Syringotropic and folliculotropic mycosis fungoides with mycosis fungoides–associated vasculopathic ulcers

Yousif A. Yonan, MD,[a] Helen J. L. Cumsky, BS,[a,b] Collin M. Costello, MD,[a] Connor J. Maly, BS,[a,c] Allison C. Rosenthal, DO,[d] Craig B. Reeder, MD,[d] William G. Rule, MD,[e] Mark R. Pittelkow, MD,[a] Fiona E. Craig, MD,[f] David J. DiCaudo, MD,[a] and Aaron R. Mangold, MD[a]
Scottsdale, Arizona; Cleveland, Ohio; and Washington, DC

Key words: folliculotropic mycosis fungoides; histopathology of folliculotropic mycosis fungoides; histology of mycosis fungoides; mycosis fungoides–associated vasculopathic ulcers; syringotropic and folliculotropic mycosis fungoides; syringotropic mycosis fungoides; ulcers in mycosis fungoides.

INTRODUCTION

Mycosis fungoides (MF), a disease of resident memory T cells, is the most common variant of cutaneous T-cell lymphoma.[1] Folliculotropic mycosis fungoides (FMF) is a well-recognized, distinct variant of MF.[2] Clinically, FMF manifests itself as acneiform lesions, with formation of comedo-like plugs and epidermal cysts, follicular papules, follicular keratoses, erythematous patches and plaques, and hair loss in the affected areas.[3,4] There is a predilection for the face, neck, and upper trunk.[3,4] Histopathologically, FMF is characterized by dense lymphocytic infiltrates surrounding and infiltrating the hair follicles and usually sparing interfollicular skin.[3,4] Follicles often show cystic dilation, plugging, and mucin deposition.[3,4] Adnexotropism in MF is not confined to hair follicles, as eccrine involvement can also be seen.[5-7] An additional variant of MF, syringotropic MF, is controversially considered a subvariant of FMF.[2,7,8] It is characterized by T-cell lymphocytic infiltration of the eccrine epithelium. Interestingly, syringotropic MF often affects the lower extremities and may be associated with superficial erosions and ulcers in up to 21% of cases.[7,8] The underlying driver of these clinical findings is unknown.

We present a case of FMF with vasculopathic lower extremity ulcers driven by MF with successful treatment with radiation therapy (RT). To the best of our knowledge, the histopathologic features of vasculopathy caused by MF infiltration have not been previously described.

Abbreviations used:

FMF:	folliculotropic mycosis fungoides
MF:	mycosis fungoides
RT:	radiation therapy
TSEBT:	total skin electron beam therapy

CASE REPORT

An 80-year-old man with a 6-year history of tumor stage IIB FMF, currently plaque stage IB presented to our clinic with nonhealing lower extremity ulcers. Prior treatments for FMF included topical corticosteroids, topical calcineurin inhibitors, narrow-band ultraviolet B, and localized RT to the tumors. He was currently on interferon-α with stable disease. Despite this, the patient had progressive painful erythema, swelling, and ulcers of the lower legs (Fig 1, *A*). Treatments for lower extremity stasis were optimized with compression garments and topical timolol ophthalmic to the ulcers without improvement. Gabapentin and pentoxifylline improved the pain without improvement of the ulcers.

From the Departments of Dermatology,[a] Hematology,[d] Radiation Oncology,[e] and Pathology,[f] Mayo Clinic, Scottsdale; Case Western Reserve University School of Medicine[b]; and Georgetown University School of Medicine.[c]

Funding sources: None.

Conflicts of interest: Dr Mangold is a Clinical Investigator for Acetilion, Soligenix, and MiRagen. The rest of the authors have no conflicts to disclose.

Correspondence to: Aaron R. Mangold, MD, Department of Dermatology, Mayo Clinic, 13400 E Shea Blvd, Scottsdale, AZ, 85259Mangold. E-mail: Aaron@Mayo.edu.

