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THERAPEUTIC HOTLINE

Tumor-stage mycosis fungoides of the vulva successfully treated with local low-dose radiotherapy

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ABSTRACT: Mycosis fungoides (MF) is the most common type of primary cutaneous T-cell lymphoma. According to the proposed guidelines for MF, skin-directed therapies are the treatment of choice for patients with limited stage disease. We present a case of early-stage MF, who progressed to tumor-stage MF during the postpartum period, showing a solitary ulcerated tumor on the vulva, which was successfully treated with local response-based, low-dose radiotherapy.

KEYWORDS: malignant neoplasms, topical therapy

Introduction

Mycosis fungoides (MF), an indolent form of non-Hodgkin lymphoma (NHL), is the most common type of primary cutaneous T-cell lymphoma (1), and has a predilection for sun-protected areas. Vulvar involvement by NHL rarely occurs and to date only two cases of MF lesions involving the vulva have been reported (2,3). Skin-directed therapies are the most appropriate option for the treatment of the early-stage MF, consisting of topical drugs (corticosteroids, nitrogen mustard, carmustine), radiation with UVB, psoralen plus ultraviolet UVA (PUVA), local radiotherapy (RT), and total skin electron beam therapy (4,5). Local RT provides the most effective treatment for individual tumor lesions in tumor-stage MF (IIB) (4,5).

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We report a patient with early-stage MF, who progressed to tumor-stage MF during the postpartum period, showing a solitary tumor on the vulva, which was successfully treated with local response-based, low-dose RT.

Case report

A 33-year-old woman presented with a sudden-onset tumor involving the left labium majus and suspicious for malignancy. The patient had a 7-year history of MF stage IA, which was restricted to patches that were seen on the trunk, arms, and inguinal regions involving 7–8% of her body surface area (BSA). Over the years, she was treated with high-potency topical steroids, narrowband UVB, PUVA, and systemic acitretin with partial improvement. She was clinically disease free for the last 5–6 months, but of note, she had given birth 1.5 months before presenting with the vulvar lesion. The tumor was sized 3 × 2 cm and was

diagnosed as tumor-stage MF by histopathology. Four months later, six erythematous scaly plaques were seen on the trunk, inguinal region, and the shoulders involving 5–6% of the BSA, and the tumor on the left labium had increased to an ulcerating tumor of 3 × 4 cm (FIG. 1). The patient was still breastfeeding. There was no systemic or lymph node involvement.

The patient was treated with low-dose intermittent local RT (two split courses 4 × 2 Gy with 2-week interval) combined with total body narrowband UVB treatment, 3/w; starting with 200 mj/cm^2, with 20% increments in each session. In order to avoid detrimental effects of RT in this highly sensitive area, we adopted a response-based treatment approach: involved field RT was applied using 9 MeV electron energy with a bolus in order to deliver a surface dose of 100% (FIG. 2). A custom block was used to protect the surrounding normal tissue. For the split course RT, a daily dose of 2 Gy, 4 days per week was given for 4 days to a total dose of 8 Gy. After a rest period of 2 weeks, the patient was re-evaluated and, given the regression of the lesion but not disappearance, a second similar course was applied to bring the total dose to 16 Gy in eight fractions.

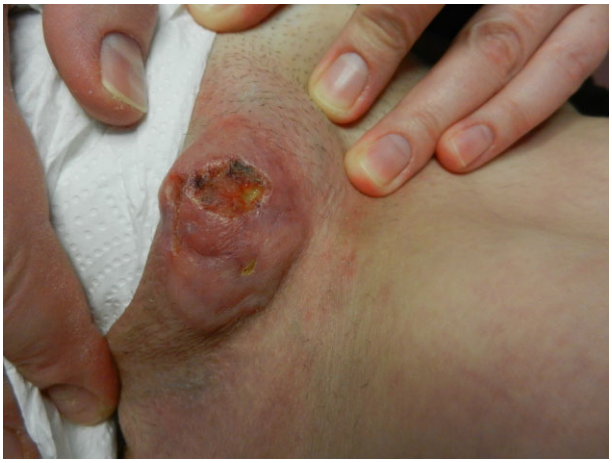

FIG. 1. Ulceration and enlargement of the initial tumor on the vulva soon after histopathological examination.

