A recurrent, painful, and indurated plaque on a 75-year-old man's back

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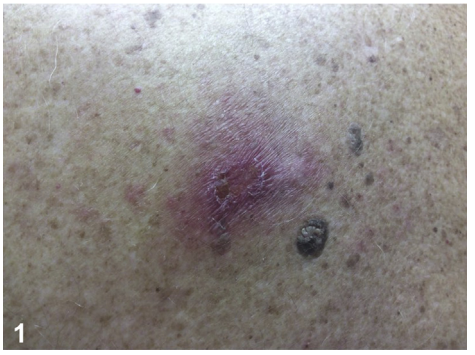

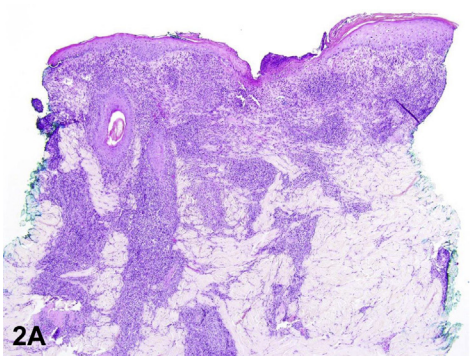

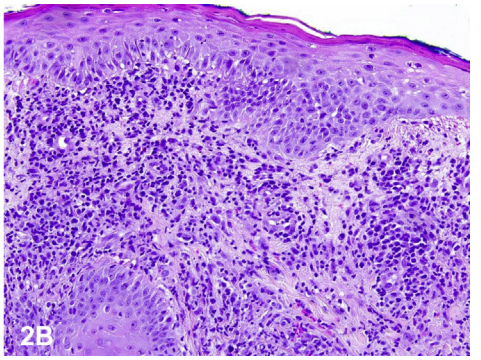

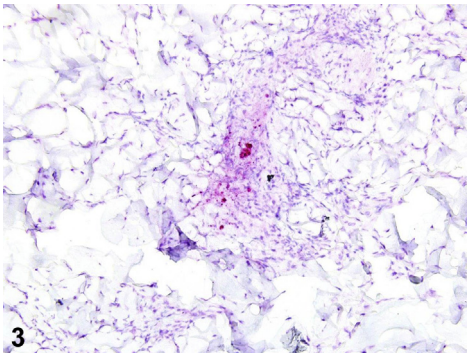

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A 75-year-old male retired physician presented with a 6-year history of an episodic, indurated and painful plaque located on the upper left side of his back that continued to recur and regress with incomplete healing every 3 to 4 months. Physical examination found a well-demarcated, tender, indurated erythematous plaque with central erosion (Fig 1).

Reoccurrence manifested with development of a pustule or bulla, which subsequently progressed to a larger indurated plaque that was tender, pruritic, and burning. Punch biopsy found a dense infiltrate of atypical small-to-medium–sized lymphocytes in the upper and middle dermis as well as around hair follicles (Fig 2, *A*). Focally, the infiltrate obscured the dermoepidermal j unction (Fig 2, *B*).

Question 1: What is the most likely diagnosis?

A. Persistent arthropod reaction

B. Actinic reticuloid

C. T-cell pseudolymphoma

D. Fixed drug eruption

E. Pagetoid reticulosis

Answers:

A. Persistent arthropod reaction — Incorrect. Arthropod reactions may reveal predominant T-cell infiltrates, but the patient's history of recurrence over 6 years would not be consistent with this diagnosis. In addition, arthropod reactions typically present with multiple pruritic papules and nodules, and not as solitary lesions.[1]

B. Actinic reticuloid — Incorrect. Actinic reticuloid is a diffuse process characterized by persistent infiltrated papules and plaques involving sun-exposed areas of the head and neck in elderly men and is typically not a solitary lesion. Therefore, this diagnosis does not correspond to the patient's clinical distribution.

C. T-cell pseudolymphoma — Correct. Cutaneous T-cell pseudolymphomas present as erythematous-to-violaceous papules or nodules that may clinically mimic a true lymphoma.[2] Often, the histologic findings cannot differentiate between the 2 entities, and additional studies are required.[1]

D. Fixed drug eruption — Incorrect. The presence of a dense infiltrate with atypical lymphocytes is not consistent with a fixed drug reaction, which is an inflammatory process with a mixed cellular infiltrate of eosinophils and lymphocytes along with epidermal necrosis.

E. Pagetoid reticulosis — Incorrect. Pagetoid reticulosis is a variant of mycosis fungoides that typically presents as a large solitary plaque, which is consistent with this patient's presentation. However, pagetoid reticulosis does not exhibit an exacerbating and remitting course and instead continues to slowly grow. Histologically, Pagetoid reticulosis is characterized by infiltrates of large atypical lymphocytes with abundant cytoplasm involving the full thickness of epidermis.

Question 2: Diagnostic studies that would better characterize this process would include all of the following, EXCEPT:

A. Giemsa stain

B. Immunohistochemical stains for T-cell markers to characterize the infiltrate

C. Gene rearrangement studies

D. Rapid polymerase chain reaction for herpes simplex virus (HSV)

E. Immunohistochemistry for HSV 1 and 2

Answers:

A. Giemsa stain — Correct. This test would be the least useful in diagnosing this suspected pseudolymphoma. Giemsa staining is notably used for diagnosis of cutaneous leishmaniasis.

