Zosteriform mycosis fungoides and lymphomatoid papulosis arising in an area of prior herpes zoster

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INTRODUCTION

Cutaneous lymphomas represent approximately 4% of all non-Hodgkin lymphomas, with mycosis fungoides (MF) comprising the majority of cases.[1,2] Classic MF presents with patches and plaques on non-sun exposed areas that may slowly evolve overtime into nodules or tumors.[1] However, there are many atypical variants of MF that may mimic benign skin conditions, including eczema, folliculitis, pigmented purpuric dermatoses, psoriasis, vitiligo, and pityriasis lichenoides chronica.[3,4] As such, MF can pose a diagnostic challenge, and clinicopathologic correlation is often necessarily to make the diagnosis, especially in the early stages of the disease.[1] Difficulties in accurate diagnosis have led to patients with MF experiencing a median delay of 36 months between first symptom development and initial diagnosis.[5]

Abbreviations used:

CD:	cluster of differentiation
CTCL:	cutaneous T-cell lymphoma
LyP:	lymphomatoid papulosis
MF:	mycosis fungoides

CASE REPORT

A 45-year-old female with a history of chronic pain syndrome and chronic obstructive pulmonary disease presented with a 20-year history of psoriasis treated in the past with topical corticosteroids and emu oil. Given that her symptoms were mild, she was not currently being treated with any systemic or topical medications. She did, however, report a long history of multiple systemic complaints, including diffuse, chronic pain and fatigue, consistent with her diagnosis of chronic pain syndrome for which she receives trigger point injections. Her family history was notable for melanoma in her mother.

Examination revealed a 30 cm light-pink, thin plaque with overlying clusters of dome-shaped, smooth, pink papules in a dermatomal distribution on the right abdomen and back (Fig 1, *A* and *B*). She recalled a different, painful, vesicular rash in this area many years prior, which was diagnosed as herpes zoster. She had similar dome-shaped papules on her bilateral ankles and eczematous plaques on her thighs. All involved areas were pruritic. The initial differential diagnosis included atopic dermatitis with prurigo papules and lichen simplex chronicus, lichen planus, and papular granuloma annulare.

A biopsy from the right lateral abdomen showed an irregularly acanthotic epidermis with overlying hyperkeratosis and parakeratosis (Fig 2, *A*). There was basilar layer tagging and epidermotropism by single and clustered cells with perinuclear halos (Fig 2, *A*). A dermal band-like infiltrate of small, atypical lymphocytes, and numerous large cells with irregular nuclear contours and prominent nucleoli were seen (Fig 2, *B*). Immunohistochemical staining

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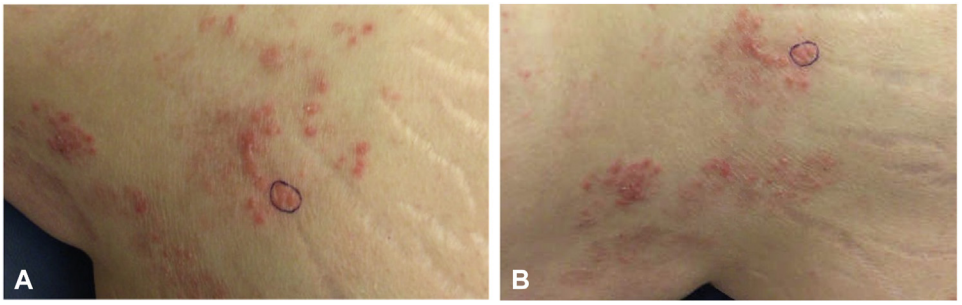

Fig 1. Physical examination revealed a 30 cm light-pink thin plaque with overlying clusters of dome-shaped, smooth, pink papules in a dermatomal distribution on the (**A**) right abdomen and (**B**) back.