JAAD Case Reports 2019;5:231-3.
2352-5126

https://doi.org/10.1016/j.jdcr.2019.01.020

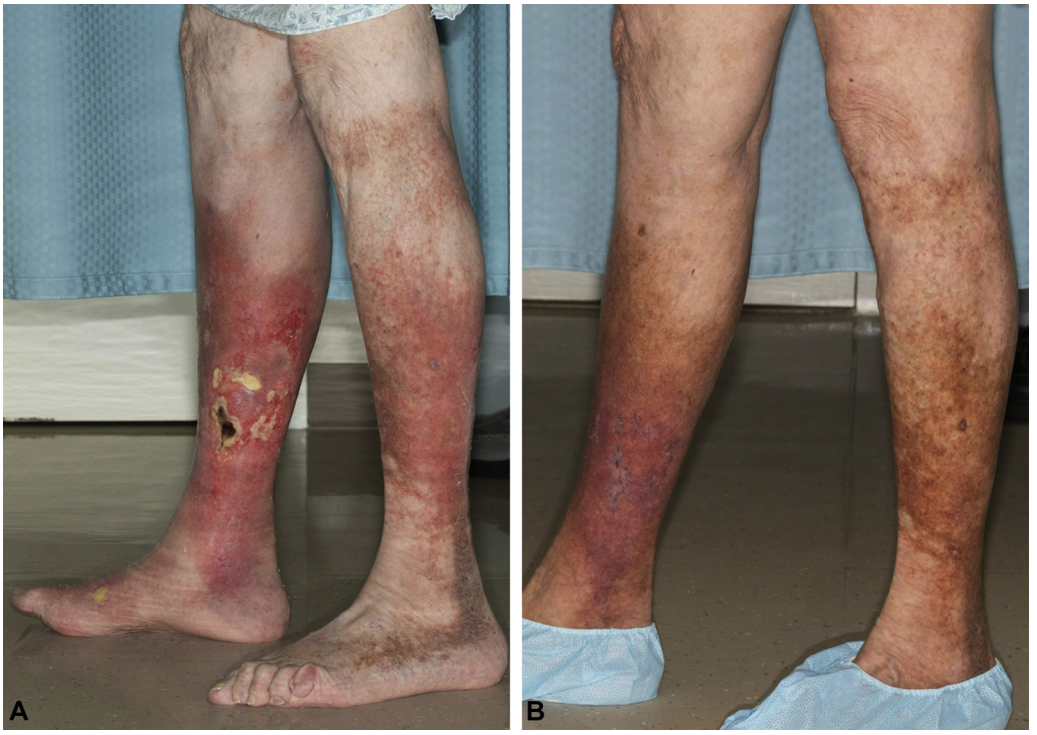

Fig 1. **A**, Folliculotropic mycosis fungoides. Vasculopathic ulcers of the lower extremity before treatment. **B**, Folliculotropic mycosis fungoides. Ten months after treatment with focal photon RT (4 Gy in 2 fractions) and 6 months after treatment with TSEBT (12 Gy in 12 fractions).

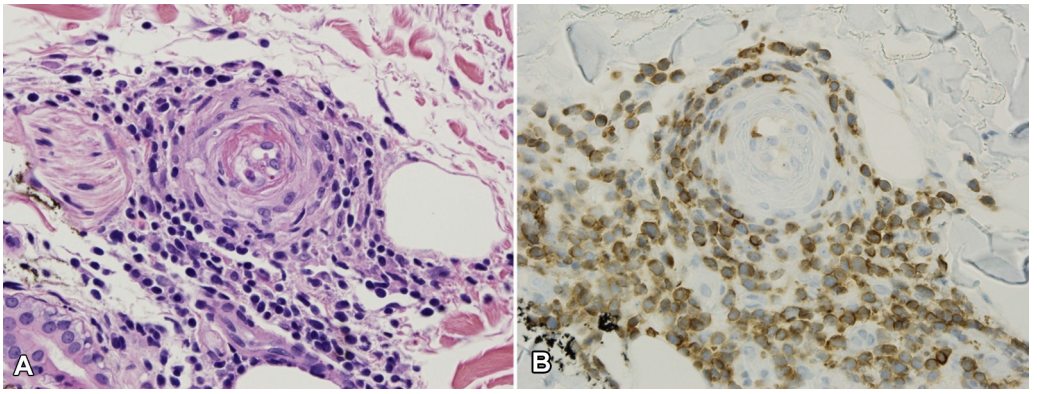

Fig 2. Folliculotropic mycosis fungoides, lower leg biopsy. **A**, Perivascular atypical lymphoid infiltrate. **B**, corresponding CD3 immunohistochemical stain. (A, hematoxylin-eosin stain; original magnifications: A and B, ×400.)

