

What Is Your Diagnosis?



A 19-year-old woman presented to the dermatology clinic with a chief concern of a pruritic eruption on her toes. The eruption started approximately 1 month prior while the patient was in London, England, for a college exchange program. Her medical history was remarkable for Graves disease that was treated with thyroidectomy and subsequent thyroid hormone replacement, Raynaud phenomenon, acne, and recurrent inguinal furunculosis. Physical examination demonstrated violaceous desquamating papules and vesicles involving the dorsal and lateral aspects of several toes on both feet. There was normal range of motion, sensation, distal pulse, and capillary refill.

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The Diagnosis: Perniosis (Chilblain)

Perniosis (or chilblain) is a cutaneous inflammatory disorder associated with exposure to cold damp conditions.¹ It presents 12 to 24 hours after exposure to cold with erythematous to violaceous papules, patches, nodules, or plaques involving acral surfaces including the fingers, toes (Figure 1), ears, and nose. Patients with perniosis often are unaware of the cold injury while it is occurring, but subsequent symptoms call their attention to the exposure.² Lesions can be pruritic or painful and are sometimes associated with vesicles, ulceration, and superficial desquamation.^{1,3} Perniosis occurs most commonly in females aged 15 to 30 years but also is frequently seen in children and the elderly. Elderly patients may have a worsening course, while younger patients often improve without therapy.¹ Perniosis generally occurs in cool, damp, or humid climates, characteristically from late fall to early spring.⁴ Moisture and humidity are thought to enhance the chilling effect of the cool environment by augmenting thermal conductivity; therefore, patients will sometimes complain that wearing socks and fitted sneakers or shoes worsens their symptoms because of an associated increase in foot perspiration.⁵ The incidence of perniosis in the United States is unknown, likely secondary to underreporting and misdiagnosis by primary care physicians and specialists alike. The annual incidence of perniosis in England, where the climate is more nationally favorable for this disease, is estimated to be approximately 10%.⁶

Accurate diagnosis of perniosis starts with eliciting a detailed history of exposure to above-freezing temperatures in the proper clinical setting. Depending on the history and clinical presentation, a broad differential diagnosis would include septic embolism or atheromatous embolism, erythromelalgia, Raynaud phenomenon, erythema multiforme, granuloma annulare, acrocyanosis, lupus pernio, and hypersensitivity vasculitis.⁷ Once the diagnosis of perniosis has been confirmed either by history and clinical presentation alone or with the help of histopathologic examination, idiopathic perniosis must be distinguished from secondary perniosis that presents as part of a primary systemic process. Perniosis can present as a secondary cutaneous manifestation of numerous systemic diseases or exposures including lupus erythematosus, rheumatoid arthritis, chronic myelomonocytic leukemia, monoclonal gammopathy, viral hepatitis, human immunodeficiency virus infection, cryoproteinemia, anorexia, use of weight



Figure 1. Erythematous to violaceous papules and plaques with superficial desquamation involving the dorsal aspects of several toes on both feet (A and B).

reduction medications, or chronic crack cocaine abuse.⁸⁻¹⁰ A thorough laboratory evaluation for secondary causes would include complete blood cell count; antinuclear antibody titer; SS-A (anti-Ro) and SS-B (anti-La) antibodies; antiphospholipid antibodies; cryoglobulins; cold agglutinin and cryofibrinogen levels; serum protein electrophoresis; and screening for hepatitis B, hepatitis C, and human immunodeficiency virus.

A 4-mm punch biopsy specimen taken from the lateral aspect of our patient's right fourth toe showed a superficial and deep perivascular lymphocytic infiltrate with perieccrine reinforcement. Additionally, there was mild spongiosis with prominent superficial papillary dermal edema (Figure 2). The constellation of these findings is suggestive of perniosis, but a thorough differential diagnosis includes other disorders with a prominent lymphocytic infiltrate

such as a morbilliform viral exanthem, acute lupus erythematosus, small plaque parapsoriasis, erythema annulare centrifugum, polymorphic light eruption, and erythema chronicum migrans. Traditionally, perniosis is described as a lymphocytic vasculitis with swelling and thickening of the vessel walls sometimes described as a “fluffy” edema.¹¹ Fibrin is not always present and is not required for diagnosis of lymphocytic vasculitis. Although the histopathologic findings in perniosis are historically considered nonspecific and somewhat controversial, Cribier et al¹² described the association of dermal edema plus superficial and deep inflammation with perieccrine reinforcement and spongiosis as suggestive of idiopathic perniosis. Lupus erythematosus-associated pernio was, in contrast, much more likely to show vacuolar changes of the basal layer. Additionally, the inflammatory infiltrate for perniosis in general was characterized as made of mononuclear cells, predominantly CD3⁺ T lymphocytes, associated with a variable number of CD68⁺ macrophages and a minority of CD20⁺ B lymphocytes.¹²

Appropriate clothing and avoidance of cold damp conditions are key preventive measures for the treatment of perniosis. Because the patient often is not conscious of the exposure, appropriate dress must be stressed, even if the patient denies ever feeling cold. Furthermore, because central cooling triggers peripheral vasoconstriction, keeping the whole body warm is paramount to improvement of the condition.¹ Patients also should be discouraged from smoking, as it may precipitate or worsen disease. In a double-blind, placebo-controlled, randomized study, Rustin et al⁵ showed nifedipine, at dosages of 20 to 60 mg daily, to substantially speed the time to clearance of disease as well as prevent recurrences of perniosis. Side effects of nifedipine, including headache, facial flushing, nausea, and edema, may limit utility in mild to moderate disease.⁵ Other treatments with some anecdotal evidence include nicotinamide, phenoxybenzamine hydrochloride, sympathectomy, and erythemogenic UVB phototherapy.¹