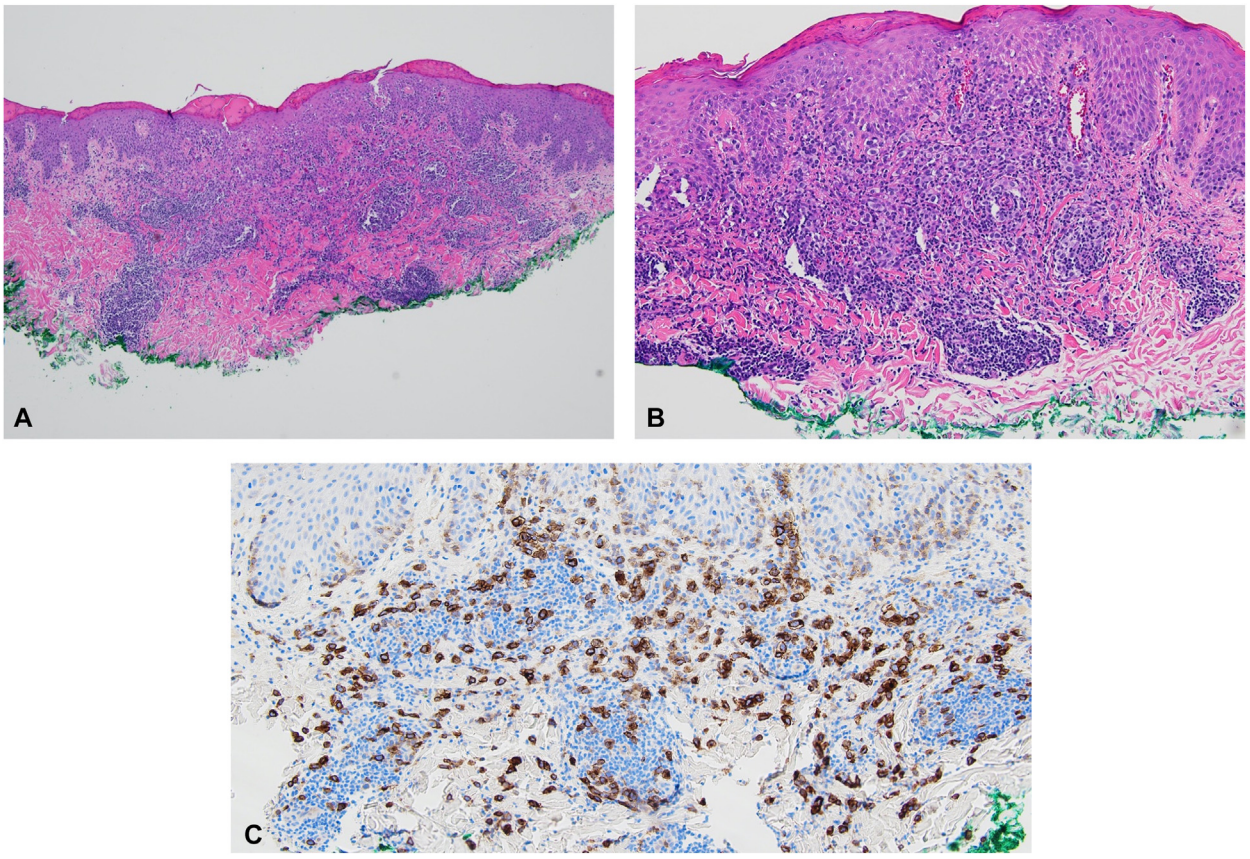

Fig 2. A, Hematoxylin-eosin section at 4× magnification showing the shave biopsy with irregularly acanthotic epidermis with overlying hyperkeratosis and parakeratosis. Basilar layer tagging and epidermotropism is seen. **B,** Hematoxylin-eosin section at 10× magnification showing the dermal band-like infiltration of small atypical lymphocytes and numerous large cells with irregular nuclear contours and prominent nucleoli (large cells are greater than 3× the size of a normal lymphocyte). **C,** CD30 immunohistochemical staining at 10× magnification highlighting some of the large cells within the dermis.

revealed that the large cells within the dermis were cluster of differentiation (CD) 30 positive (Fig 2, *C*). The majority of CD3 positive dermal lymphocytes had loss of CD7 expression (Fig 3, *A* and *B*). CD4 staining was diffusely positive whereas CD8 staining was largely negative in the intraepidermal cells (Fig 4, *A* and *B*). Ki67 staining confirmed an elevated proliferative rate (Fig 4, *C*).

Flow cytometry from peripheral blood showed a small population of CD4 positive T cells with loss of

