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CASE REPORT

Generalized syringotropic mycosis fungoides responsive to total skin electron beam therapy

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ABSTRACT

A case of syringotropic mycosis fungoides without internal organ involvement received total skin electron beam therapy (TSEBT) and evolved into poikilodermatous mycosis fungoides. Subsequent oral psoralen plus ultraviolet A (PUVA) therapy achieved complete remission. The value of TSEBT for syringotroopic mycosis fungoides is illustrated in this case.

Introduction

Syringotropic mycosis fungoides (MF) is a rare variant characterized by prominent involvement of the eccrine glands with syringometaplastic lymphoepithelial lesions.[1] It is currently classified in adnexotropic MF, which also includes folliculotropic MF.[2] Typically, MF manifests as patches, plaques, and tumors.[3] According to the largest case review of syringotropic MF to date,[1] the individual lesions were mainly punctate erythematous papules, plaques, and nodules. Seventy percent of patients had concomitant follicular involvement and may have shown alopecia or anhidrosis. Given the rarity of the disease, no consensus of treatment has been published. Generalized syringotropic MF has been reported to be responsive to extracorporeal photophoresis,[4] which is not available at our institution so far. We report a case of generalized syringotropic MF responsive to the total skin electron beam therapy (TSEBT) and presenting a transition to poikilodermatous MF.

Case report

A 31-year-old man presented with a 5-year history of generalized erythematous papules and plaques. Some red papules were in the corresponding follicular area. Painful ulcers were also noted on the left chest wall and left lower back (Figure 1A). No alopecia on the skin was observed. The patient reported decreased sweat production on the affected chest wall. The skin lesions were unresponsive to topical corticosteroids. A skin biopsy taken from his left chest wall showed focal epidermal necrosis, diffuse heavy infiltrates of small- to medium-sized atypical lymphoid cells throughout the dermis with little epidermotropism (Figure 1B). These atypical lymphoid cells were found in syringometaplastic lymphoepithelial lesions (Figure 1C). Immunohistochemical study showed that the lymphoid cells were mainly CD2+, CD3+, and CD8+ T cells. The clonal proliferation of T cells was confirmed by a T-cell receptor (TCR) gene rearrangement analysis using the BIOMED-2 multiplex polymerase chain reaction assay with both heteroduplex and GeneScan analyses (Figure 2).[5] After the complete staging work-up for lymphoma, including whole body computed tomography scan and bone marrow biopsy, the patient was diagnosed to have syringotropic MF stage IB (T2N0M0).

Subsequently, the patient received TSEBT modified from the Stanford protocol for 3600 cGy in 36 fractions.[6] According to the results of *in vivo* dose measurement with a thermo-illuminescent dosimeter, several localized regions of extreme dose nonuniformity (underdose) on the patient's surface received additionally local electron boost during the course of TSEBT. These underdose regions included soles (electron boost with 2210 cGy in 13 fractions) and perineum (1800 cGy in 13 fractions). Moreover, a simultaneous electron boost to the lesions with deep infiltration during the course of TSEBT was also delivered at the left chest wall and the left flank (additionally 1300 cGy in 15 fractions).

After the TSEBT, hyperpigmented patches, telangiectasia on mildly hypopigmented atrophic and scarring skin developed on the

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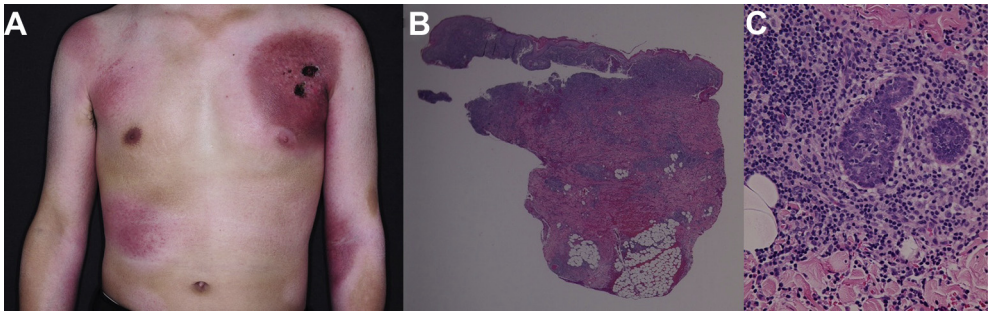

Figure 1 Clinical picture of the patient before total skin electron beam therapy. (A) Multiple erythematous plaques on the trunk and upper extremities. Note ulcers on the left upper chest lesion. (B) Heavy lymphoid cell infiltrates are seen in the upper dermis and scattered aggregates in the lower part (hematoxylin and eosin stain, ×20). (C) Islands of lymphoepithelial lesions are infiltrated by lymphoid cells indicating syringotropic mycosis fungoides (hematoxylin and eosin stain, ×200).

