folliculitis, and arthropod insult. Baseline labs were also ordered which included complete blood count (CBC), complete metabolic panel (CMP), fasting lipid panel, amylase, lipase, hemoglobin A1C, and thyroid stimulating hormone (TSH).

On histology, hematoxylin and eosin (H & E) stained sections demonstrated foamy, xanthomatous histiocytes scattered throughout multiple levels of the dermis, being most concentrated in the superficial dermis (Fig. 3, Fig. 4). These histologic findings are consistent with xanthoma.

The results of the blood work came back with the following remarkable results: triglycerides 4931 mg/dL, total cholesterol 410 mg/dL, hemoglobin A1C 12% (avg. glucose – 298 mg/dL), amylase normal, lipase normal.

Based on the clinical history with confirmation through laboratory values, the diagnosis of eruptive xanthoma was given. The patient was given clobetasol 0.05% cream to use twice daily on lesions for two weeks. Laboratory values were sent to the primary care physician to allow for appropriate treatment regarding the hypertriglyceridemia, hypercholesterolemia, and uncontrolled diabetes.

The patient returned for follow-up one month later after having been seen by his primary care physician, who started him on gemfibrozil 600mg twice daily for the hypertriglyceridemia.
demia. The lesions had started to resolve and were less pruritic (Fig. 5). Repeat fasting lipid levels were drawn and the following changes were noted: triglycerides 575 mg/dL, total cholesterol 286 mg/dL. Because of the patient’s uncontrolled diabetes and accompanying visual complaints, he was sent to ophthalmology to be evaluated. A report was sent from the ophthalmologist that did not show any abnormalities.

Due to our patient’s personal history of extremely elevated triglycerides, coupled with his father’s history of having high cholesterol, it is probable that he has an underlying hyperlipoproteinemia (HLP). However, the patient refused to be tested for any underlying genetic disorders secondary to the high cost of the test, as well as him having little interest in the test results. Despite not having genetic testing done, we can come to a relatively strong conclusion that our patient suffers from type IV HLP. Type IV HLP is favored because he exhibited all of the associated concomitant diseases that coincide with eruptive xanthoma, which include; diabetes mellitus, obesity, and/or alcoholism.¹

**DISCUSSION**

Xanthomas are deposits of lipids in the skin and sometimes of the subcutaneous tissue that are expressed clinically as yellowish to erythematous papules and plaques.² The lipid deposits in xanthomas are thought to be derived from circulating plasma lipoproteins.³ In many cases, this condition is secondary to a metabolic condition, such as hyperlipidemia, but not in all cases. It is important to determine if there is an underlying hyperlipidemia, as this can lead to atherosclerotic disease attributing to severe morbidity and mortality. It is also important to assess the cause of the hyperlipidemia, as it may be a manifestation of other systemic diseases. Some common conditions that can lead to hyperlipidemia include diabetes, obstructive liver disease, thyroid disease, renal disease, and pancreatitis. If recognized and treated early enough, progression to atherosclerotic disease and/or pancreatitis may be prevented, as well as resolution of the xanthomas.⁴

Eruptive xanthomas are often the result of elevated serum triglyceride levels. They present in a disseminated manner, with predilection for the buttocks, extensor surfaces of the thighs and arms, knees, intertriginous areas, and oral mucosa. Pruritus is variable, but is often severe and the presenting complaint of the outbreak.⁵ Hypertriglyceridemia levels associated with eruptive xanthoma often exceed levels of 3,000-4,000 mg/dL.⁶ When levels these high are achieved, one must consider the possibility that there is an associated HLP. Table 1 demonstrates the five different types of HLPs.

In addition to hyperlipidemia, certain medications have been shown to cause eruptive xanthomas. The most common inciting medications to cause eruptive xanthomas include systemic estrogens, systemic corticosteroids, systemic retinoids, and olanzapine.⁵⁷

