Primary cutaneous diffuse large B-cell lymphoma, leg type, presenting as subcutaneous nodules: Case series and comparison of treatment outcomes

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INTRODUCTION

Primary cutaneous diffuse large B-cell lymphoma, leg type (PCDLBCL-LT) is a rare and aggressive subtype of primary cutaneous B-cell lymphoma with high rates of local recurrence, frequent extracutaneous progression, and poor prognosis, with 5-year survival rates of 55%.[1] First-line therapy is combination chemotherapy with cyclophosphamide, doxorubicin vincristine, prednisone (CHOP) plus rituximab (R-CHOP).[1] There have been few reports highlighting subcutaneous masses or nodules as the primary manifestation of PCDLBCL-LT, and further characterization of this unique presentation is needed.[1-4]

A retrospective review of primary cutaneous B-cell lymphoma across the Mayo Clinic enterprise was performed. This search yielded 20 patients with a clinical and pathologic diagnosis of PCDLBCL-LT. Chart review was performed, and demographic, diagnostic, treatment, and outcome data were tabulated. Six of these patients were found to have presented with subcutaneous nodules. We compared these subcutaneous cases with 12 cases of classically presenting PCDLBCL-LT. Two patients were excluded because of diagnostic uncertainty.

Clinically, the 6 patients in the subcutaneous group most frequently presented with an enlarging, asymptomatic, "lump" on the lower extremity with minimal to no overlying cutaneous changes, prompting dermatologic evaluation (Figs 1 and 2). Lipoma was listed in the differential diagnosis for several of these patients. The method used to make a diagnosis varied, particularly in the subcutaneous group, and included punch biopsy, excisional biopsy, and fine-needle aspiration under ultrasound guidance. Imaging, including computed tomography and positron emission tomography scans, were utilized to aid in diagnosis in most patients in both groups. Demographic and clinical information can be found in Table I. There were no demographic differences between the cutaneous and subcutaneous groups. The average age at diagnosis was 67.2 years (SD = 13.3). Similarly, there was no difference seen in mean size of lesion or T stage. Average overall follow-up was 1944.7 days (SD = 1626.4) and was similar between groups. No difference was seen in histologic staining for CD20, CD79a, MUM1, BCL2, or CD10 between the 2 groups.

Abbreviations used:

PCDLBCL-LT:	Primary cutaneous diffuse large B-cell lymphoma, leg type
R-CHOP:	cyclophosphamide, Adriamycin, vincristine, prednisone plus rituximab

Fig 1. Primary cutaneous diffuse large B-cell lymphoma, leg type presenting as subcuatneous nodules with minimal to no overlying cutaneous changes on the lower extremities of 2 patients. **A,** Nodule denoted by *arrow.* **B,** Nodule denoted by *circle.*

Fig 2. Subcutaneous nodule seen on ultrasound of the lower extremity, diagnosed by aspiration as primary cutaneous diffuse large B-cell lymphoma, leg type.

Treatment and outcome data can be found in Table II. All patients received systemic rituximab as part of their treatment course, with the most common treatment modality being R-CHOP. R-CHOP was utilized in all subcutaneous patients, and (9/12) classic PCDLBCL-LT. Rituximab monotherapy was used in 3 of 12 patients with classic PCDLBCL-LT. Radiation therapy was used in 5 of 6 patients in the subcutaneous group and 7 of 12 patients with classic PCDLBCL-LT. Overall treatment response was worse in patients who presented with subcutaneous lesions

(P = .009), with all 6 of these patients having progressive disease. All patients in the subcutaneous groups had recurrence of their disease, compared with 7 of 12 patients with classic PCDLBCL-LT (P = .114). Disease-specific death occurred in 4 of 6 subcutaneous patients, as compared with 2 of 12 cutaneous patients (P = .107). Survival at 5 years was 66.7% (37.9%-100%) in the subcutaneous group and 71.4% (48.2%-100%) in the cutaneous group.

PCDLBCL-LT is a rare and aggressive disease with variable clinical presentation.[1] Patients who present initially with subcutaneous lesions without cutaneous involvement have significantly higher rates of progressive disease and worse overall treatment response. There does not appear to be a difference in overall survival or recurrence; however, sample size in our study was limited.

A previous study showed that there are common alterations in immune evasion genes in PCDLBCL-LT, and that there are distinct genetic differences between PCDLBCL-LT and cutaneous DLBCL-not otherwise specified, suggesting the need for distinct treatment strategies.[5] Additional research is needed to determine if there are genetic differences between subcutaneous and classically presenting PCDLBCL-LT that differentiate their clinical course and response to treatment and if patients who present with subcutaneous lesions should be managed more aggressively.

