Ice-Pack Dermatosis
A Cold-Induced Dermatitis With Similarities to Cold Panniculitis and Perniosis That Histopathologically Resembles Lupus

Sara E. West, MD; Timothy H. McCalmont, MD; Jeffrey P. North, MD

Cold panniculitis typically occurs in infants and young children, appearing as indurated erythematous plaques or nodules after cold exposure, that typically affects infants and children. Recently, a variant involving the lateral thighs of equestrians has been described. Since the original report of this variant, some confusion has arisen in the literature in which the terms equestrian cold panniculitis and equestrian perniosis are both used. Outside of this presentation, cold panniculitis in adults is exceedingly rare.

Importance

Cold panniculitis is a self-limited condition, manifesting as erythematous plaques or nodules after cold exposure, that typically affects infants and children. Recently, a variant involving the lateral thighs of equestrians has been described. Since the original report of this variant, some confusion has arisen in the literature in which the terms equestrian cold panniculitis and equestrian perniosis are both used. Outside of this presentation, cold panniculitis in adults is exceedingly rare.

Observations

We describe 2 adult patients using ice-pack therapy for chronic back pain who developed erythematous, purpuric plaques at the site of ice-pack application. Histopathologic findings from both patients were similar and showed overlapping features of perniosis and cold panniculitis that closely resembled the pattern seen in cutaneous lupus erythematosus.

Conclusions and Relevance

Ice-pack dermatosis is an uncommon cold-induced process that occurs in adults using long-term ice-pack therapy. The clinical manifestations include erythematous to purpuric plaques with a livedo-like appearance and superficial ulceration. The histopathologic features resemble those seen in cutaneous lupus erythematosus with a superficial and deep perivascular and periadnexal dermatitis with increased dermal mucin and a superficial lobular panniculitis.

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Case Report/Case Series

Case 1
A woman in her late 50s presented with a 2- and-a-half-year history of recurrent erythematous purpuric papules with retiform-like purpura with ulceration on the lower back (Figure 1). The patient had chronic low back pain that she treated intermittently with ice packs. Histopathologic findings from two 4-mm punch biopsies showed a superficial and deep lymphocytic infiltrate with a striking predilection for neurovascular bundles and adnexa (Figure 1 and Figure 2). Mild vacuolar alteration of the basal epidermis with occasional apoptotic keratinocytes and focal epidermal necrosis were present. The lymphocytic infiltrate extended into the subcutaneous fat with a predominantly lobular distribution and focal fat necrosis (Figure 2). Increased dermal mucin was present, highlighted by a colloidal iron stain. Additionally, small clusters of CD123+ mononuclear cells (plasmacytoid dendritic cells) were detectable in the inflammatory infiltrate. Further characterization...
of the inflammatory infiltrate showed that most of the lymphocytes were CD3+ T cells (CD4+ count > CD8+ count) with scattered CD20+ B cells.

Case 2
A man in his late 20s with chronic low back pain presented with a similar history of recurrent erythematous to purpuric papules with ulceration on the lower back. He had been treating his low back pain with frequent ice-pack use. Histopathologic findings in a punch biopsy specimen appeared very similar to those in case 1 with a superficial and deep lymphocytic infiltrate involving the neurovascular bundles and adnexa, subtle changes of a vacuolar interface dermatitis, and a lobular lymphocytic panniculitis (Figure 3). Increased dermal mucin was again confirmed with a colloidal iron stain. Most of the lymphocytes were CD3+ T cells (CD4+ count > CD8+ count) with
scattered CD20+ B cells. Small clusters of CD123+ plasmacytoid dendritic cells were present as well.

**Discussion**

Cold panniculitis was first reported in 1902 by Hochsinger in a description of submental plaques occurring in children after cold exposure. In 1941, Haxthausen described plaques on the cheeks of infants and toddlers days after exposure to cold temperatures that he termed *adiponecrosis e frigore*. A biopsy specimen from 1 of the patients revealed necrosis and inflammation of the subcutaneous fat.

In 1963, a case of panniculitis within hours of cold exposure was reported in a 28-year-old woman on the cheeks, thighs, and lower legs. Histopathologic findings showed acute adiponecrosis. The inflammatory infiltrate was composed of lymphocytes with a few neutrophils and eosinophils in a lobular pattern as well as around blood vessels in the deep dermis. The patient’s lesions were readily reproducible with ice-cube exposure.

In 1966, when they described a 6-month old boy who manifested symptoms of cold panniculitis on serial skin biopsy specimens after his skin was exposed to ice. The cold-induced inflammatory response started with perivascular lymphocytes and histiocytes concentrated at the dermal-subdermal junction that extended into the adjacent reticular dermis and superficial subcutis 24 hours after cold exposure. At 48 to 72 hours, these changes intensified, and necrosis of adipocytes was evident. Increasing ice exposure times were required to produce the inflammatory reaction as the child aged, and the reaction no longer occurred at age 22 months.