Other forms of xanthomas include, tuberous/tuberoeruptive xanthomas, tendinous xanthomas, plane xanthomas, and verruciform xanthomas. Tuberous/tuberoeruptive xanthomas are described as being pink-yellow papules or nodules, most commonly found on the extensor surfaces, most notably on the elbows and knees. These lesions are usually seen in individuals with elevated serum cholesterol. Similar to eruptive xanthomas, tuberous/tuberoeruptive xanthomas are often associated with a HLP, most commonly types II and III.⁶ Tendinous xanthomas are described as being firm, smooth deposits of lipid that affect the Achilles tendon, as well as extensor tendons of the hand, knees or elbows. These lesions are also closely associated with types II and III HLP.⁶ Plane xanthomas are described as being orange-yellow macules, papules, patches, and plaques. Plane xanthoma location is often predictive of underlying disease. For example, lesions in intertriginous areas are suggestive of type II HLP.⁶ Lesions located within palmar creases (xanthoma striatum palmaris) suggests type III HLP.⁶ Xanthelasmas (xanthelasma palpebrarum) are plane xanthomas of the eyelids. While about half of these patients have an underlying hyperlipidemia, the presence of these lesions is not pathognomonic for such conditions. Plane xanthomas in the setting of a normolipemic individual raises the concern of an underlying monoclonal gammopathy, including multiple myeloma, B-cell lymphoma.
or Castleman’s disease. Verruciform xanthomas are typically solitary lesions that average 1-2 cm in diameter. These lesions usually arise in and around the mouth or in the anogenital region. Unlike the other forms of xanthomas, verruciform xanthomas are not associated with underlying hyperlipemic states. Verruciform xanthomas are often found in the presence of other disease states, such as lymphedema, epidermolysis bullosa, graft-versus-host disease, and CHILD syndrome. Table 1 demonstrates the different HLPs and the form of xanthomas that are commonly associated with each.

Treatment of eruptive xanthomas is directed at lowering the serum triglyceride levels. An overview of the patient’s medication list will show if an offending agent is being used, and if so it should be stopped or switched to an alternative medication that is not known to trigger eruptive xanthomas. Well balanced diet and exercise is the cornerstone for lipid lowering techniques; however, in most cases this is not enough to normalize the extremely elevated triglyceride levels that are associated with eruptive xanthomas. The best medications for lowering serum triglycerides specifically are the fibrac acid derivatives (fibrates) and omega-3 fatty acids. The fibrates decrease VLDL synthesis and increase lipoprotein lipase LPL which aid in lowering serum triglycerides. Omega-3 fatty acids increase triglyceride catabolism, which also aids in lowering serum triglyceride levels. Failure to treat the extremely elevated serum triglyceride levels that are associated with eruptive xanthomas can lead to more serious sequel, including pancreatitis and atherosclerosis. Once serum triglyceride levels approach reasonable levels, not only does the risk of pancreatitis and atherosclerosis decrease, but the cutaneous lesions also will resolve over several days to weeks. In addition to oral medications, other treatment modalities have been described for lesions resistant to contemporary medical treatment options. Surgery, lasers, and cryotherapy are the most commonly used of these alternative treatment options.

Cutaneous lesions are often the initial finding in otherwise systemic disease processes, placing the dermatologist in a position of great importance in relation to disease prevention and management.

Doug Richley, DO, is a second-year dermatology resident at Northeast Regional Medical Center/ATSU, Kirksville, Missouri.

Steven J. Plumb, DO, is a dermatopathologist at Cleaver Dermatology, Kirksville, Missouri.

Jonathan Cleaver, DO, FAOCD, is an attending dermatologist at Northeast Regional Medical Center/ATSU, Kirksville, Missouri.

Lloyd Cleaver, DO, FAOCD, is Program Director at Northeast Regional Medical Center/ATSU, Kirksville, Missouri.

Table 1

<table>
<thead>
<tr>
<th>Type</th>
<th>Pathogenesis</th>
<th>Laboratory Findings</th>
<th>Skin Findings</th>
<th>Systemic Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I</td>
<td>Deficiency in LPL</td>
<td>Elevated serum chylomicrons</td>
<td>Eruptive xanthomas</td>
<td>None</td>
</tr>
<tr>
<td>Type II</td>
<td>Deficiency in LDL receptor</td>
<td>Elevated serum LDLS</td>
<td>Tendinous, tuberoeruptive, tuberos, or plane xanthomas</td>
<td>Atherosclerosis</td>
</tr>
<tr>
<td>Type III</td>
<td>Deficiency in APO</td>
<td>Elevated serum chylomicrons, IDLs, triglycerides</td>
<td>Tendinous, tuberoeruptive, tuberos, or plane xanthomas</td>
<td>Atherosclerosis</td>
</tr>
<tr>
<td>Type IV</td>
<td>Increased production of VLDL</td>
<td>Elevated serum VLDLS and triglycerides</td>
<td>Eruptive xanthomas</td>
<td>Diabetes mellitus, obesity, alcoholism</td>
</tr>
<tr>
<td>Type V</td>
<td>Unknown</td>
<td>Decreased serum LDLS ad HDLS</td>
<td>Eruptive xanthomas</td>
<td>Diabetes mellitus</td>
</tr>
</tbody>
</table>