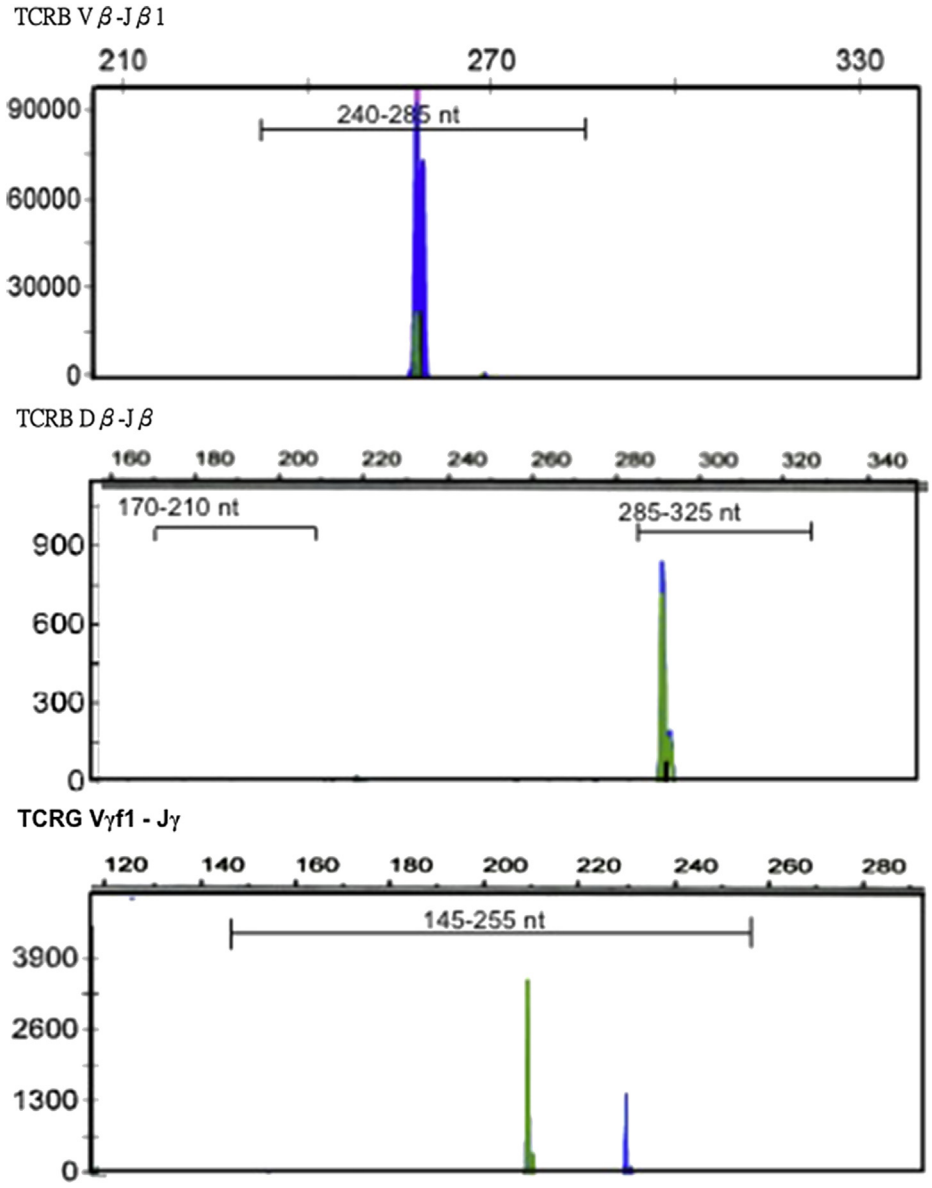

Figure 2 T-cell receptor gene rearrangement study of the original syringotropic mycosis fungoides lesion showing clonal Vβ-Jβ1, Dβ-Jβ, and Vγf1-Jγ rearrangements in GeneScan analysis.

