Radiation therapy for primary cutaneous γδ T-cell lymphoma: Case report and literature review

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INTRODUCTION

Primary cutaneous γδ T-cell lymphoma (PCGD-TCL) is a rare non-Hodgkin lymphoma arising from mature, activated cytotoxic γδ T cells. Patients typically present with generalized skin lesions with disease commonly involving the extremities.[1,2] Although radiation therapy (RT) is an important treatment modality in the management of more common cutaneous T-cell lymphomas, such as mycosis fungoides, its role in the management of this disease has not been established. Although it is commonly reported that PCGD-TCLs are resistant to both chemotherapy and RT,[3-5] published data on the role of RT for this disease are limited.[6] We report a challenging case in which local RT provided significant clinical benefit for a patient with widespread PCGD-TCL.

CASE REPORT

A 63-year-old African-American female presented to our clinic with a history of widespread nodular skin plaques that were initially diagnosed as psoriasis. Neither topical steroids nor narrow-band ultraviolet B light therapy proved effective. After approximately 2 years of symptoms, she was started on adalimumab (Humira). Her skin lesions worsened within weeks of starting adalimumab, and ulcers developed on her hands, feet, and posterior thigh.

A biopsy was performed with histologic examination finding an atypical lymphoid infiltrate involving the entire dermis with extension into the subcutis and prominent epidermotropism (Fig 1, *A*).

Abbreviations used:

PCGD-TCL:	primary cutaneous γδ T-cell lymphoma
RT:	radiation therapy

The infiltrate consisted of medium-sized to large lymphocytes with oval, indented, or irregular nuclear contours, vesicular chromatin, and scant-to-moderate amounts of amphophilic or clear cytoplasm (Fig 1, *B*). Immunohistochemical analysis found that most of the infiltrating lymphoid cells were positive for CD3 (Fig 1, *C*), CD2 (Fig 1, *D*), CD7, and T-cell receptor δ with loss of CD5 (Fig 1, *E*) and negative β-F1 (Fig 1, *F*). CD56 and CD30 stains showed scattered positive cells. Granzyme-B and TIA-A stains were focally positive. Polymerase chain reaction–based T-cell receptor gene rearrangement analysis detected a clonal rearrangement of the T-cell receptor γ gene, confirming a clonal nature of the T-cell infiltration.

Subsequent bone marrow biopsy was negative for lymphomatous involvement. Positron emission tomography/computed tomography found hypermetabolic skin thickening at sites involved clinically without evidence of systemic disease. The histopathologic features, molecular diagnostic findings, and clinical presentation supported a diagnosis of PCGD-TCL.

The patient was in severe pain from her disease, and she required narcotic analgesics. Ambulating was difficult because of the ulcerated lesions on the soles of her feet. After evaluation by the medical

