Localized skin-limited blastic plasmacytoid dendritic cell neoplasm: A subset with possible durable remission without transplantation

Iris Amitay-Laish, MD,[a,b] Uma Sundram, MD, PhD,[c,d] Richard T. Hoppe, MD,[e] Emmilia Hodak, MD,[a,b] Bruno C. Medeiros, MD,[f] and Youn H. Kim, MD[c]
Petah Tikva and Tel Aviv, Israel, and Stanford, California

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INTRODUCTION

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) was defined in the 2008 World Health Organization Classification of Tumors of Hematopoietic and Lymphoid Tissue as a malignant proliferation of blastic plasmacytoid dendritic cells.[1] The skin lesions appear as bruiselike erythematous nodules or tumors and are usually found already at presentation. BPDCN is highly malignant, with a mean survival time of 15.2 months.[2] Data are limited concerning patients with localized skin-limited BPDCN (LS-BPDCN).

We report our experience with 2 patients with LS-BPDCN, both of whom achieved potential cure with hyper-CVAD chemotherapy (cyclophosphamide, vincristine, doxorubicin, dexamethasone) followed by consolidative localized radiotherapy (LRT), without hematopoietic stem cell transplantation (HSCT).

Abbreviations used:

ALL:	acute lymphoblastic leukemia
BPDCN:	blastic plasmacytoid dendritic cell neoplasm
CVAD:	cyclophosphamide, vincristine, doxorubicin, dexamethasone
CVAD A+B:	cyclophosphamide, vincristine, doxorubicin, dexamethasone alternating with methotrexate and cytarabine
HSCT:	hematopoietic stem cell transplantation
LRT:	localized radiotherapy
LS-BPDCN:	localized skin-limited blastic plasmacytoid dendritic cell neoplasm

CASE DESCRIPTIONS

The first patient was a 38-year-old white man and the second was a 23-year-old Asian woman. Sites of occurrence were the forearm (patient 1; Fig 1, *A*) and forehead (patient 2; Fig 1, *B*). In both cases, the lesion started as a solitary papule/plaque. The forehead lesion was initially diagnosed clinically as a pimple. The lesions enlarged within weeks to months to form tumors (largest diameter, 6-8 cm) with a dusky, purplish/violet, or bruiselike appearance; in one case, the lesion was ulcerated (Fig 1, *B*). The patients had no systemic complaints. No lymphadenopathy or hepatosplenomegaly was noted on examination.

Complete blood count, comprehensive metabolic profile, and serum lactate dehydrogenase level were within normal range. Findings on bone marrow biopsy, whole-body positron emission tomography–computed tomography were unremarkable.

Histopathologic findings were remarkable for a dense dermis-based monomorphous infiltrate

From the Department of Dermatology, Rabin Medical Center–Beilinson Hospital, Petah Tikva[a]; Sackler Faculty of Medicine, Tel Aviv University[b]; and the Departments of Dermatology,[c] Surgical Pathology,[d] Radiation Oncology,[e] and Hematology,[f] Stanford Cancer Center, Stanford Hospital and Clinics.

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Correspondence to: Iris Amitay-Laish, MD, Department of Dermatology, Rabin Medical Center–Beilinson Hospital, Petach Tikva, Israel 49100. E-mail: amitaylaishiris@gmail.com.

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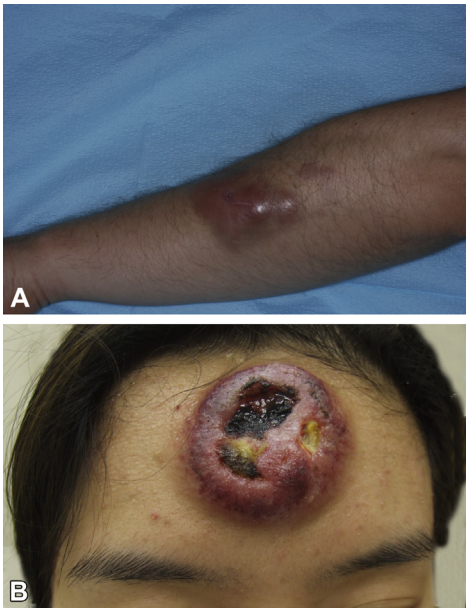

Fig 1. LS-BPDCN lesion pretreatment. **A**, Patient 1. Well-demarcated erythematous tumor, adjacent to a small infiltrated plaque, observed on the forearm. **B**, Patient 2. Bulky tumor mass on the forehead with ulceration.