Complete clinical response of the tumoral lesion was achieved after eight treatments of local low-dose RT (FIG. 3). No RT-related side effects were observed. The patient continued to have occasional flares of lesions on the trunk, involving 1–2% of the BSA while still being under the treatment of narrowband UVB (3/w, total cumulative dose of 125 j/cm^2). As soon as the patient stopped breastfeeding, the treatment was switched to PUVA, 3/w, starting with 1.5 j/cm^2 with 0.5 j/cm^2 increments per week and 3/w subcutaneous (s.c.) injections of interferon (IFN), followed by 50 µg/m^2/w of pegylated IFN alpha (PegIntron®, Merck & Co. Inc., Whitehouse Station, NJ, USA). After receiving a cumulative dose of 167.5 j/cm^2 PUVA, and 14-week injections of IFN and 16-week injections of PegIntron, the patient only had two small erythematous patches on the inguinal regions with no new nodules or plaques. So, PUVA treatment was ended and the patient has been treated with s.c. injections of 50 µg/m^2/w, PegIntron for the last 3.5 months with no new lesions.

Discussion

We describe here a patient suffering from early-stage MF (stage IA) with a fairly stable course of 7

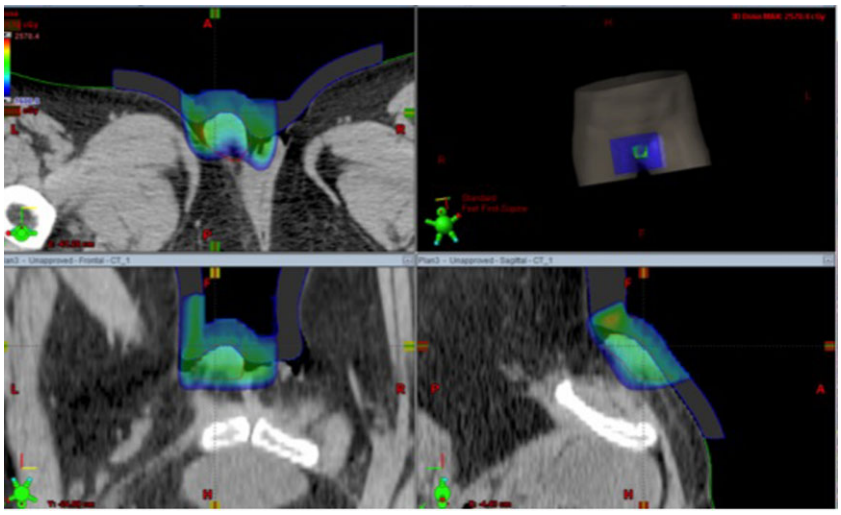

FIG. 2. Involved field radiotherapy (RT) was applied using 9 MeV electron energy with a bolus.

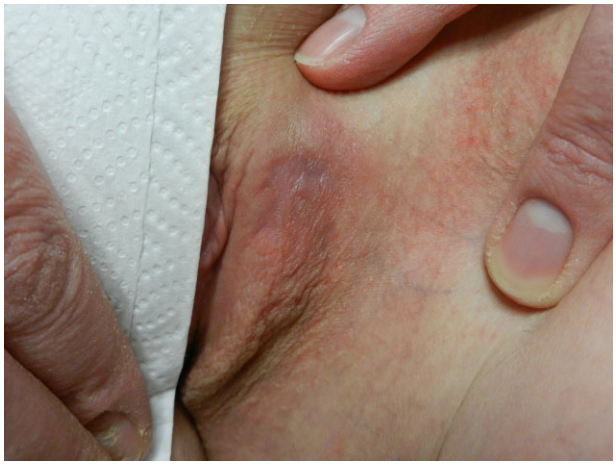

FIG. 3. Complete clearance of the nodule was attained in 1 month, with a total radiotherapy (RT) dose of 16 Gy that was given in eight fractions together with 66 sessions of narrow-band UVB treatment given in 3/w sessions.

years, including a period of pregnancy, but postpartum suddenly progressing to tumor-stage MF, showing a solitary ulcerating nodule on the vulva. Although the effects of pregnancy and delivery on MF are still unknown, it is tempting to speculate that the delivery may have caused the progression of MF in our patient. There are few case reports about pregnancy and its adverse effect on the clinical course of MF, such as CD30-positive large-cell transformation (6,7).

Although MF lesions have a predilection for sun-protected areas, the vulva is uncommon as a site of onset or as manifestation of an advance stage of MF (2,3). One of the reasons that vulvar MF lesions are hardly reported might be that most patients with MF have generalized tumoral skin involvement, thereby offering other involved anatomic sites than the vulva to sample material for pathological analysis.

