Hematopoietic stem cell transplantation for primary cutaneous γδ T-cell lymphoma and refractory subcutaneous panniculitis-like T-cell lymphoma

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Background: The panniculitic T-cell lymphomas (TCLs) comprise 2 distinct entities, αβ subcutaneous panniculitis-like TCL (SPTCL) and the γδ cutaneous TCLs with pannicular involvement primary cutaneous γδ (PCGD)-TCL. Although outcomes for most patients with SPTCL are favorable, those with PCGD-TCLs generally have an inferior outcome, and treatment strategies have not been well defined. Allogeneic hematopoietic stem cell transplantation (HSCT) has been shown to be a potentially curative strategy in aggressive TCLs and in refractory and advanced-stage mycosis fungoides.

Objective: We sought to analyze the outcomes of HSCT for panniculitic cutaneous TCL.

Results: Fourteen patients (4 SPTCL, 10 PCGD-TCL) presented with primarily pannicular T-cell infiltrates. Seven patients underwent allogeneic HSCT from matched-related donors and matched-unrelated donors of which 4 (57%) are alive (1 SPTCL, 3 PCGD-TCL) at 7.8, 6.9, 6.2, and 0.25 years. Two patients underwent autologous HSCT (1 SPTCL, 1 PCGD-TCL) and both are alive at a median follow-up of 1.91 years.

Limitations: This study is limited by its retrospective nature and small sample size because of the rarity of SPTCL and PCGD-TCL.

Conclusion: Aggressive therapy followed by allogeneic HSCT is a promising treatment modality for patients with PCGD-TCL. (J Am Acad Dermatol 2015;72:1010-5.)

Key words: γ-δ; hematopoietic stem cell transplantation; primary cutaneous γδ T-cell lymphoma; subcutaneous panniculitis-like T-cell lymphoma; T-cell lymphoma.

Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) was accepted as a provisional entity in the European Organization for the Research and Treatment of Cancer (EORTC) classification in 1991 and in the World Health Organization (WHO) classification of hematopoietic and lymphoid tumors in 2001. However, in the past decade, it has become clear that there is significant clinical, immunophenotypic, and histopathologic heterogeneity within this entity, with γδ variants having a more aggressive course and carrying a worse prognosis than αβ variants.[1] For this reason, diagnostic criteria have been redefined, and the WHO/EORTC classification in 2005 and the WHO classification in 2008 now recognize the 2 variants as distinct clinical entities.

Both SPTCL and primary cutaneous γδ (PCGD) T-cell lymphomas (TCLs) are extremely rare, accounting for 0.9% and 0.1% of all TCLs, respectively.[2,3] The clinical course reported for patients with SPTCL is highly variable, because in part of the small number of cases reported and the fact that until

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recently the distinction between the $\alpha\beta$ and $\gamma\delta$ subtypes had not been uniformly made at diagnosis. There is no consensus on the best treatment for SPTCL and PCGD-TCL. Indolent presentations have been successfully treated with radiation therapy and immunosuppressive agents such as prednisone and cyclosporine. However, in a review of 154 cases of SPTCL published in 2004, it was reported that although corticosteroids are often used as a first-line therapy in these patients, with 50% of patients achieving partial response (PR) or complete response (CR), responses were often short lived, lasting less than 6 months.[4] Perhaps more controversial is the question of the most effective therapy for patients with advanced or refractory disease. In this review, 13 patients underwent stem cell transplantation (SCT), with all but 1 undergoing autologous SCT.[4] Twelve patients (92%) had a CR with a median duration of response of 14 months; only 1 patient developed recurrent disease at 3 months. The single patient who underwent allogeneic SCT had the longest follow-up time, remaining in remission at 70 months after transplantation. These data suggest the use of transplantation as a potentially curative treatment for aggressive disease.

CAPSULE SUMMARY

- The best treatment for cutaneous T-cell lymphomas (TCLs) with primarily pannicular involvement is not known. Allogeneic hematopoietic stem cell transplantation offers a potentially curative treatment for subcutaneous panniculitis-like TCL (SPTCL) and primary cutaneous $\gamma\delta$ (PCGD)-TCL, yet fewer than 20 cases have been reported since 2000.
- In this series, 7 of 14 patients (4 SPTCL, 10 PCGD-TCL) underwent allogeneic hematopoietic stem cell transplantation and 4 (57%) of these patients are alive (1 SPTCL, 3 PCGD-TCL) at 7.8, 6.9, 6.2, and 0.25 years.
- The treatment approach to PCGD-TCL and refractory SPTCL should be similar to that of other aggressive poor-prognosis TCLs and should include multiagent chemotherapy, followed by stem cell transplantation from an allogeneic donor if one is available.

METHODS

We conducted a retrospective analysis of patients given the diagnosis of SPTCL and cutaneous γ-δ TCL between 2000 and 2012 evaluated at the Yale Cancer Center. Yale University's Institutional Review Board granted exempt status for this limited retrospective case series. All patients met the clinical, histopathologic, and molecular criteria for either SPTCL or PCGD-TCL defined by the 2008 WHO classification. Immunohistochemistry was performed using antibodies against CD2, CD3, CD4, CD5, CD7, CD8, CD20, CD30, CD56, TIA-1, and/or granzyme B. The diagnosis of PCGD-TCL was made on the basis of $\gamma\delta$ expression by flow cytometry in lesional tissue, $\gamma\delta$ immunohistochemical staining, and/or lack of βF1 immunohistochemical staining in conjunction with other typical histopathological findings. Clinical staging, treatment, outcome, and follow-up information were obtained (Tables I and II; available at http://www.jaad.org).

A retrospective review of the literature was conducted to identify previously reported cases where SCT was used for SPTCL and panniculitic PCGD-TCL dating back to 2000. A MEDLINE search was performed using the key words "panniculitis," "subcutaneous panniculitis-like T cell lymphoma," "cutaneous T cell lymphoma," "primary cutaneous $\gamma\delta$ T cell lymphoma," and "γ-δ," along with "allogeneic stem cell transplant," "autologous stem cell transplant," and "stem cell transplant." Seventeen cases were identified (Table III; available at http://www.jaad.org).

RESULTS

Clinical characteristics

Of the 14 patients, 10 had PCGD-TCL and 4 had SPTCL. The median age in the PCGD-TCL group was 42 (26-63) years and in the SPTCL group was 43 (34-49) years. All patients presented with skin nodules or ulcerations (visible by positron emission tomography scan) that tended to be single nodules in the SPTCL group and more generalized in the PCGD-TCL group (Fig 1). In the PCGD-TCL group, involvement of the lower extremities or generalized disease occurred more often than upper extremity involvement. In the PCGD-TCL group, 1 developed involvement of the liver, 2 had bone-marrow involvement, and 3 developed peripheral blood involvement. In the SPTCL group, only 1 patient had an equivocal bone-marrow biopsy. See Table I for detailed patient characteristics.

Pathology

The 4 cases of SPTCL were adipocentric with dense lymphocytic infiltrates rimming the fat (Fig 2). They all lacked epidermotropism, necrosis, and angiocentrism/angioinvasion. In contrast, the PCGD-TCL cases more often had dermal and/or epidermal (in addition to pannicular) involvement