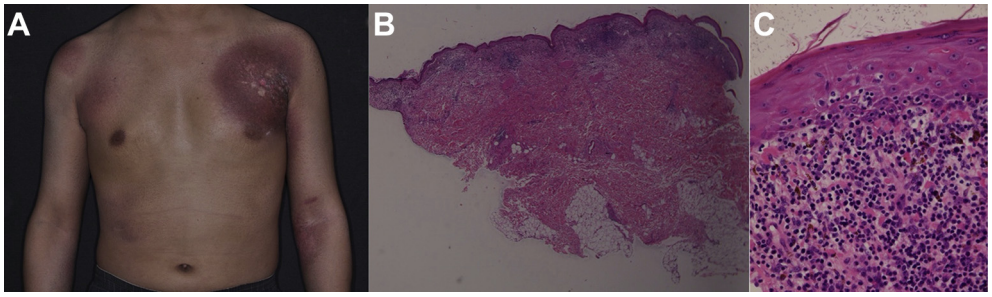

Figure 3 (A) The skin lesions after total skin electron beam treatment. The plaques became flattened with poikilodermatous change. (B) Lymphoid cell infiltrates are present only in the superficial dermis (hematoxylin and eosin stain, ×20). (C) Higher magnification shows epidermotropic lymphoid cells and vacuolar degeneration of basal cells with melanin incontinence consistent with poikilodermatous mycosis fungoides (hematoxylin and eosin stain, ×200).

previously involved area (Figure 3A). A skin biopsy from the left chest wall showed diffuse heavy infiltrates of small to medium sized lymphoid cells in papillary dermis (Figure 3B) with vacuolar degeneration of the basal layer, melanin incontinence and atrophic epidermis (Figure 3C). No syringotropic infiltration was seen. The lymphoid cells were mainly positive for CD3 and CD4. Repeated TCR gene rearrangement study showed identical patterns for clonality status in the skin biopsy tissue from skin lesions after TSEBT (Figure 4). The patient's diagnosis was changed from syringotropic MF to poikilodermatous MF. Since the involvement of

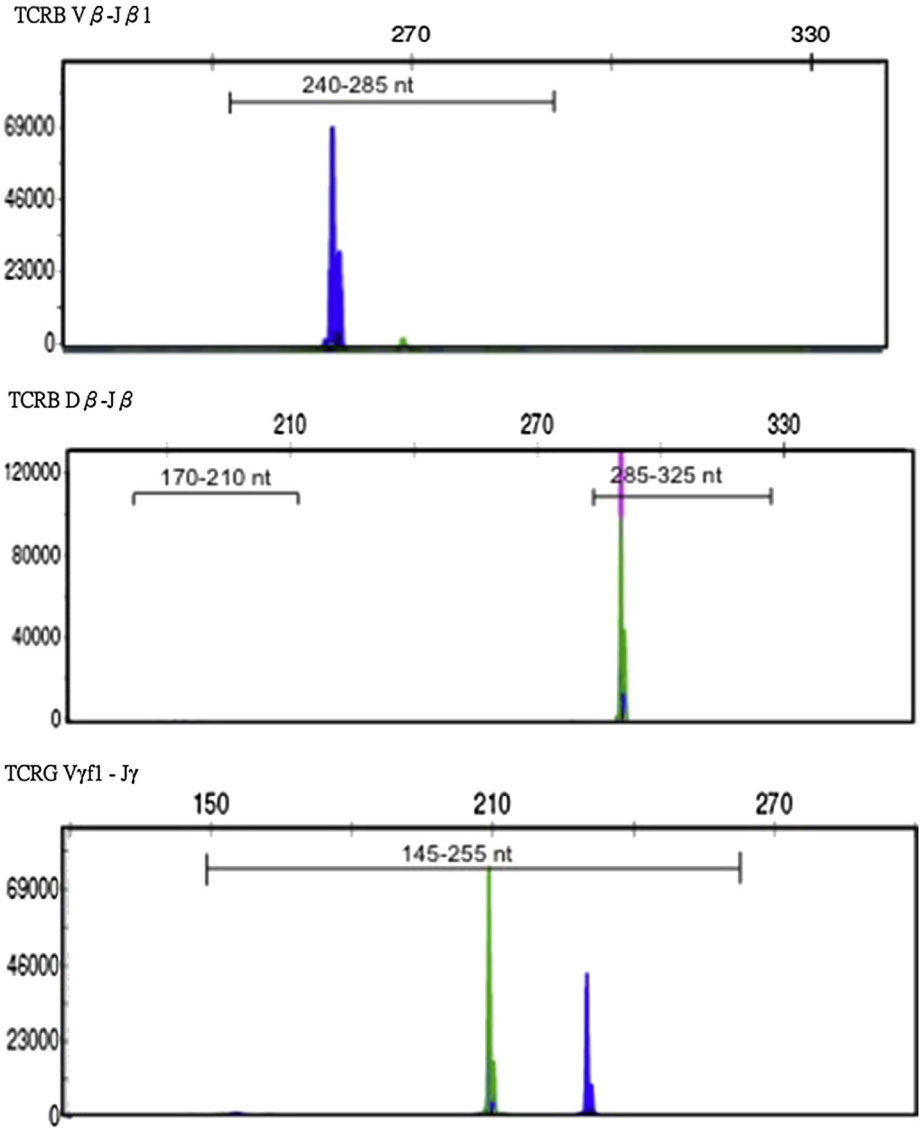

Figure 4 T-cell receptor gene rearrangement study on skin biopsy tissue of poikilodermatous mycosis fungoides after total skin electron beam therapy detected identical clonal patterns as seen in the initial study shown in Figure 2.

