A case of mixed mycosis fungoides and superficial morphea: A clinicohistopathologic challenge

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To the Editor:

Morphea, or localized cutaneous scleroderma, is a distinctive autoimmune fibrosing condition of skin and/or subcutaneous tissue [1]. Lesions present as erythematous to violaceous indurated patches and plaques. Histopathologically, morphea is characterized by a thickened collagen bundle, periadnexal fat loss with decreased adnexal structures, and a variable lymphocytic and plasmacytic infiltrate in the mid- and deeper dermis [2]. Superficial morphea, early presclerotic inflammatory cases, and morphea overlapping with inflammatory lichen sclerosus can mimic cutaneous T-cell lymphoma (CTCL), namely mycosis fungoides (MF), including interstitial variants [3]. Herein, we report a novel case of the superficial morphea subtype coexisting with MF in the same patient and illustrate the diagnostic challenge between these two conditions, which often requires continued clinicohistopathologic evaluation.

A 51-year-old woman presented to our cutaneous oncology center with a four-year history of multiple hyperpigmented patches. Since onset, the patient continually developed hyperpigmented patches on various parts of her body, in addition to scattered hypopigmented patches on the back and legs. One year prior to presenting at our institution, she had a biopsy performed by a local dermatologist, which showed a low density atypical epidermotropic lymphocytic infiltrate suggestive of MF and was started on narrowband ultraviolet B therapy with some improvement in her skin. The patient was subsequently referred to us for diagnostic confirmation and further management.

On her initial presentation to us, physical examination showed multiple hyperpigmented and hypopigmented patches over the abdomen, upper and lower extremities, back, and buttocks (**Figure 1**). The patient was asymptomatic except for occasional mild pruritus. Her presentation was concerning for MF, although the presence of an overlapping inflammatory condition could not be completely excluded. Biopsy of the left flank and buttocks revealed very prominent fibroplasia commencing in the superficial dermis, whereby the collagen bundles were of a wider caliber and assumed a parallel orientation to the long axis of the epidermis. Vascular dropout was noted and the sclerosing process was hypocellular (**Figure 2A**). There was a supervening lymphoplasmacytic infiltrate of modest degree accentuated around the nerves, blood vessels, and hair follicles. The CD34 expression was

markedly diminished in the superficial dermis in the zone of fibrosis (**Figure 2B**). Conversely, there was a very striking expression of smooth muscle actin focally amidst fibroblasts of the superficial dermis (**Figure 2C**). The findings were therefore diagnostic of superficial morphea.

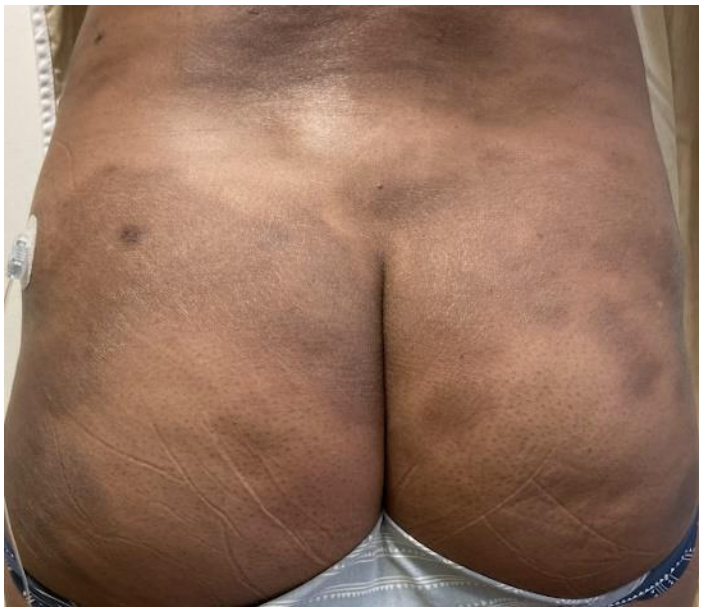

Figure 1. *Multiple hypopigmented and hyperpigmented patches of the lower back and buttocks of the first patient at her screening visit, prior to initiating treatment with extracorporeal photopheresis.*

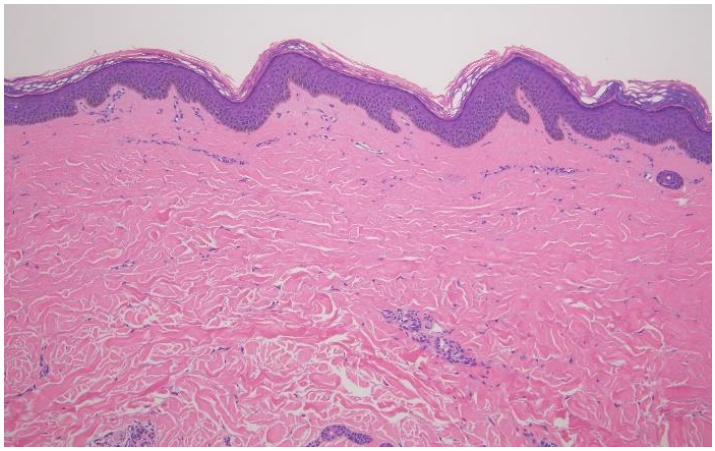

Figure 2A. *The biopsy shows a striking superficial subepidermal pauci-cellular fibrosing reaction associated with vascular drop out. There are no concurrent changes of overlying lichen sclerosis. The collagen bundles appear hyalinized whereby the interstitial spaces between the thickened bundles are markedly attenuated (hematoxylin and eosin staining 100x).*

