Acetaminophen-induced lichenoid keratosis: a new way to look at an old lesion

Editor

Acetaminophen (paracetamol) is a widely used analgesic-antipyretic drug, easily obtained over the counter and generally well tolerated. Its potential for drug interactions is often underestimated. Adverse skin reactions, some life threatening, involve almost all arms of the innate and acquired immune systems, and include urticarial anaphylactoid reactions, fixed drug eruptions, pigmented purpuras, acute generalized exanthematous pustulosis, toxic epidermal necrolysis, and even a case of IgA bullous dermatosis. The association of acetaminophen with lichenoid eruption is rare.

We encountered a case of what appeared to be acetaminophen-induced lichenoid keratosis (LK) in a 63-year-old, otherwise healthy Ashkenazi Jewish woman who presented with a 2-week history of an asymptomatic, solitary, flat-topped, small ovoid plaque on the ventral side of the right arm. The plaque was erythematous, with a brownish hue. She had ingested acetaminophen for a headache 1 day prior to appearance of the lesion. She reported a previous episode of clinically diagnosed lichenoid eruption in the same area following ingestion of acetaminophen, which disappeared and reoccurred after challenge, leaving no pigmentary changes. The lag time between ingestion of the drug and appearance of the lesions at that time was much longer than in the current incident.

Histological examination of a completely excised lesion revealed a lichenoid inflammatory infiltrate obscuring the dermo-epidermal junction, with vacuolar changes, occasional Civatte bodies and pigment incontinence. The inflammatory infiltrate consisted mainly of T cell lymphocytes, with mixed CD4 and CD8 populations (fig. 1), but no eosinophils or plasma cells. The epidermis showed focal acanthosis without hypergranulosis or parakeratosis. Hyperpigmentation features of solar lentigo were encountered.

In vitro interferon gamma release test performed on the patient’s lymphocytes, described previously, showed a rise in interferon release, with acetaminophen over the predrug test level (480 pg/mL vs. 350 pg/mL, respectively). This test is recognized as a safe, informative tool for identifying drugs associated with various forms of adverse cutaneous drug reactions.

Table 1 summarizes the major clinical and histological features of LK-associated lesions, showing the overlap between entities. Our case exhibited LK clinically, with mixed histological evidence of LK and lichenoid drug eruption, suggesting that the two are in fact reactive immunological processes, probably to the same insult. This observation was supported by the positive rechallenge to acetaminophen, accompanied by the in vitro rise in the release of interferon gamma, a key orchestrating cytokine in T-lymphocyte processes. In view of the usual slow growth of lichenoid lesions, their appearance the third time only 1 day after ingestion of acetaminophen is intriguing. This might be explained by the fact that in reactive recurrent cases like ours, local T cells are already activated, rendering a shortened lag time.
Lichenoid keratosis has not previously been reported as drug induced. We suggest including it in the spectrum of lichenoid reactive lesions, and recommend searching for an inducing or exacerbating factor in appropriate recurring cases.

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References

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Table 1 Clinical and histological features of lichenoid lesions

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<thead>
<tr>
<th>Lichenoid lesions</th>
<th>Clinical</th>
<th>Histology</th>
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<tr>
<td>Lichenoid keratosis</td>
<td>Solitary round brown to red scaling on sun-exposed extremity.</td>
<td>Lichenoid lymphocytic infiltrate with hyperkeratosis, focal acanthosis and parakeratosis. Vacular alteration with individual necrotic keratinocytes. No atypia or acantholysis.</td>
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<tr>
<td>Lichen planus</td>
<td>Pruritic, numerous erythematous to violet polygonal lesions, sometimes with Wicham’s stria. Initial lesion appears on extremity, disseminates in a few weeks. Flexural symmetrical distribution.</td>
<td>Hyperkeratosis, hypergranulosis, saw-tooth lichenoid interface infiltrate.</td>
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<tr>
<td>Fixed drug reaction</td>
<td>Single or few sharply demarcated erythematous lesions on face or genitalia. Recurrence on same location with each challenge. Residual local hyperpigmentation on subsequent appearance.</td>
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Acquired ichthyosis with pravastatin

Editor
Acquired ichthyosis (AI) has the clinical and histological appearance of vulgaris ichthyosis. AI has even been reported in association with neoplasia (in particular Hodgkin’s disease or non-Hodgkin’s lymphoma), endocrinopathy, metabolic pathology, autoimmune disease and others pathologies such as Crohn’s disease and HIV.

However, many drugs that modify lipid metabolism can cause acquired ichthyosis too. These include clofazimine, nicotinic acid, diazacholesterol, triparanol, dixyrazine, allopurinol, cimetidine (by antiandrogenic action), feno-fibrate, nafoxidine (by hormonal action), butyrophenone, isotretinioine, and hydroxyuree.1

We report the first case of acquired ichthyosis induced by pravastatin treatment.

A 52-year-old woman presented with a 2-month history of localized acquired ichthyosis on her arms and forearms, and fatigue (fig. 1). She had no personal and familial history of ichthyosis. There was no relevant medical history except for pulmonary tuberculosis treated at the age of 9 years. Our patient was treated for 2 months with pravastatin (Vasten®, Aventis, France), a hydroxy-methyl-glutaryl coenzyme A reductase inhibitor for hypercholesterolaemia.

Clinical examination showed localized ichthyosis on the arms and forearms with brown scales, with no hepatomegaly, splenomegaly and lymphadenopathy. There was no weight loss and fever. Full blood count and electrophoresis