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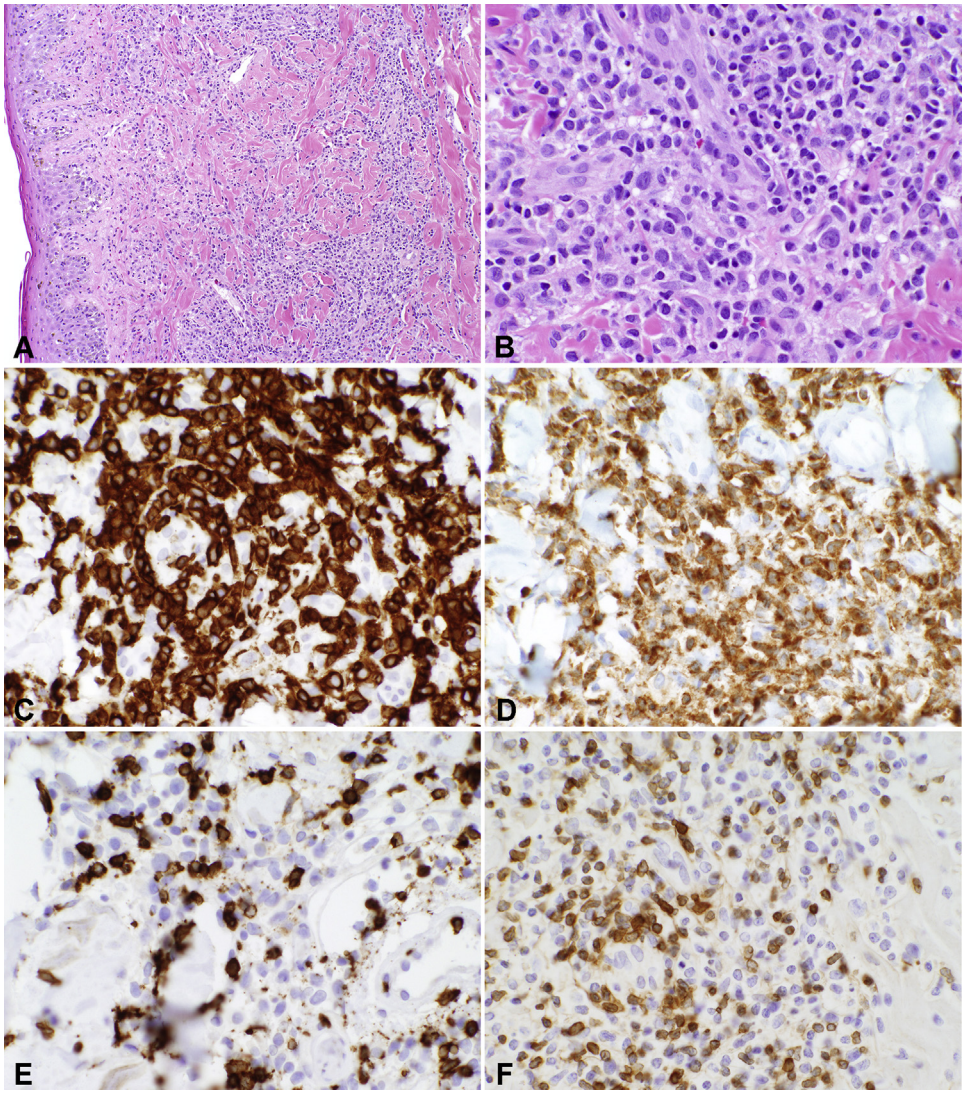

Fig 1. Histopathologic evaluation of the skin punch biopsy. The hematoxylin-eosin stained section (×100) shows an extensive lymphoid infiltrate in the papillary to reticular dermis (**A**). The lymphoid infiltrate appears mainly interstitial in distribution with significant perivascular and periadnexal infiltrates. Note the psoriasiform epidermal changes and epidermotropism with vacuolar degeneration in the basal layer of epidermis. Pigmentary incontinence and extravasation of red blood cells can be seen in the papillary dermis. A high magnification hematoxylin-eosin stained section shows an interstitial infiltrate by medium-to-large lymphocytes in the mid to reticular dermis (**B**). Note the oval, indented to irregular nuclear contours, vesicular chromatin and moderate amount of amphophilic or clear cytoplasm of the atypical lymphocytes. One mitotic figure (upper middle field of the image) and a few karyorrhexis can be seen. Scattered small lymphocytes with dense chromatin likely represent benign lymphoid components. CD3 (**C**) and CD2 (**D**) stains are positive in most lymphocytes. Note their medium-to-large size highlighted by the stains. The atypical lymphocytes are negative for CD5 (**E**). Note the scattered positive cells are small in size, in contrast to the larger size of the negative cells; these small $CD5^+$ cells likely represent reactive T cells. The atypical lymphocytes are negative for β-F1 (**F**). As in the CD5 stain, scattered β-$F1^+$ cells are smaller and likely represent reactive T cells. (Original magnifications: **A**, ×100; **B**, ×400.)

oncology, dermatology, and radiation oncology departments, an immediate course of RT was administered to the hands and feet and a deeply ulcerated mass on her left thigh.

Given the extent of disease, a single 6x photon field was used to treat both hands and wrists with 1.5 cm of overlying bolus. Lateral fields were used to treat both feet and ankles in a customized box filled

