A 62-year-old white man presented with blistering of the skin on his lower extremity. The rash began two weeks prior on the anterior surface of his right ankle and did not improve with a one-week course of ciprofloxacin (Cipro). A similar rash subsequently developed on the lateral surface of his right thigh. He denied any foreign travel, trauma, or insect bites. He had a history of hypothyroidism, for which he took levothyroxine. He had no known medication allergies. He worked as a truck driver and had no pets. The patient did not have fever, gastrointestinal symptoms, or joint pain. Apart from the skin changes and swelling of the leg, the review of systems was unremarkable.

Physical examination revealed large, confluent, erythematous patches with clusters of clear and hemorrhagic vesicles, bullae, and sporadic ulcerations over the right lateral leg and anterior ankle (see accompanying figure). There was no mucosal involvement or inguinal lymphadenopathy. The rash was pruritic, but there was no pain or numbness. The examination was negative for Nikolsky sign (i.e., epidermal detachment from minimal pressure applied to normal skin adjacent to the lesion).

**Question**

Based on the patient’s history and physical examination, which one of the following is the most likely diagnosis?

- A. Bullous pemphigoid.
- B. Dermatitis herpetiformis.
- C. Erythema multiforme.
- D. Pemphigus vulgaris.
- E. Porphyria cutanea tarda.

See the following page for discussion.
Photo Quiz

Discussion

The correct answer is A: bullous pemphigoid. The autoimmune condition is characterized by tense bullae on normal or erythematous skin. Typical age of onset is between 60 and 80 years; however, cases of juvenile bullous pemphigoid occur. Incidence of the disease increases with age. Patients may present with pruritus or urticaaria with bullous formation occurring over weeks to months. Fluid contained in the bullae may be clear, or hemorrhagic if the base is bleeder. Rupture of the bullae results in erosions and crusting. Skin involvement can be localized, with lesions confined to the lower extremities, abdomen, and forearms; or generalized, with a widespread distribution of bullae. Mucosal involvement occurs in 10 to 25 percent of affected patients.

The diagnosis is based on histologic examination, which reveals separation of the epidermis and dermis. Direct immunofluorescence testing shows deposition of immunoglobulin G autoantibodies targeting two hemidesmosomal proteins on the basement membrane of the epidermis. Serum antibody titers for the two antigens may also be performed. Prednisone, alone or in combination with a steroid-sparing agent, is the cornerstone of treatment.

Topical corticosteroids may be sufficient for mild cases. More potent topical or systemic corticosteroids, or combinations thereof, may be necessary for severe disease. Serum antibody titers for the two antigens may also be measured periodically to assess treatment response. Flaccid blisters located on head, trunk, and intertriginous areas, and “target” lesions may contain a small bulla. The blisters are typically between 40 and 60 years of age

Erythema multiforme is an acute type IV hypersensitivity reaction characterized by macules, papules, and “target” lesions; begins on distal extremities and spreads proximally; minimal involvement of mucous membranes.

Pemphigus vulgaris is associated with Nikolsky sign and has a mortality rate of 5 to 15 percent. It is associated with other autoimmune diseases, including myasthenia gravis and thyromma.

Porphyria cutanea tarda results from a deficiency in a heme-synthesizing enzyme. Blistering of the skin occurs on sun-exposed areas, especially the hands and forearms, and occasionally the face. Patients may also exhibit hypertrichosis of the forehead and cheeks, hyperpigmentation, and urine discoloration. Risk factors for the disease include hepatitis C, hemochromatosis, and alcoholism.

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