The results of our patient’s laboratory workup, including complete blood cell count, antinuclear antibody titer, SS-A (anti-Ro) and SS-B (anti-La) antibodies, anticardiolipin antibody panel, cold agglutinin, lupus anticoagulant panel, C3, C4, and screening for hepatitis B and hepatitis C, were entirely within reference range and she was diagnosed with idiopathic perniosis. Given her history of Raynaud phenomenon and newly diagnosed idiopathic perniosis, she might more accurately be described as having neurovascular instability syndrome, a term coined by George et al¹³ to describe cases of aberrant neurovascular response to environmental

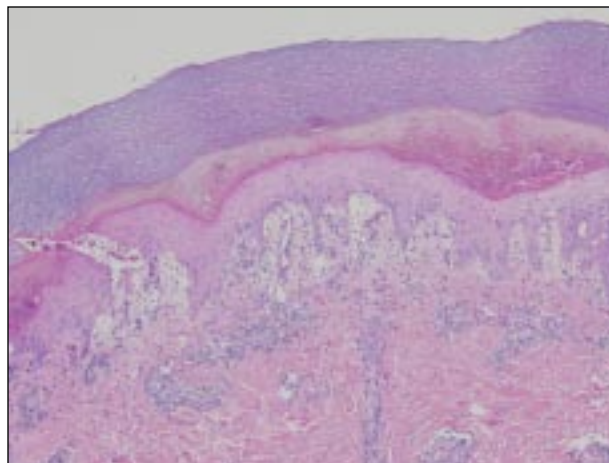


Figure 2. A 4-mm punch biopsy specimen taken from the right fourth toe demonstrating a superficial and deep perivascular lymphocytic infiltrate with perieccrine reinforcement and superficial papillary dermal edema (H&E, original magnification $\times 10$).

stimuli manifesting as perniosis, erythromelalgia, or Raynaud phenomenon. These patients are hypothesized to have small fiber neuropathy causing inappropriate neural responses to temperature, which in turn leads to abnormal vascular responses.¹³ Fortunately, our patient’s symptoms gradually improved with conservative environmental measures and a return to the warm temperate climate of San Antonio, Texas. She was counseled on her susceptibility to recurrence of disease and advised to take preventive environmental precautions to avoid future episodes of perniosis.

REFERENCES

1. Smith ML. Environmental and sports-related skin diseases. In: Bologna JL, Jorizzo JL, Rapini RP, eds. *Dermatology*. Vol 2. 2nd ed. Philadelphia, PA: Mosby Elsevier Limited; 2008:1353-1375.
2. James WD, Berger TG, Elston DM, eds. Dermatoses resulting from physical factors. In: James WD, Berger TG, Elston DM, eds. *Andrews’ Diseases of the Skin: Clinical Dermatology*. 10th ed. Philadelphia, PA: Saunders Elsevier; 2006:21-49.
3. Simon TD, Soep, JB, Hollister JR. Pernio in pediatrics. *Pediatrics*. 2005;116:472-475.
4. Parlette EC, Parlette HL. Erythrocyanotic discoloration of the toes. *Cutis*. 2000;65:223-224, 226.
5. Rustin MH, Newton JA, Smith NP, et al. The treatment of chilblains with nifedipine: the results of a pilot study, a double-blind placebo-controlled randomized study and a long-term open trial. *Br J Dermatol*. 1989;120:267-275.
6. Crowson AN, Magro CM. Idiopathic perniosis and its mimics: a clinical and histological study of 38 cases. *Human Pathol*. 1997;28:478-484.

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7. Bauer JH, Krusinski PA. Violaceous plaques on the feet. *J Am Acad Dermatol.* 2004;51:494-496.
8. Payne-James JJ, Munro MH, Rowland Payne CM. Pseudosclerodermatous triad of perniosis, pulp atrophy and “parrot-beaked” clawing of the nails—a newly recognized syndrome of chronic crack cocaine use. *J Forensic Leg Med.* 2007;14:65-71.
9. McCleskey PE, Winter KJ, DeVillez RJ. Tender papules on the hands. *Arch Dermatol.* 2006;142:1501-1506.
10. Yazawa H, Saga K, Omori F, et al. The chilblain-like eruption as a diagnostic clue to the blast crisis of chronic myelocytic leukemia. *J Am Acad Dermatol.* 2004;50(suppl 2):S42-S44.
11. Weedon D. The vasculopathic reaction pattern. In: Weedon D. *Skin Pathology.* 2nd ed. St. Louis, MO: Churchill Livingstone; 2002:250-251.
12. Cribier B, Djeridi N, Peltre B, et al. A histologic and immunohistochemical study of chilblains. *J Am Acad Dermatol.* 2001;45:924-929.
13. George R, Fulchiero GJ, Marks JG, et al. Neurovascular instability syndrome: a unifying term to describe the coexistence of temperature-related vascular disorders in affected patients. *Arch Dermatol.* 2007;143:275-276.