B. Immunohistochemical stains for T-cell markers to characterize the infiltrate — Incorrect. Immunohistochemistry is an important tool for the differential diagnosis of lesions that clinically resemble cutaneous lymphomas. Loss of pan–T-cell markers CD 2, 3, and 5 has been observed in cutaneous T-cell lymphomas but not pseudolymphomas.[1] Similarly, aberrant loss of CD7 expression is common in cutaneous T-cell lymphomas such as mycosis fungoides but is rare in pseudolymphomas.

C. Gene rearrangement studies — Incorrect. Gene rearrangement studies are useful in differentiating between malignant and reactive cutaneous infiltrates. Malignant processes contain monoclonal cell populations, whereas benign or reactive process such as pseudolymphomas typically lack clonal populations.[1] However, pseudolymphomas with clonal T-cell populations have been reported; thus, molecular findings should be interpreted in the context of the entire clinicopathologic picture for proper diagnosis.[2]

D. Rapid polymerase chain reaction for HSV — Incorrect. The patient's clinical history of a painful cutaneous lesion that continually reoccurs and regresses should raise suspicion for potential HSV infection. HSV infection can present atypically without the characteristic clinical and histologic findings. HSV-associated pseudolymphoma is one such rare and atypical presentation of viral infection, described in a handful of case reports and small case series to date.[3,4] In a retrospective review of 65 cutaneous herpes cases, 8 presented with clinical features compatible with pseudolymphoma, with histology revealing lymphoid infiltrates with numerous atypical lymphocytes and subtle to absent HSV-associated epithelial cell changes.[4]

E. Immunohistochemistry for HSV 1 and 2 — Incorrect. This method is useful in demonstrating HSV within a lesion. Immunoperoxidase staining for HSV 1 and 2 revealed focal positivity for HSV 2 within the endothelium of a dermal blood vessel (Fig 3).

Question 3: What is the next best step in the treatment of this patient?

A. Observation

B. Oral valacyclovir

C. Topical 0.05% betamethasone dipropionate cream under occlusion

D. Topical imiquimod 5%

E. Topical mechlorethamine

Answers:

A. Observation — Incorrect. In cutaneous pseudolymphomas with an identifiable cause, removal or retreatment of the causative agent typically resolves the lesion.[1,2]

B. Oral valacyclovir — Correct. The patient was started on valacyclovir, 500 mg daily. At follow-up visits 6 months and 1 year later, his lesion remained in remission. Two years after his initiation of daily valacyclovir with no lesion reoccurrence, the patient began a trial of medication cessation. There have since been no reports of lesion recurrence.

C. Topical 0.05% betamethasone dipropionate cream under occlusion — Incorrect. Although topical or intralesional corticosteroids can be used to treat pseudolymphomas, this would not be an indicated treatment for a proved HSV-induced T-cell pseudolymphoma.[2] The patient had tried a topical corticosteroid and received no relief.

D. Topical imiquimod 5% — Incorrect. Immunomodulatory therapies such as imiquimod or thalidomide are useful in treating immunosuppressed patients with HSV infection. However, the case patient is not immunosuppressed and therefore does not require immunomodulation therapy. Immunosuppressed patients may have more extensive, persistent, and/or atypical HSV 2—related lesions. Sbidian et al[5] reported that daily thalidomide, 100 to 200 mg, in 4 HIV^+ patients with pseudotumoral HSV 2 infection resulted in a quick and dramatic regression of all lesions with a sustained complete response after treatment cessation. Treatment with topical imiquimod 5% also completely resolved the lesions, but relapse occurred shortly after stopping the treatment.

E. Topical mechlorethamine — Incorrect. Topical mechlorethamine is used for topical treatment of mycosis fungoides and would not address the underlying cause of this patient's lesion.

Abbreviation used:

HSV: herpes simplex virus

REFERENCES

1. Ploysangam T, Breneman DL, Mutasim DF. Cutaneous pseudolymphomas. *J Am Acad Dermatol*. 1998;38(6 Pt 1):877-895. quiz 896-897.
2. Mitteldorf C, Kempf W. Cutaneous pseudolymphoma. *Surg Pathol Clin*. 2017;10(2):455-476.
3. Mitteldorf C, Geissinger E, Pleimes M, Schon MP, Kempf W. T-cell pseudolymphoma in recurrent herpes simplex virus infection. *J Cutan Pathol*. 2019;46(10):717-722.
4. Leinweber B, Kerl H, Cerroni L. Histopathologic features of cutaneous herpes virus infections (herpes simplex, herpes varicella/zoster): a broad spectrum of presentations with common pseudolymphomatous aspects. *Am J Surg Pathol*. 2006;30(1):50-58.
5. Sbidian E, Battistella M, Legoff J, et al. Recalcitrant pseudotumoral anogenital herpes simplex virus type 2 in HIV-infected patients: evidence for predominant B-lymphoplasmocytic infiltration and immunomodulators as effective therapeutic strategy. *Clin Infect Dis*. 2013;57(11):1648-1655.