Several studies (2) reported progression of the disease after vulvar involvement, and therefore, the vulvar involvement was concluded as a poor prognostic feature. Vang and colleagues (2) reported six cases of NHL involving the vulva. One patient was diagnosed as MF stage IVA/Sézary syndrome and was treated with chemotherapy and phototherapy (2). Although initially complete clinical remission was achieved, the patient had relapses in the peripheral blood and stayed alive for 4 years after vulvar involvement (2).

RT is a highly effective therapy for both early and advanced-stage MF, in which patients continue to develop new plaques and tumors (4). Partial regression of disease may be observed with single doses as low as 1.0 Gy (8). It is postulated that MF tumor cells have little ability to repair sublethal damage; therefore, even low daily fraction doses can provide local control while minimizing the toxicity to the surrounding tissue (8).

The approach for localized disease is similar to the management of other low-grade lymphomas: to treat such patients with local RT with "curative" intent to a dose of approximately 30–36 Gy (9–11). There have also been retrospective studies reporting good outcomes with a single high dose of 7–8 Gy RT for localized unilesions with complete response rates of 94.4% (12). Neelis et al. (5) achieved a complete response rate of 92% with an RT schedule of 4 Gy ×2 to a total dose of 8 Gy. However, the tenderness of the vulvar localization limited the use of higher single dose and we designed a gentler response-based radiation regimen in multiple fractions with a comparatively lower dose than other series.

To the best of our knowledge, the presented patient is the first MF patient of whom the involved vulva showed complete clinical remission with a good cosmetic result, 2 weeks after low-dose RT to a total dose of 16 Gy applied in split course fashion. There have been several retrospective studies with different RT schedules and doses; however, none of them based their dose on treatment response. Although our patient has been nodule free for 1 year now, the effect of response-based dose approach on long-term local control is not well determined.

We believe that accurate diagnosis, risk evaluation, and selection of appropriate therapy according to the stage remains critical in MF patients and each treatment protocol should be tailored on individual basis concerning patient age, overall health status, pregnancy, associated symptoms, or cost–benefit features of treatments.

Conflict of interest

None of the authors have any conflict of interest to declare. No primer presentation.

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Financial disclosure

None of the authors have any financial disclosure to declare.

References

1. Willemze R, Jaffe ES, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. Blood 2005: **105**: 3768–3785.
2. Vang R, Medeiros LJ, Silva EG, et al. Non-Hodgkin's lymphoma involving the vagina: a clinicopathologic analysis of 14 patients. Am J Surg Pathol 2000: **24**: 719–725.
3. Reichman O, Sobel JD, Bentley G. Chronic vulvar fissure – a rare manifestation of mycosis fungoides. J Low Genit Tract Dis 2010: **14**: 65–67.
4. Trautinger F, Knobler R, Willemze R, et al. EORTC consensus recommendations for the treatment of mycosis fungoides/Sézary syndrome. Eur J Cancer 2006: **42**: 1014–1030.
5. Neelis KJ, Schimmel EC, Vermeer MH, et al. Low-dose palliative radiotherapy for cutaneous B- and T-cell lymphomas. Int J Radiat Oncol Biol Phys 2009: **74**: 154–158.
6. Naeini FF, Najafian J, Nilforoushzadeh M. CD30+ large cell transformation of mycosis fungoides during pregnancy. Indian J Dermatol 2013: **58**: 160.
7. Amitay-Layish I, David M, Kafri B, et al. Early-stage mycosis fungoides, parapsoriasis en plaque, and pregnancy. Int J Dermatol 2007: **46**: 160–165.
8. Kim JH, Nisce LZ, D'Anglo GJ. Dose-time fractionation study in patients with mycosis fungoides and lymphoma cutis. Radiology 1976: **119**: 439–442.
9. Wilson LD, Kacinski BM, Jones GW. Local superficial radiotherapy in the management of minimal stage IA cutaneous T-cell lymphoma (Mycosis Fungoides). Int J Radiat Oncol Biol Phys 1998: **40**: 109–115.
10. Smith BD, Glusac EJ, McNiff JM, et al. Primary cutaneous B-cell lymphoma treated with radiotherapy: a comparison of the European Organization for Research and Treatment of Cancer and the WHO classification systems. J Clin Oncol 2004: **22**: 634–639.
11. Cotter GW, Baglan RJ, Wasserman TH, et al. Palliative radiation treatment of cutaneous mycosis fungoides – a dose response. Int J Radiat Oncol Biol Phys 1983: **9**: 1477–1480.
12. Thomas TO, Agrawal P, Guitart J, et al. Outcome of patients treated with a single-fraction dose of palliative radiation for cutaneous T-cell lymphoma. Int J Radiat Oncol Biol Phys 2013: **85**: 747–753.