Infants have a higher saturated to unsaturated fat ratio, resulting in a higher freezing point of fat. This differential fat composition is thought to underlie the predilection in young children for this disease. Cases of cold panniculitis developing on the cheek of a 6-month-old child 2 days after contact with a popsicle and in a 4-month-old child following induced hypothermia for cardiac surgery have also been reported. A biopsy specimen from the younger child demonstrated a chronic inflammatory reaction in the subcutis with areas of fat necrosis, with no further histopathologic information provided.

Cold panniculitis in adults is rare. In 1980, a case series of 4 young, healthy women with panniculitis involving the lateral thighs that occurred after long periods of equestrian activities in cold weather was reported. These patients developed erythematous, pruritic papules on the superior and lateral portions of one or both thighs that progressed to indurated, tender, erythematous plaques and nodules. The lesions seemed to clear within 3 weeks, but new lesions continued to appear throughout the winter with reexposure. Test results for cold agglutinins, cryoglobulins, and cryofibrinogens were negative. Two subsequent cases of equestrian panniculitis were associated with the detection of cold agglutinins.

The histopathologic features of these 4 patients were similar. They included an inflammatory infiltrate of lymphocytes, neutrophils, and histiocytes most prominent at the border of the dermis and subcutis with ruptured adipocytes. The inflammatory infiltrate also involved adnexa and neurovascular bundles within the dermis and subcutaneous tissue as...
well as increased mucin. The authors hypothesized that regional differences in chemical composition of adult fat could possibly result in cold sensitivity of the lateral thighs and also that the patients wore tight-fitting riding pants that may have decreased skin blood flow.

Four cases of “perniosis” affecting the thighs after wading across mountain rivers in New Zealand were reported in 2001.7 The histopathologic characteristics of 1 of these cases included edema of the papillary dermis with prominent perivascular and perifollicular lymphocytic inflammation and fat necrosis of the upper subcutaneous tissue.

A study from Finland described 3 female equestrians with cold panniculitis and sought to examine the prevalence and risk factors of cold panniculitis among horse riders.60 Data from questionnaires found that 25% of the respondents reported similar symptoms occurring during the winter. Increasing severity of symptoms seemed to correlate with age younger than 35 years, heavy smoking, wearing tight riding clothes, and longer riding times.

Multiple types of cold-induced dermatitis have been described, including cold panniculitis, perniosis, cold-induced urticaria, cryoglobulinemic vasculitis, and frostbite. While cold panniculitis is classified as a panniculitis and perniosis as a dermatitis, overlapping histopathologic features do occur in these 2 diseases and may indicate that they represent ends of a spectrum rather than distinct diseases. In Weedon’s Skin Pathology,11 he refers to equestrian perniosis instead of equestrian cold panniculitis. The changing of the name is interesting, since the histopathologic description of the originally reported cases closely mirrors the description of findings in the characterization of cold panniculitis in an infant by Duncan et al.4 The 2 cases in our present report have features of both perniosis and cold panniculitis, supporting the hypothesis that these diseases lie on a spectrum with variable histopathologic findings depending on the clinical scenario, including the age of the patient, site of involvement, and the amount and composition of the fat in the subcutis. King et al20 reported 2 cases of perniosis after anterior cruciate ligament repair and postoperative treatment with cold-therapy systems. Biopsy revealed a superficial and deep perivascular and perianadial lymphocytic infiltrate quite similar to that found in our cases. The subcutaneous fat was not pictured, and so we could not see if any panniculitis was present in those cases.

There are similarities both clinically and histopathologically between perniosis and lupus erythematosus. Cribier et al13 studied the histopathologic findings of perniosis (chilblains) in contrast to lupus to identify differentiating features. Cases of pernio had abundant dermal edema and necrotic keratinocytes with superficial and deep lymphocytic inflammation in a perivascular distribution as well as a striking perieccrine involvement. Compared with cases of lupus erythematosus, idiopathic perniosis had more spongiosis, more dermal edema, greater deep perieccrine inflammation, and less vacuolization of the basal layer.

The histopathologic findings in our 2 cases also bear similarity to those of lupus erythematosus (Table). These include a superficial and deep perivascular and perianadial lymphocytic infiltrate with a lobular lymphocytic panniculitis and increased dermal mucin. Large clusters of CD123+ plasmacytoid dendritic cells are often found in lupus erythematosus and can also be seen in perniosis.44 Our cases demonstrated clusters of CD123+ cells in the inflammatory infiltrate, though the clusters were smaller than those that have a more specific association with lupus.