The patient's initial biopsy was also reviewed which confirmed the presence of a sparse atypical epidermotropic lymphocytic infiltrate. Flow cytometry showed 2% atypical T-cells and a positive TCR gene rearrangement, consistent with the presence of a clonal T-cell population. Thus, the patient was diagnosed with both MF with minor blood involvement and concomitant morphea. Treatment options were discussed, including light therapy, low dose methotrexate, and a clinical trial testing efficacy of extracorporeal photopheresis (ECP) in MF. The patient opted for enrollment into the clinical trial and was treated with ECP with excellent response in both types of her skin lesions, with near complete resolution of the patches and significant improvement in the appearance and texture of her skin 9 months after starting ECP (**Figure 3**). Almost two years after beginning ECP, the patient achieved complete remission with residual post-inflammatory hyperpigmentation and resolution of blood involvement (**Figure 4**).

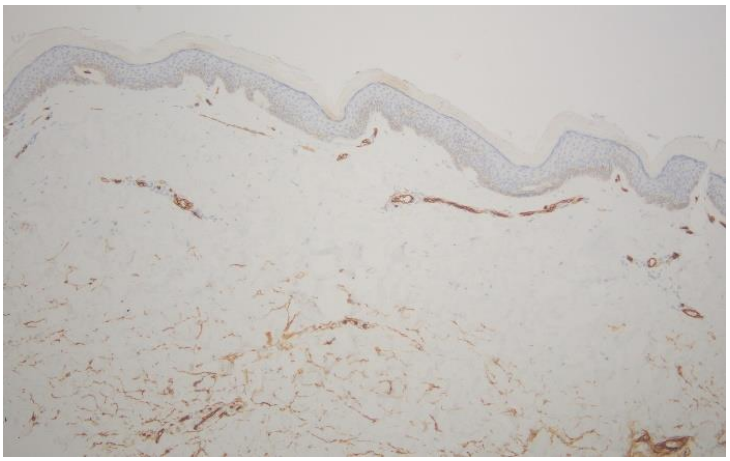

Figure 2B. *Within the zone of superficial sclerosis, there is a noticeable absence for CD34 staining in fibroblasts whereas in the subjacent zone where fibrosis is not discernible, the interstitial fibroblasts show a normal expression pattern for CD34 qualitatively and quantitatively (CD34, diaminobenzidine, 100x).*

Herein, we present a mixed presentation of MF and morphea, two conditions which bear clinicopathologic resemblance to each other. Superficial morphea is a variant of morphea that occurs almost exclusively in women and is characterized by hypo- and hyperpigmented patches and plaques in symmetric intertriginous sites [4]. Clinically, the patient's presentation is congruent with previously reported cases of superficial morphea, although the extensive nature

of her presentation not restricted to the skin folds is a unique finding. Aside from classic morphea, entities in the differential diagnosis include MF, idiopathic atrophoderma of Pasini-Pierini, which typically presents in adolescence and early adulthood, and lichen sclerosus et atrophicus [4]. The differential diagnosis might be even more challenging in patients with skin of color, as with this patient [5].

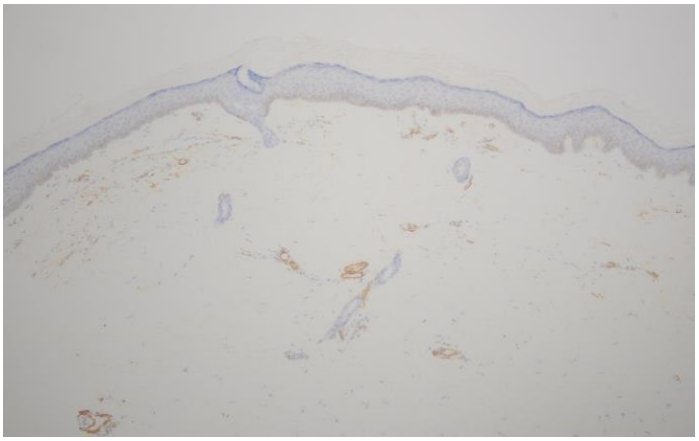

Figure 2C. *In contradistinction to the loss of CD34 expression within the zone of sclerosis, the fibroblasts have acquired a procollagen myofibroblastic phenotype and express smooth muscle actin (SMA). The classic scleroderma fibroblast phenotype is therefore defined (i.e. CD34 positive, SMA negative) (SMA, diaminobenzidine, 100x).*