lymphoma infiltration was confined within the papillary dermis, we shifted the therapy to oral psoralen plus ultraviolet-A (PUVA) treatment. Local radiotherapy was delivered to the lesions of residual disease with unsatisfactory response. The patient had generalized hyperpigmentation after PUVA treatment. His ulcers healed, and he maintained the PUVA treatment three times a week for 6 months. The follow-up biopsy showed no lymphoma cells in the skin finally. The patient achieved complete remission status, and maintenance PUVA treatment was given once a week. He has since been alive without disease for 6 months.

Discussion

Our case was unique in the presentation of painful shallow ulcers in addition to the punctate follicular corresponding papules. The ulceration in syringotropic MF may stand for more advanced disease. In addition, the poikilodermatous lesions developed after TSEBT. Poikilodermatous MF is another variant of MF with hypopigmentation, hyperpigmentation, skin atrophy, and telangiectasia in addition to the red patches and plaques seen in conventional MF.[7] After the TSEBT, the atrophy of the skin and aggravated ulceration could be attributed to the side effects from the treatment *per se*.[8] However, the radiation would not cause the vacuolar degeneration of the basal layer. The true mechanism of the transition from syringotropic MF to poikilodermatous MF remains unknown. Our case also showed the shift from CD8+ MF to CD4+ MF, which has been observed in other case of T-cell lymphoma and the pathogenesis is unclear.[9]

The diagnosis of syringotropic MF and poikilodermatous MF in our case were supported by the clonal T-cell proliferation. The use of the TCR gene rearrangement study aids in the confirmation of lymphoma cells. The clonality detection rate by BIOMED-2 TCR multiplex polymerase chain reaction protocol is 99% for T-cell malignancy.[5] However, clonality *per se* does not necessarily equal malignancy, careful clinicopathologic correlation is mandatory for making an accurate diagnosis.

Because of involvement of deeper structures in syringotropic MF, topical therapies are often unsuccessful.[4] Only two cases of syringotropic MF have reported complete remission.[1,4] The first was the solitary syringotropic MF, but the treatment modality given was not mentioned.[1] The second was the generalized syringotropic MF responsive to extracorporeal photophoresis and maintenance use of oral bexarotene.[4] In other cases of syringotropic MF, patients had variable response to PUVA treatment,[10] narrow-band ultraviolet-B phototherapy, and topical treatments with bexarotene gel and clobetasol ointment.[11] In our case, TSEBT is a good treatment modality for generalized syringotropic MF without the evidence of internal organ involvement. Whole-skin irradiation treatment can be delivered to a mean depth of 3 mm with a 6 MeV electron beam produced by a linear accelerator and accumulated to a total dose of 24 Gy in 8 fractions divided into 3 times a week.[12] Because the eccrine glands are located at the junction between the reticular dermis and subcutaneous layer, regular PUVA treatment cannot reach the level of eccrine glands. Our case showed good response to TSEBT, which should be considered as one of the first-line treatments in cases of generalized syringotropic MF without any internal organ involvement. After our case showed only superficial involvement of MF in the epidermis and papillary dermis, we used the PUVA treatment since there was limitation of the highest dose of electron beam and PUVA can only reach less than 160 um deep in the skin.[13]

One review of 20 cases of syringotropic cutaneous T-cell lymphoma indicated that the disease had a prognosis similar to chronic forms of conventional MF, with 10-year survival ranging from 83% to 97% depending on the extent of cutaneous involvement.[14] We had followed our case for 3 years after the initial diagnosis of syringotropic MF and he was still alive without disease for 6 months. As in the treatment for conventional MF, continuous follow-up with maintenance treatment are considered mandatory in treating syringotropic MF.

Syringotropic MF is a rare variant of MF warranting further clinical and pathologic identification by the dermatologists and dermatopathologists. The transition from syringotropic MF to poikilodermatous MF might be associated with the effect of TSEBT. The pathophysiology and prognosis of syringotropic MF require further studies. Different treatment modalities should be considered when treating various types of MF.

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