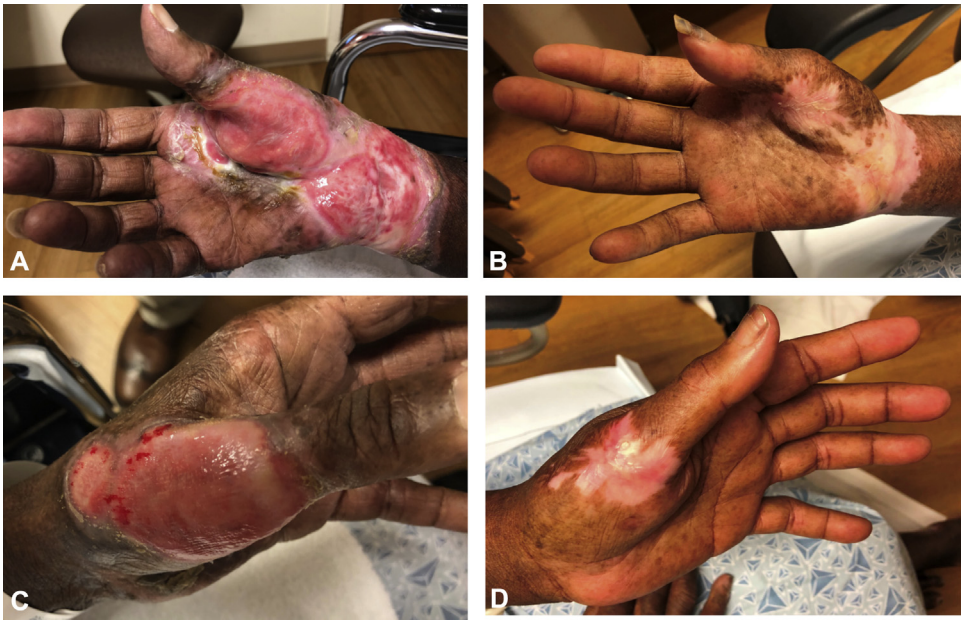

Fig 2. Right hand before (**A**) and after (**B**) radiation therapy. Left hand before (**C**) and after (**D**) radiation therapy.

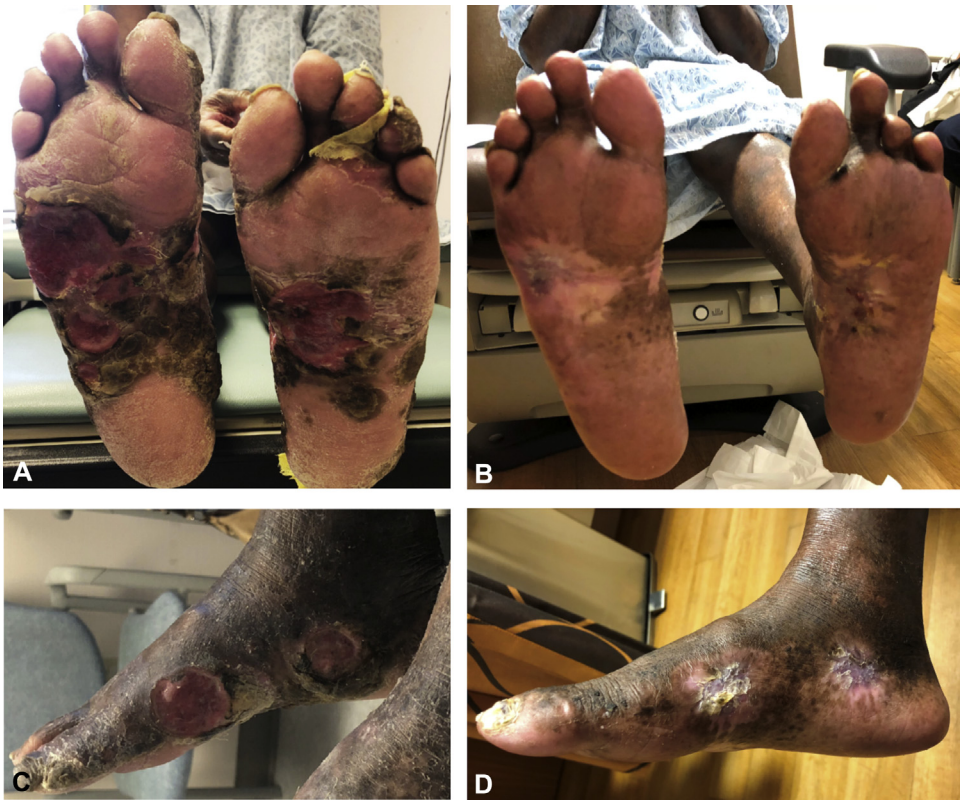

Fig 3. Soles of feet before (**A**) and after (**B**) radiation therapy. Right lateral foot before (**C**) and after (**D**) radiation therapy.

with bolus material. The right thigh mass was treated with opposed photon fields. A dose of 30 Gy was delivered in 2-Gy daily fractions. Within 2 months, the ulcerated disease involving the hands had improved dramatically. The lesions on the feet took longer to heal, but within 8 months both the disease