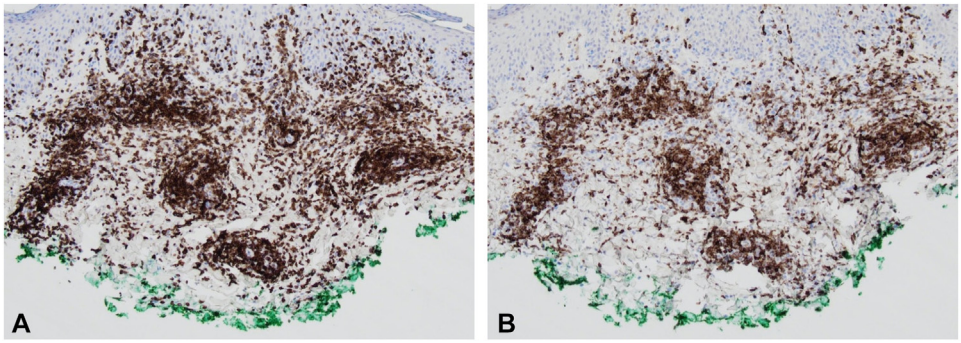

Fig 3. A, Close-up of CD3 immunohistochemical staining at 4× magnification showing positive-staining T cells within the dermal lymphocyte population. **B,** Close-up of CD7 immunohistochemical staining at 4× magnification showing loss of CD7 expression in the majority of the CD3 positive T cells.

CD7 and CD26 (2% of lymphocytes). Positron emission tomography imaging was without visceral involvement. She was seen in cutaneous T-cell lymphoma (CTCL) clinic where she was diagnosed with patch stage MF (<10% body surface area) in addition to lymphomatoid papulosis (LyP) as the cause of the large, CD30 positive, atypical cells. While the pathology could be consistent with either LyP or MF with large cell transformation, a diagnosis of LyP was made based on the clinical morphology, specifically the small papules, which was classic for LyP. Additionally, the patient had typical patches of MF. She was treated with methotrexate 10 mg weekly and topical clobetasol for symptomatic relief. After 1 month of treatment, her skin was completely clear without evidence of active disease.

DISCUSSION

Multiple cutaneous malignancies have been reported within areas of prior herpes zoster, including squamous cell carcinoma, angiosarcoma, Kaposi sarcoma, CTCL, and cutaneous B-cell lymphoma.[6-10] Zosteriform MF is an exceedingly rare variant of MF characterized by lesions that occur in a dermatomal distribution.[11] In 1991, Williams et al[12] described a case in which several firm nodules in a zosteriform distribution over the left neck and shoulder were found to be MF on biopsy. Since then, a total of 6 patients have been reported to have zosteriform MF or CTCL, including our case (Table I).[9,12-15] The average reported age was 57 with a range of 21 to 86 years. Both sexes were affected although females (5) significantly more than males (1). All 6 patients underwent skin biopsy due to uncertainty of the diagnosis. Following biopsy, 6 patients were diagnosed with MF while 1 patient was diagnosed with CTCL.

Of the previously reported cases, only 1 patient developed zosteriform MF at the site of previous herpes zoster eruption. In that case, the patient was a 55-year-old male who had experienced a herpes zoster eruption 4 years prior.[9] While the exact mechanism between herpes zoster and the development of MF is unknown, varicella-zoster virus is thought to play an important role in the development and maintenance of zosteriform skin lesions.[11] Lewis et al[13] described a case of zosteriform MF that was successfully suppressed with oral valacyclovir. Interestingly, the patient experienced disease recurrence on 4 separate occasions when antiviral therapy was either discontinued or the dose was reduced. Additional hypotheses have implicated varicella-zoster virus reactivation in the pathogenesis of MF and herpes zoster as an infectious trigger initiating MF development.[11,16] However, given the rarity of this clinical variant of MF in the literature, more information is still needed on the exact mechanism linking varicella-zoster virus to MF development and the role of antiviral agents in the treatment of zosteriform MF.

We present this case to highlight both the possible role of herpes zoster in the development of MF and the years-long diagnostic delay that patients with MF often face. Patients with seemingly common skin conditions that do not respond to conventional therapy should be promptly referred to dermatology. Additionally, cutaneous eruptions that follow a dermatomal distribution are not always herpes zoster. Cutaneous malignancies or metastases, although rare, should be considered in the differential diagnosis of zosteriform eruptions of the skin. Lastly, given the numerous variants and presentations of MF that have been described, a skin biopsy may be needed to rule out malignancy.

