Case Letter

Herpes Simplex Virus–Associated Pseudolymphoma

To the Editor:

Pseudolymphomas consist of benign reactive T- or B-cell lymphoproliferative processes that clinically and/or histologically simulate cutaneous lymphomas. It is important to identify herpes infections, as they may mimic diseases such as cellulitis and cutaneous lymphoma with markedly disparate therapeutic and prognostic consequences.

An 18-year-old woman was admitted to the hospital for treatment of recurrent cellulitis of the right elbow. Prior to admission, the plaque failed to respond to treatment with oral trimethoprim-sulfamethoxazole and cephalexin for 4 days. The patient reported 2 prior episodes of cellulitis in the same location within the last 2 years; on one of these occasions, intravenous antibiotics were deemed necessary for treatment. Her medical history was otherwise unremarkable.

Clinical examination revealed a large, ill-defined, warm, indurated, erythematous plaque overlying the right elbow. Numerous confluent vesicles and small bullae were noted at the center of the plaque (Figure 1). A complete blood cell count revealed a normal white blood cell count, and the patient was afebrile. Bacterial and viral cultures were obtained from a sample vesicle, and a punch biopsy was performed from the lateral aspect of the plaque. Gram stain and bacterial culture revealed no organisms or white blood cells. The viral culture was positive for herpes simplex virus (HSV) type 1. Histologic examination revealed a dense superficial and deep perivascular, slightly interstitial, periecrine and perifollicular infiltrate of $CD3^+$ T lymphocytes and plasma cells with overlying mild vacuolar changes. No viral cytopathic changes were detected (Figure 2). Antibiotics were discontinued and the patient was treated with oral acyclovir for 10 days, leading to resolution of the eruption.

A study by Xu et al[1] (1988-1994) of 13,904 Americans aged 12 years and older revealed that 51.0% of individuals tested positive for HSV-1 only, 5.3% were positive for HSV-2 only, and 16.6% were coinfected with HSV-1 and HSV-2.[1] Although cutaneous eruptions associated with HSV infections (ie, HSV-1, HSV-2, varicella-zoster virus [VZV]) are common, the clinical and histopathologic presentations of these infections are widely varied. Atypical clinical features often lead clinicians to biopsy these lesions, yielding histology that ranges from isolated epithelial involvement with minimal to absent inflammatory infiltrates to florid pseudolymphomatous patterns.[2] It is vital to accurately characterize HSV infections, as they may mimic diseases such as cellulitis and cutaneous lymphoma with markedly disparate therapeutic and prognostic consequences.

Pseudolymphomas are classified as B cell, T cell, and mixed based on the predominant cell type in the infiltrate and the pattern of inflammation.[3] Although

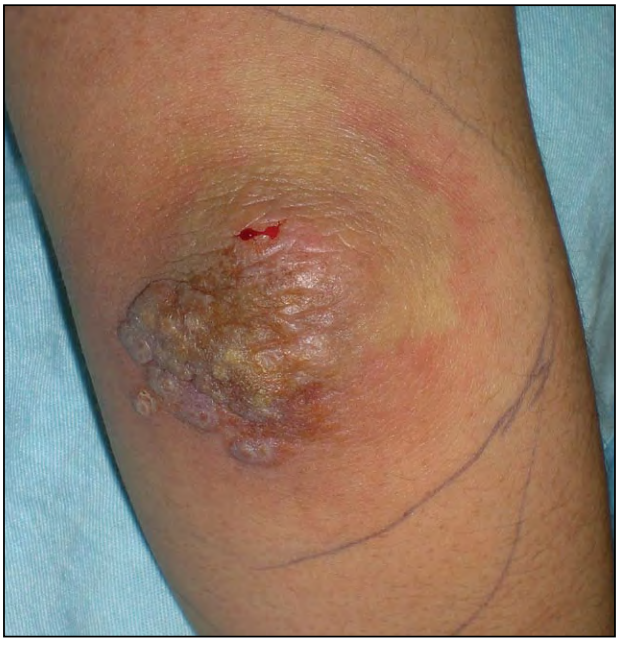

Figure 1. A warm, indurated, erythematous plaque with central vesicles and bullae developed on the right elbow.