Table I. Demographic and clinical information

Data	Subcutaneous (*N* = 6)	Cutaneous (*N* = 12)	Total (*N* = 18)	*P* value
Age at diagnosis (y)				.7415[†]
N (Missing)	6 (0)	12 (0)	18 (0)	
Mean (SD)	68.2 (13.1)	66.8 (14.0)	67.2 (13.3)	
Median (IQR)	75 (53-76)	62 (61-74)	64 (61-76)	
Range	50.0, 80.0	48.0, 92.0	48.0, 92.0	
Race, *n* (%)				1.0000[*]
Vietnamese	0 (0.0%)	1 (8.3%)	1 (5.6%)	
White	6 (100.0%)	11 (91.7%)	17 (94.4%)	
Sex, *n* (%)				.6199[*]
Female	2 (33.3%)	7 (58.3%)	9 (50.0%)	
Male	4 (66.7%)	5 (41.7%)	9 (50.0%)	
PET, *n* (%)				1.0000[*]
No	0 (0.0%)	1 (8.3%)	1 (5.6%)	
Yes	6 (100.0%)	11 (91.7%)	17 (94.4%)	
CT, *n* (%)				.5147[*]
No	0 (0.0%)	3 (25.0%)	3 (16.7%)	
Yes	6 (100.0%)	9 (75.0%)	15 (83.3%)	
Bone marrow biopsy, *n* (%)				.5294[*]
No	0 (0.0%)	2 (16.7%)	2 (11.1%)	
Yes	6 (100.0%)	10 (83.3%)	16 (88.9%)	
Nodal biopsy, *n* (%)				.0980[*]
No	4 (66.7%)	12 (100.0%)	16 (88.9%)	
Yes	2 (33.3%)	0 (0.0%)	2 (11.1%)	
Location of biopsy *n* (%)				.9741[*]
Left arm and hand	1 (16.7%)	3 (25%)	4 (22.3%)	
Left leg and foot	2 (33.3%)	3 (25%)	5 (27.8%)	
Right arm and hand	0 (0.0%)	3 (25%)	3 (16.7%)	
Right leg and foot	3 (50%)	3 (25%)	6 (33.3%)	
Size, greatest dimension (cm)				.9529[†]
N (Missing)	6 (0)	9 (3)	15 (3)	
Mean (SD)	4.1 (3.2)	3.8 (2.4)	3.9 (2.7)	
Median (IQR)	3 (2, 5)	3 (3, 5)	3 (2, 5)	
Range	1.0, 10.0	1.0, 9.0	1.0, 10.0	
TNM classification NCCN: T, *n* (%)				1.0000[*]
Missing	0	2	2	
1a	3 (50.0%)	4 (40.0%)	7 (43.8%)	
2a	1 (16.7%)	2 (20.0%)	3 (18.8%)	
2b	0 (0.0%)	1 (10.0%)	1 (6.3%)	
2c	1 (16.7%)	1 (10.0%)	2 (12.5%)	
3a	0 (0.0%)	1 (10.0%)	1 (6.3%)	
3b	1 (16.7%)	1 (10.0%)	2 (12.5%)	
Days F/U				.4537[*]
N (Missing)	6 (0)	12 (0)	18 (0)	
Mean (SD)	2128.0 (914.3)	1853.1 (1918.4)	1944.7 (1626.4)	
Median (IQR)	1920 (1811-3031)	992 (515-2759)	1841 (673-3031)	
Range	787.0-3300.0	60.0-5509.0	60.0-5509.0	

CT, computed tomography; *PET* , positron emission tomography.
[*]Kruskal-Wallis *P* value.
[†]Fisher Exact *P* value.

Table II. Treatment and treatment outcomes

Data	Subcutaneous (*N* = 6)	Cutaneous (*N* = 12)	Total (*N* = 18)	*P* value
R-CHOP				.5147*
No	0 (0.0%)	3 (25.0%)	3 (16.7%)	
Yes	6 (100.0%)	9 (75.0%)	15 (83.3%)	
Rituximab monotherapy				.5147*
No	6 (100.0%)	9 (75.0%)	15 (83.3%)	
Yes	0 (0.0%)	3 (25.0%)	3 (16.7%)	
Radiation therapy				.6000*
No	1 (16.7%)	5 (41.7%)	6 (33.3%)	
Yes	5 (83.3%)	7 (58.3%)	12 (66.7%)	
Other therapy (methotrexate, pembrolizumab, lenalidomide, etc.)				.3156*
No	1 (16.7%)	6 (50.0%)	7 (38.9%)	
Yes	5 (83.3%)	6 (50.0%)	11 (61.1%)	
R-CHOP or rituximab response, *n* (%)				.0245*
Complete response	3 (50.0%)	11 (91.7%)	14 (77.8%)	
Partial response	0 (0.0%)	1 (8.3%)	1 (5.6%)	
Progressive disease	3 (50.0%)	0 (0.0%)	3 (16.7%)	
Other therapy response, *n* (%)				.0350*
Missing	0	2	2	
Complete response	1 (16.7%)	7 (70.0%)	8 (50.0%)	
Partial response	0 (0.0%)	1 (10.0%)	1 (6.3%)	
Progressive disease	5 (83.3%)	2 (20.0%)	7 (43.8%)	
Treatment overall response, *n* (%)				.0090*
Complete response	0 (0.0%)	8 (66.7%)	8 (44.4%)	
Partial response	0 (0.0%)	1 (8.3%)	1 (5.6%)	
Progressive disease	6 (100.0%)	3 (25.0%)	9 (50.0%)	
Vital status (alive/deceased), *n* (%)				.1312[†]
Alive	1 (16.7%)	8 (66.7%)	9 (50.0%)	
Deceased	5 (83.3%)	4 (33.3%)	9 (50.0%)	
Disease-specific death (yes/no), *n* (%)				.1070[†]
No	2 (33.3%)	10 (83.3%)	12 (66.7%)	
Yes	4 (80.0%)	2 (50.0%)	6 (33.3%)	
Recurrence, *n* (%)				.1141[†]
No	0 (0.0%)	5 (41.7%)	5 (27.8%)	
Yes	6 (100.0%)	7 (58.3%)	13 (72.2%)	
Progressive disease, *n* (%)				.0090[†]
No	0 (0.0%)	9 (75.0%)	9 (50.0%)	
Yes	6 (100.0%)	3 (25.0%)	9 (50.0%)	

R-CHOP, cyclophosphamide, Adriamycin, vincristine, prednisone plus rituximab.
*Kruskal-Wallis *P* value.
[†]Fisher Exact *P* value.

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