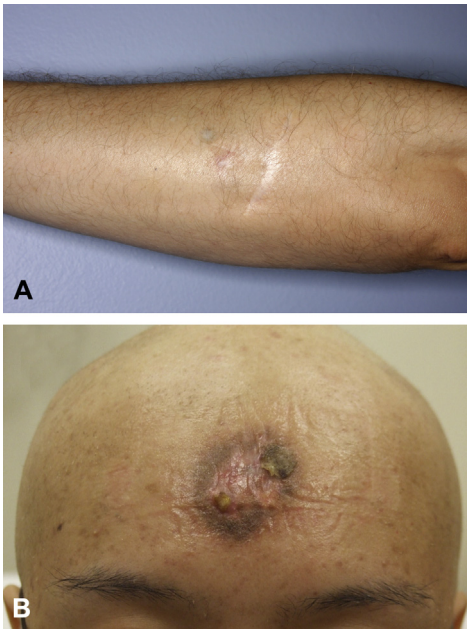

Fig 2. LS-BPDCN lesion after treatment. **A** and **B**, After treatment with hyper-CVAD × 4 cycles and consolidative LRT; only a residual scar remains.

composed of blast cells with irregular nuclei and 1 to several small nucleoli, without epidermal involvement. Cells in patient 1 were positive for CD4, CD56, CD123, TCL-1, CD2, CD7, and terminal deoxynucleotidyl transferase-1 and negative for CD3, CD8, CD5, CD30, CD20, CD34, myeloperoxidase, and Epstein-Barr virus (in situ hybridization).

In patient 2, cells were positive for CD4, CD56, CD123, CD43, CD68, and terminal deoxynucleotidyl transferase-1 and negative for CD3, CD8, CD20, CD30, CD117, myeloperoxidase, and Epstein-Barr virus (in situ hybridization).

Both patients were treated with combination chemotherapy, completing 4 cycles of hyper-CVAD, alternating with methotrexate and cytarabine (A+B). One month after chemotherapy, both underwent consolidative LRT (36 Gy). Clinical remission was achieved (Fig 2, *A* and *B*) and has been sustained so far for 6 years (patient 1) and 9 years (patient 2), without HSCT.

DISCUSSION

Only 19 patients with LS-BPDCN have been reported in the literature since the latest classification of BPDCN in 2008,[3-12] (their data are summarized in Table I). Median age of the reported patients at presentation was 46 years (range, 5-83), which is younger than the median age documented for all patients with BPDCN (67.8 years).[2] None of the reports mentioned time to diagnosis from initial evaluation by a clinician. In our patient 2, the diagnosis was delayed by 5 months, suggesting that LS-BPDCN is not always recognized by clinicians at presentation. A delay in diagnosis poses a risk of disease progression.

In 15 of the total 21 patients with LS-BPDCN (current work and the literature, 71%), the lesion was located on the upper part of the body. It was clinically described as a violaceous, bruiselike erythematous nodule/tumor.

There is no established standard frontline treatment for BPDCN. Some evidence supports the use of an acute lymphoblastic leukemia (ALL)-like protocol (eg, hyper-CVAD) over acute myelogenous leukemia—like protocols.[13] Current active clinical trials are exploring novel treatments including targeted therapies (SL-401, XmAb14045) and genetically modified T-cell immunotherapy. Promising results have been reported for SL-401, a diphtheria toxin conjugated to interleukin-3, directed to the interleukin-3 receptor (CD123), a target overexpressed on BPDCN. According to the preliminary results of a phase 2 registration clinical trial in patients with BPDCN, SL-401 showed robust single-agent activity, including 100% overall response rate in first-line patients and 87% in all lines, with multiple complete responses; response duration data are being processed and are so far encouraging (presented at the 2016 American Society of Clinical Oncology and American Society of Hematology Annual Meetings, NCT02113982).