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The authors report no conflict of interest.

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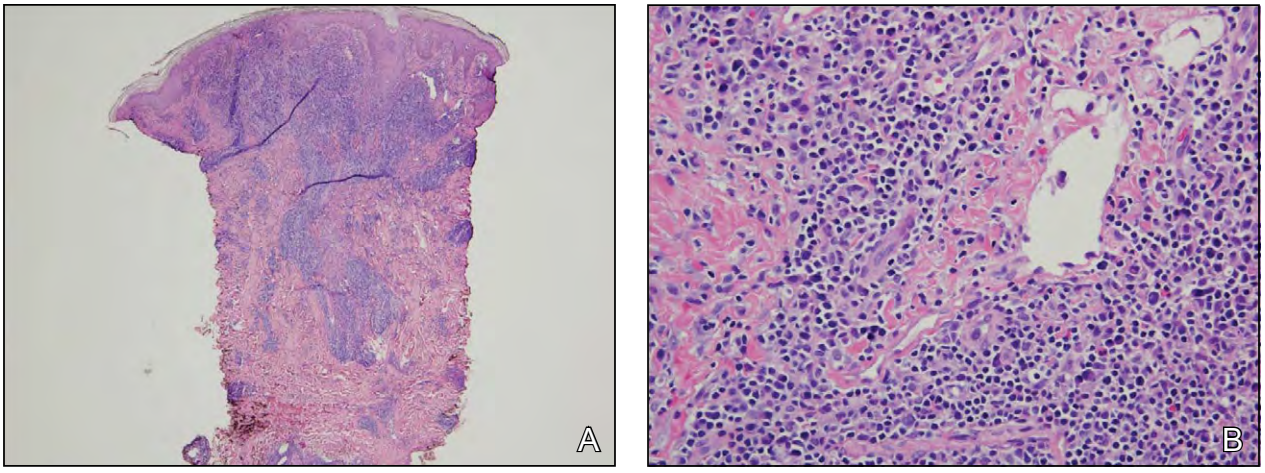

Figure 2. Dense superficial and deep perivascular, slightly interstitial, perieccrine and perifollicular lymphocytes and plasma cells with overlying mild vacuolar changes (A and B)(H&E; original magnifications ×4 and ×20, respectively).

many cases of pseudolymphomas are considered idiopathic, foreign agents (eg, tattoo dyes, insect bites) and infections (eg, *Borrelia burgdorferi*, VZV, human immunodeficiency virus) have been implicated as stimuli.[4] One retrospective study of biopsy specimens from 65 patients with cutaneous eruptions caused by HSV-1, HSV-2, or VZV revealed 8 cases with a pseudolymphomatous infiltrate, numerous atypical lymphocytes, and subtle epithelial changes resembling cutaneous lymphoma.[2]

Pseudolymphomas represent a diagnostic challenge in clinical practice as well as dermatopathology. One challenge in the diagnosis of pseudolymphoma is its differentiation from lymphoma. It has been suggested that the majority of pseudolymphomas can be distinguished from lymphomas by clinical correlation and morphologic assessment with immunohistochemistry when necessary.[3]

Our patient initially was treated with intravenous vancomycin for presumed cellulitis, but this therapy was discontinued after results of the viral culture were obtained. The clinical response to oral acyclovir supported the diagnosis of HSV-associated pseudolymphoma. Because our patient was concomitantly treated with antibiotics, the presence of secondary cellulitis cannot be reliably excluded. Nonetheless, prompt recognition of this entity based on the clinical findings, viral culture, and histopathology described may prevent subsequent unnecessary treatment with antibiotics and hospitalizations for future recurrences.

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