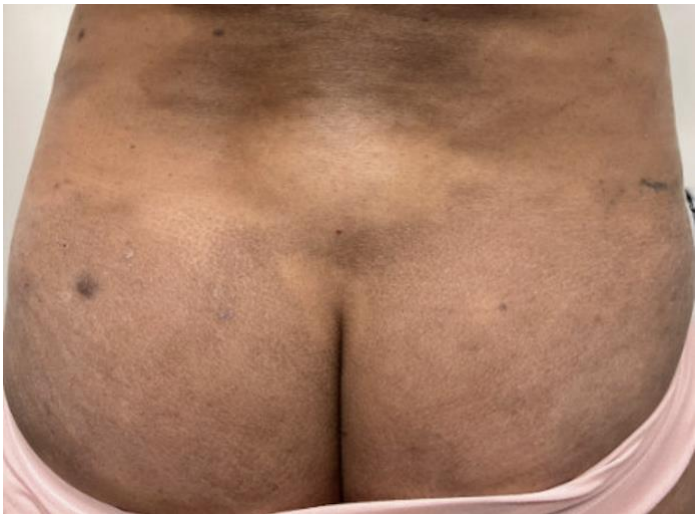

Figure 3. *Clinical improvement of the patient's morphea after 9 months of treatment.*

ECP is an approved therapy for systemic sclerosis in Canada and other countries [6]. ECP is also an US Food and Drug Administration-approved leukapheresis-based therapy for CTCL and has been shown to be an effective therapy for patients with MF and peripheral blood involvement [7]. Not surprisingly, our patient experienced significant clinical response of her MF and morphea lesions after therapy with ECP. Moreover, she had a remarkable improvement in her abnormal peripheral blood counts, including the disappearance of her clone. The presence of a dominant clone is a characteristic feature of CTCL and has also been identified in scleroderma [8]. Consequently, diagnosis of CTCL can be challenging given the lack of markers specific for the disease, a challenge which may be further exacerbated when it presents coincidentally with other skin conditions as in this case.

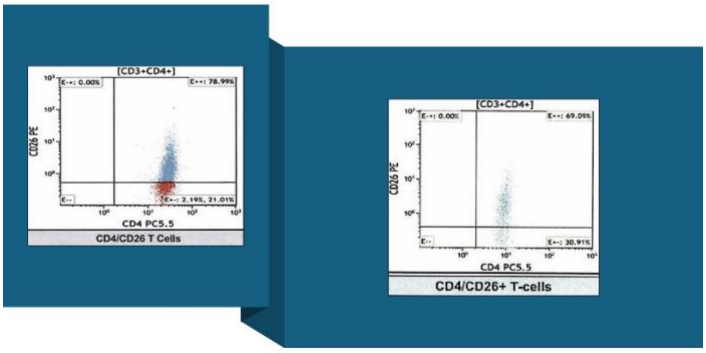

Figure 4. *Flow cytometry showing the presence of a malignant population (CD4+/CD26- T-cells, highlighted in red) at initial visit (left), compared to resolution of blood involvement almost two years after starting ECP (right).*

To our knowledge, this is the first case of the superficial morphea subtype co-existing with early stage CTCL in the same patient. ECP proved to be a very effective treatment for the management of both her conditions. In this letter, we highlight the diagnostic difficulty between MF and morphea and call for in-depth clinical and histopathologic correlation when faced with this diagnostic dilemma. We also offer a promising therapeutic option for concurrent MF with morphea.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Laxer RM, Zulian F. Localized scleroderma. *Curr Opin*

Rheumatol. 2006;18:606-13. [PMID: 17053506].

2. Fujimoto M, Basko-Plluska JL, Petronic-Rosic V, Shea CR. Early morphea simulating patch-stage mycosis fungoides. *The American Journal of Dermatopathology*. 2015;37:409-12. [PMID: 25768945].
3. Go J, Wu Y. Generalized early inflammatory morphea mimicking interstitial T-cell lymphoma: A diagnostic pitfall. *J Cutan Pathol*. 2024;51:34-9. [PMID: 37596808].
4. Loyal J, Norris II, Lester EB, Pierson JC. Superficial morphea: Case report, look-alikes, pathogenesis, and treatment. *Dermatology Online Journal*. 2017;23. [PMID: 28537856].
5. Nakamura M, Huerta T, Williams K, Hristov AC, Tejasvi T. Dermoscopic features of mycosis fungoides and its variants in patients with skin of color: A retrospective analysis. *Dermatol Pract Concept*. 2021;11:e2021048. [PMID: 34123556].
6. Lagacé F, Netchiporouk E, Turchin I, et al. Extracorporeal photopheresis and its use in clinical dermatology in Canada. *Skin Therapy Lett*. 2022;27:1-6. [PMID: 36469458].
7. Zic JA. Extracorporeal photopheresis in the treatment of mycosis fungoides and Sézary Syndrome. *Dermatol Clin*. 2015;33:765-76. [PMID: 26433848].
8. Dereure O, Gubler B, Bessis D, et al. The presence of dominant T-cell clones in peripheral blood of patients with collagen vascular disorders: A prospective study of 97 cases: Dominant T-cell clones, peripheral blood and collagen vascular disorders. *British Journal of Dermatology*. 2006;154:445-9. [PMID: 16445773].