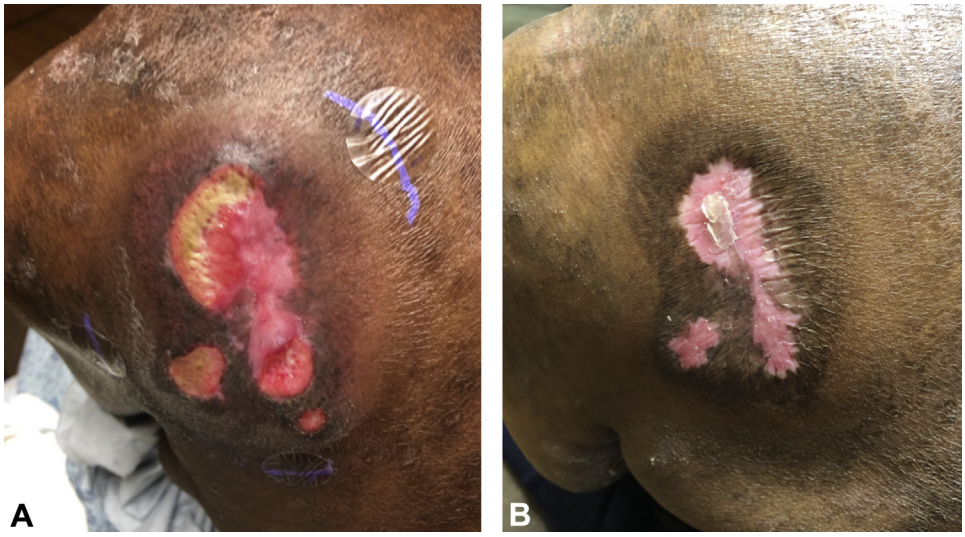

Fig 4. Left side of the back before (**A**) and after (**B**) radiation therapy.

on her hands and feet had completely resolved (Figs 2 and 3). The deeply ulcerated thigh lesion continues to heal 11 months after treatment. She tolerated RT well and was eventually able to discontinue narcotic analgesics. One concern with circumferential treatment of her ankles and wrists was the possibility of lymphedema development, but this has not been observed to date.

After completing RT, she received 2 cycles of CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone). Her chemotherapy course was complicated by sepsis and clinical deterioration requiring hospitalization. Approximately 7 months after completing the first course of RT, a new ulcerated plaque developed involving the left side of the back that was hypermetabolic on positron emission tomography/computed tomography with a maximum standardized uptake value of 5.1. This lesion was treated with a second course of RT (30 Gy; electrons) without further chemotherapy (Fig 4). A complete response was achieved. She is currently being evaluated for additional systemic therapy.

DISCUSSION

The most common cutaneous T-cell lymphomas are mycosis fungoides and primary cutaneous anaplastic large cell lymphoma. As with most hematologic malignancies, both diseases are particularly sensitive to RT. When treating symptomatic plaques or tumors, complete response rates exceed 90% for both entities.[7,8]

The World Health Organization currently recognizes several other cutaneous T-cell lymphomas that are much less common. These include PCGD-TCL, primary cutaneous $CD8^+$ aggressive epidermotropic cytotoxic T-cell lymphoma, primary cutaneous acral $CD8^+$ T-cell lymphoma, and primary cutaneous $CD4^+$ small/medium T-cell lymphoproliferative disorder.[9] The first 2 diseases are clinically aggressive with a poor prognosis, whereas patients with the latter 2 entities have a favorable prognosis. Although RT plays an important role in the management of mycosis fungoides and primary cutaneous anaplastic large cell lymphoma, there is far less experience treating these less-common cutaneous T-cell lymphomas.

Given this patient's clinical presentation, with deeply ulcerated symptomatic disease from a high-grade lymphoma, we elected to treat to 30 Gy. A lower dose may have achieved a similar response. Although the first course of RT was followed immediately by chemotherapy, albeit only 2 cycles, no systemic therapy was administered after the second course of RT. Thus, one can reasonably conclude that the RT itself was successful in achieving an excellent response at all sites treated, and this has remained durable for the last year. A case report of PCGD-TCL treated with RT and denileukin diftitox also used 30 Gy with a favorable response.[6]

RT can play a significant role in the overall management of PCGD-TCL. Although most patients present with widespread disease necessitating systemic therapy, modest doses of RT can successfully palliate symptomatic sites of disease.

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