In conclusion, we present 2 cases of adult patients with chronic low back pain treated with ice packs that had histopathologic findings typical of a cold-induced dermatosis with overlapping features of cold panniculitis and perniosis. There is increasing evidence that these 2 diseases represent 2 points on a spectrum of cold-induced dermatoses in which there is significant overlap. Histopathologic changes in both cases demonstrated a superficial and deep perivascular and perianadial lymphocytic infiltrate with a lobular lymphocytic panniculitis, mild vacuolar alteration of the basal epidermis, and increased dermal mucin. The characteristics bear similarity to those found in cutaneous lupus erythematosus. A thorough clinical history is important in such cases to avoid misdiagnosing cold-induced dermatoses and connective tissue diseases such as lupus erythematosus.

### Table. Histopathologic Features of Cold-Induced Dermatoses and Cutaneous Lupus

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Perniosis</th>
<th>Cold Panniculitis</th>
<th>Ice-Pack Dermatosis</th>
<th>Lupus Erythematosus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papillary dermal edema</td>
<td>++</td>
<td>–</td>
<td>+/−</td>
<td>+/−</td>
</tr>
<tr>
<td>Location of inflammation</td>
<td>Superficial lichenoid, deep perivascular, and perieccrine</td>
<td>Deep perivascular with a lobular panniculitis</td>
<td>Superficial and deep perivascular, perifollicular, perieccrine, and perineural with a lobular panniculitis</td>
<td>Superficial and deep perivascular, perifollicular, perieccrine, lobular panniculitis, +/−</td>
</tr>
<tr>
<td>Thickened basement membrane</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Vascular change with keratinocyte necrosis</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>++</td>
</tr>
<tr>
<td>CD123+ cells</td>
<td>Small or large clusters</td>
<td>Unknown</td>
<td>Small clusters</td>
<td>Large clusters</td>
</tr>
<tr>
<td>Panniculitis</td>
<td>–</td>
<td>Lobular, lymphocytic, centered at dermal-subcutaneous junction</td>
<td>Lobular, lymphocytic, centered at dermal-subcutaneous junction</td>
<td>Lobular, lymphocytic, more diffuse with prominent hyaline fat necrosis</td>
</tr>
<tr>
<td>Increased dermal mucin</td>
<td>+/−</td>
<td>–</td>
<td>+</td>
<td>++/++</td>
</tr>
</tbody>
</table>

Abbreviations: –, Absent; +, present; +/−, rarely; ++/++, strongly present.
Tommaso Campailla and the Syphilis Museum in Sicily

Ismaël Maatouk, MD, Roy Moutran, MD

The Museo Tommaso Campailla, or Syphilis Museum, is devoted to the treatment of syphilis. Tommaso Campailla (1668-1740) was first famous as a poet and philosopher. It was not until the death of his father that Campailla was able to indulge his passion for medicine, for at that time, the profession was not considered respectable. He became interested in the treatment of venereal diseases. He was known for creating wooden botti (barrels) for the patients to sit in and inhale mercury infusions. The idea was pioneered in France; there, the patient’s head would project from the top of the barrel. Campailla’s design was squarer, and the patient’s whole body sat in the “cabin.” The wood was of a special kind, which Campailla ordered from abroad, and to this day, no one knows exactly what it was. The treatment was administered in 2 rooms in a hospital, Ospedale Santa Maria della Pietà.

First the cabin was heated to 70°F (21.1°C) by a brazier, and then, the brazier removed, the patient would enter, carrying a small oil lamp for light, which he would hang on a nail, and a smaller brazier, which he would place on the ground beneath his feet.1,2

There were 2 holes in the door of the cabin, and through the top one the patient was monitored. Through the second, at the bottom of the door, the mercury infusion was poured onto the small brazier. The dose for a first treatment was half a gram of cinnabar and a pinch of incense (being added to facilitate breathing). This was doubled at the next treatment. Eventually, the patient would sweat off the infusion back onto the small brazier. The sessions lasted for 10 minutes, on alternate days, and normally a patient would have 9 or 10 treatments.

In more serious cases, 2 g of cinnabar would be used, and the patient would receive up to 13 treatments. After a cabin session, the patient would lie on a bed to continue the “sweating it out” process. By all accounts, the treatments worked, provided the disease was caught early enough, and some patients with rheumatic conditions were also treated.1,2 Campailla treated many prostitutes. His methods were used until the discovery of penicillin. The Tommaso Campailla Museum is now a municipal office building behind the Piazza Matteotti in Modica Bassa.

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