Dermacase

Answer to Dermacase continued from page 537

3. Eruptive xanthomas

Xanthomas are nodules or plaques composed of lipid-laden macrophages, which are also known as foam cells. They can be a clinical presentation of various metabolic disorders or just a local aggregation of foam cells without a true underlying lipoprotein disorder. Only a small number of cases of hyperlipidemia will be further complicated by xanthomas. However, eruptive xanthomas (EXs) are usually associated with severe hypertriglyceridemia. The levels of triglycerides in these patients are usually higher than 30 mmol/L.

Pathogenesis

The detailed mechanisms of xanthomas are not entirely understood. Lipids found in the different xanthomas are the same as those in plasma. The plasma lipids consist of triglycerides and cholesterol, which are transported to peripheral cells by lipoproteins. Lipoproteins are classified by their density as chylomicrons, very low-density lipoproteins, intermediate-density lipoproteins, low-density lipoproteins (LDLs), and high-density lipoproteins. Extravasated and oxidized LDLs induce vascular adhesion molecules and E-selectin, which can activate foam cell aggregation. Macrophages ingest lipids through the capillary walls via the scavenger receptors for LDLs and then form the foam cells.

Diagnosis

The cutaneous manifestations of xanthomas are named based on clinical morphology and location, which are summarized in Table 1. The different clinical phenotypes are associated with specific lipid disorders (Table 2). Clinically, EXs are multiple, small, reddish to yellowish, waxy papules with erythematous halos (Figure 1). They develop rapidly in crops over the trunk and limbs, especially the extensor surfaces, such as elbows, buttocks, and knees. Eruptive xanthomas can vary in presentation according to plasma lipoprotein levels. In general, EXs are asymptomatic but pruritus, tenderness, or an isomorphic response might occur. Local predisposing factors such as heat and friction might increase the capillary leakage of LDLs, which corresponds to the isomorphic response.

Related disorders

Eruptive xanthomas actually indicate the presence of hypertriglyceridemia, chylomicronemia, and high levels of LDL—low-density lipoprotein, VLDL—very low-density lipoprotein.

Data from Rader and Hobbs and Fredrickson and Lees.

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**Table 1. Clinical classification of xanthomas**

<table>
<thead>
<tr>
<th>TYPE OF XANTHOMA</th>
<th>CLINICAL MORPHOLOGY</th>
<th>USUAL LOCATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eruptive</td>
<td>Multiple papules to small nodules</td>
<td>Extensor surface of the extremities and buttocks</td>
</tr>
<tr>
<td>Tendinous</td>
<td>Firm subcutaneous nodules</td>
<td>Achilles tendons or extensor tendons of the knees and elbows</td>
</tr>
<tr>
<td>Tuberous</td>
<td>Dermal nodules</td>
<td>Extensor surface of the elbows, knees, knuckles, and buttocks</td>
</tr>
<tr>
<td>Planar</td>
<td>Soft papules or small plaques</td>
<td>Palms and intertriginous areas</td>
</tr>
</tbody>
</table>

Data from White.

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**Table 2. Frederickson classification of familial hyperlipidemia**

<table>
<thead>
<tr>
<th>TYPE OF HYPERLIPIDEMIA</th>
<th>CONDITION</th>
<th>TYPE OF XANTHOMAS</th>
<th>TRIGLYCERIDE LEVELS</th>
<th>CHOLESTEROL LEVELS</th>
<th>ELEVATED LIPOPROTEIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Familial chylomicronemia</td>
<td>Eruptive</td>
<td>Very highly elevated</td>
<td>Slightly elevated</td>
<td>Chylomicrons</td>
</tr>
<tr>
<td>IIa</td>
<td>Familial hypercholesterolemia; familial defective apolipoprotein B</td>
<td>Tendinous, tuberous, planar</td>
<td>Normal</td>
<td>Highly elevated</td>
<td>LDL</td>
</tr>
<tr>
<td>IIb</td>
<td>Familial combined hyperlipidemia</td>
<td>None</td>
<td>Elevated</td>
<td>Elevated</td>
<td>LDL and VLDL</td>
</tr>
<tr>
<td>III</td>
<td>Familial dysbetalipoproteinemia</td>
<td>Planar, tuberous, tuberoeruptive</td>
<td>Highly elevated</td>
<td>Elevated</td>
<td>Chylomicron and VLDL remnants</td>
</tr>
<tr>
<td>IV</td>
<td>Familial hypertriglyceridemia</td>
<td>Eruptive (rare)</td>
<td>Elevated</td>
<td>Normal</td>
<td>VLDL</td>
</tr>
<tr>
<td>V</td>
<td>Mixed hyperlipidemia</td>
<td>Eruptive</td>
<td>Very highly elevated</td>
<td>Elevated</td>
<td>Chylomicrons and VLDL</td>
</tr>
</tbody>
</table>

LDL—low-density lipoprotein, VLDL—very low-density lipoprotein.

Data from Rader and Hobbs and Fredrickson and Lees.
very low-density lipoprotein. These conditions can be seen in type I, IV, and V familial hyperlipidemia. Eruptive xanthomas might also be caused by secondary hyperlipidemia due to uncontrolled diabetes, obesity, cholestasis, alcoholism, and drugs. Some drugs, including retinoids, estrogen, and protease inhibitors, might also affect plasma lipid levels. Atherosclerosis, coronary artery disease, and acute pancreatitis, which are all complications of hyperlipidemia, might appear in patients with EXs. Therefore, blood tests for lipid levels, liver function, pancreatic enzyme levels, and fasting glucose levels should be arranged for patients with EXs. When triglyceride levels are above 20 mmol/L, the risk of acute pancreatitis for these patients is very high. If the plasma concentration of triglycerides exceeds 45 mmol/L, lipemia retinalis might develop.

Treatment
The treatment of EXs depends on the underlying lipoprotein disorder and the possible predisposing factors. Dietary modification is an important part of the management of dyslipidemia. The fatty acids of medium-chain triglycerides are not incorporated into chylomicrons, so medium-chain triglycerides can make up a maximum of 10% of the total calorie intake of patients with type I hyperlipidemia. Fibric acid derivatives are effective agents for reducing triglyceride levels and might also raise high-density cholesterol levels. Fibrates are the treatment of choice for patients with type IV or V familial hyperlipidemia or severe hypertriglyceridemia (triglyceride level of >10 mmol/L). Regular exercise and weight reduction also have beneficial effects on lipid profiles. Management of secondary hyperlipidemia is mainly focused on the underlying diseases. Eruptive xanthomas usually improve progressively 6 to 8 weeks after plasma lipid levels are corrected.

Conclusion
Family physicians should recognize that EXs might be a clinical reflection of underlying hyperlipidemia and should be alert to the consequences of hyperlipidemia, such as atherosclerosis, coronary artery disease, pancreatitis, and lipemia retinalis. Correctly identifying EXs and arranging laboratory tests are essential for initiation of adequate treatment and prevention of further complications.

Dr Yeh completed a surgical residency at the Song-Shan Armed Forces General Hospital in Taipei, Taiwan, and is a second-year dermatology resident in the Department of Dermatology at the Tri-Service General Hospital in Taipei. Drs Chen and Wu are attending dermatologists in the Department of Dermatology at the Tri-Service General Hospital.

Competing interests
None declared

References