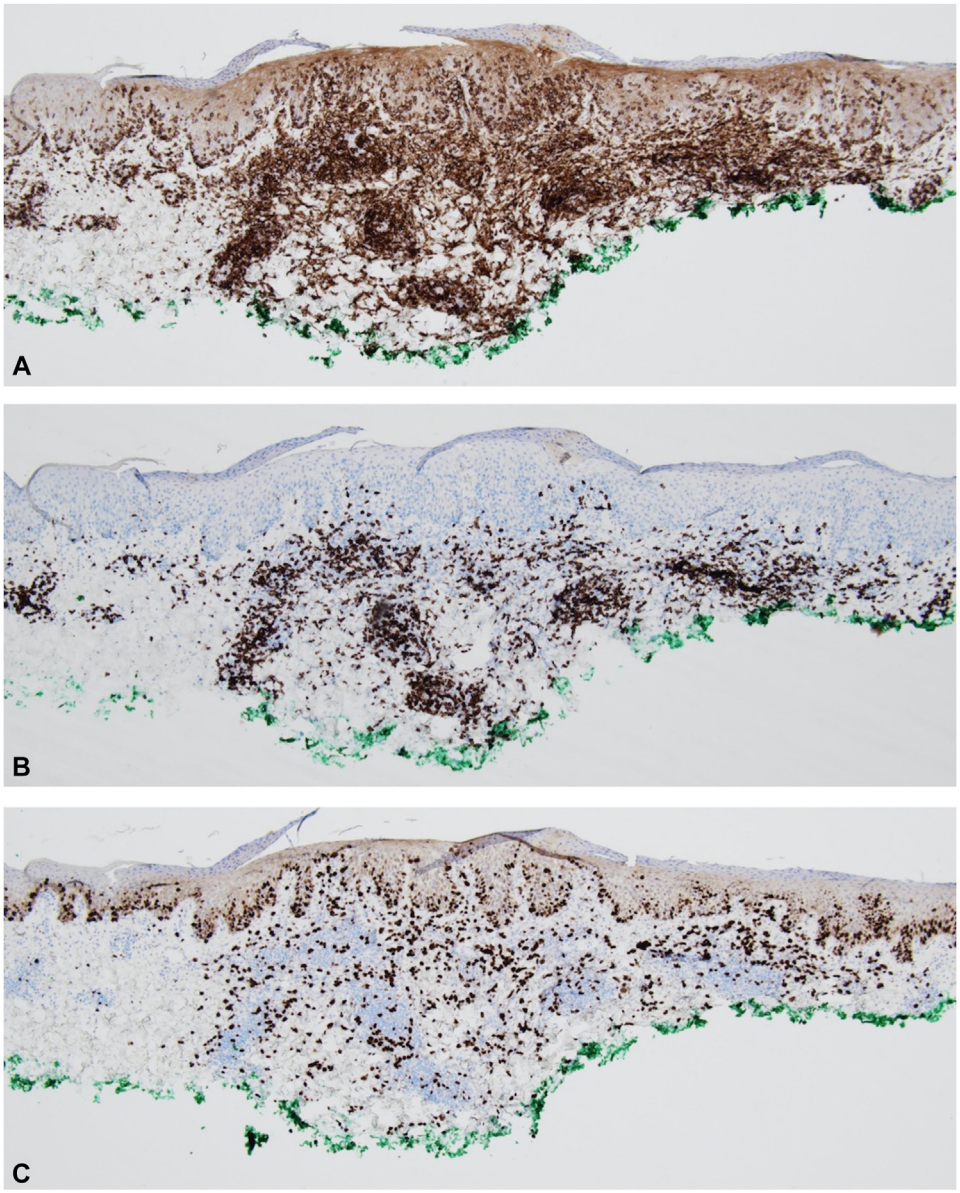

Fig 4. A, CD4 immunohistochemical staining at 4× magnification showing diffuse positivity. **B,** CD8 immunohistochemical staining at 4× magnification showing positive-staining dermal lymphocytes. However, CD8 is largely negative in the intraepidermal cells. **C,** Ki67 immunohistochemical staining at 4× magnification showing elevated proliferative rate.

Table I. Reported cases of zosteriform mycosis fungoides or primary cutaneous T-cell lymphoma, including our case

Authors and year	Diagnosis	Age and sex	Location	Previous site of herpes zoster
Zhao et al (2023)	Mycosis fungoides	45 y.o. F	R abdomen and back	Yes
Huang et al[9] (2018)	Mycosis fungoides	55 y.o. M	R upper thigh	Yes
Lewis et al[13] (2018)	Mycosis fungoides	69 y.o. F	L upper back, chest, arm	No
Rieger et al[14] (2017)	Mycosis fungoides	21 y.o. F	R abdomen, flank, back	No
Ricci et al[15] (1995)	Cutaneous T-cell lymphoma	66 y.o. F	R anterior thorax	No
Williams et al[12] (1991)	Mycosis fungoides	86 y.o. M	L neck and shoulder	No

F, Female; *L*, left; *M*, male; *R*, right; *y.o.*, year old.

Conflicts of interest

None disclosed.

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