A biopsy found syringotropic MF with small-vessel vasculopathy with a dense tumor infiltration of vessels (Fig 2, *A* and *B*). The papillary dermis contained a dense, band-like infiltrate of small lymphocytes with variably irregular nuclear contours. Focal epidermotropism was present. In the reticular dermis, the small lymphocytes surrounded eccrine glands and infiltrated the walls of adjacent small vessels. The affected vessels had thickened walls with an onion skin appearance and narrowed lumina. Fibrin deposits were evident within the vessel walls.

The patient underwent focal photon RT to the lower legs (4 Gy in 2 fractions) with a plan for total skin electron beam therapy (TSEBT), and noted significant improvement in his leg ulcers. At 6-month follow-up after TSEBT (12 Gy in 12 fractions), the patient experienced a near-complete response, was feeling well, and was off all systemic therapies

(Fig 1, *B*). No recurrence of lower extremity ulcers was noted at 15-month follow-up.

DISCUSSION

We present a case of FMF and lower extremity vasculopathy associated with a dense perivascular infiltrate of MF and provide the first detailed histopathologic description of vasculopathy in FMF. Vasculotropism has been previously reported in association with lower extremity ulcers in syringotropic mycosis fungoides.[7] Cases of poikiloderma vasculare atrophicans with associated small-vessel vasculitis and MF with necrotizing vasculitis have also been described.[9,10] However, the histopathologic description of vasculopathy in FMF has not been previously reported. For the vasculopathy presented clinically as lower extremity ulcers and on histopathologic examination, the atypical lymphocytes were not only syringotropic, but also vasculotropic. The lymphocytes infiltrated the walls of adjacent vessels. Evidence of vascular damage included the onion skin appearance of the thickened vessel wall and the presence of vascular fibrin deposits. Although this is a single report, perivascular involvement of MF may be the underlying driver of lower extremity ulcers in syringotropic MF.

We present a case of FMF and lower extremity vasculopathy associated with a dense perivascular infiltrate of MF that was treated successfully with RT. We provide the first detailed histopathologic description, to our knowledge, of vasculopathy in MF. One should consider syringotropic MF when ulcers are present in a patient with FMF.

REFERENCES

1. Scarisbrick JJ, Prince HM, Vermeer MH, et al. Cutaneous lymphoma international consortium study of outcome in advanced stages of mycosis fungoides and sezary syndrome: effect of specific prognostic markers on survival and development of a prognostic model. *J Clin Oncol*. 2015;33(32):3766-3773.
2. Willemze R, Jaffe ES, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. *Blood*. 2005;105(10):3768-3785.
3. Hodak E, Amitay-Laish I, Atzmony L, et al. New insights into folliculotropic mycosis fungoides (FMF): a single-center experience. *J Am Acad Dermatol*. 2016;75(2):347-355.
4. van Santen S, Roach RE, van Doorn R, et al. Clinical Staging and prognostic factors in folliculotropic mycosis fungoides. *JAMA Dermatol*. 2016;152(9):992-1000.
5. Kazakov DV, Burg G, Kempf W. Clinicopathological spectrum of mycosis fungoides. *J Eur Acad Dermatol Venereol*. 2004;18(4):397-415.
6. Mantaka P, Helsing P, Gjersvik P, Bassarova A, Clausen OP, Delabie J. Clinical and histopathological features of folliculotropic mycosis fungoides: a Norwegian patient series. *Acta Derm Venereol*. 2013;93(3):325-329.
7. de Masson A, Battistella M, Vignon-Pennamen MD, et al. Syringotropic mycosis fungoides: clinical and histologic features, response to treatment, and outcome in 19 patients. *J Am Acad Dermatol*. 2014;71(5):926-934.
8. Pileri A, Facchetti F, Rutten A, et al. Syringotropic mycosis fungoides: a rare variant of the disease with peculiar clinicopathologic features. *Am J Surg Pathol*. 2011;35(1):100-109.
9. Warin AP, Eady RA. Poikiloderma vasculare atrophicans with vasculitis. *Clin Exp Dermatol*. 1977;2(2):171-173.
10. Granstein RD, Soter NA, Haynes HA. Necrotizing vasculitis within cutaneous lesions of mycosis fungoides. *J Am Acad Dermatol*. 1983;9(1):128-133.