

Low-Grade Cutaneous B-cell Lymphoma in African American Patients

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ABSTRACT

Introduction: Cutaneous marginal zone lymphoma (CMZL) and cutaneous follicle center lymphoma (CFCL) are rare indolent cutaneous B-cell lymphomas (CBCL). Their incidence in African American (AA) patients is extremely low. While cutaneous T-cell lymphomas appear to be more aggressive in AA individuals, there is no data on the presentation and course of disease of CBCL in this group. In this study, we aimed to characterize CMZL/CFCL in AA patients.

Methods: A retrospective chart review identified 10 AA patients with CMZL/CFCL. We compared demographics, clinical features, and systemic disease incidence between AA and white patients.

Results: Of 288 patients with CMZL/CFCL, 10 patients were AA (3.5%), and 266 were white. AA patients trended toward diagnosis at a younger age compared to white individuals (median age of 41 vs 54 years; *P*=0.07). AAs presented with more regional and generalized cutaneous disease (T2-T3 in 70%), while most white patients presented with a solitary lesion (T1 in 55%). Head and neck involvement was more common in AA patients. Extracutaneous systemic disease at initial staging was not significantly different between the groups. One AA patient with primary CMZL developed extracutaneous MZL after16 years. No deaths were reported among AAs.

Discussion: CMZL/ CFCL in this series of AA patients had an earlier age of onset with preferential head and neck involvement and a higher T classification at presentation. Despite these features, systemic involvement was uncommon, and no deaths were recorded. This data supports an indolent course of CMZL and CFCL in the AA population; larger studies are needed to confirm these findings.

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INTRODUCTION

Cutaneous B-cell lymphomas (CBCLs) are indolent lymphomas presenting in the skin. Primary CBCL is classified according to the WHO/EORTC into three types[1]: primary cutaneous marginal zone lymphoma (PCMZL), primary cutaneous follicle center lymphoma (PCFCL), and primary cutaneous diffuse large B-cell lymphoma, leg type (PCDLBCL-LT). While PCMZL and PCFCL are generally recognized as indolent diseases with 95% to 99% 5-year survival rate, PCDLBCL-LT has a more aggressive behavior with 5-year survival rates of 50%.[2]

The incidence of cutaneous T-cell lymphomas (CTCL), specifically of mycosis fungoides (MF), is increased significantly in African Americans (AAs) versus white individuals.[3-6] AA patients with CTCL present with an earlier age of onset, and a higher stage at presentation.[3] MF in AA patients is associated with disease progression and poorer survival.[7-9]

Primary CBCL is much less common than MF.[4] Unlike MF, its incidence in AA patients is significantly lower compared to white patients.[3,4,10,11] Given its rarity, there is limited data on presentation and clinical behavior of CBCL in AAs.[12] We attempted to characterize the disease presentation and course in this group.

METHODS

We retrospectively searched the tumor registry and pathology reports database for patients with CMZL/CFCL who were diagnosed and followed at our institution between 1997-2016. We defined CMZL/CFCL as skin lesions with histology either consistent with primary CBCL or secondary cutaneous presentation of systemic B-cell lymphoma. Our inclusion criteria were: (1) CMZL/CFCL histology confirmed by pathologists at MSKCC; (2) skin as initial site of involvement by the lymphoma; (3) staging imaging study [positron emission tomography (PET) scan and/or chest, abdomen, and pelvic computed tomography (CT) scan] completed within 12 months of diagnosis. This study was approved by the institutional review board of Memorial Sloan Kettering Cancer Center.

Demographic and clinical data were collected from the medical records including age, sex, race and ethnicity, disease distribution, and clinical T classification (according to the ISCL/EORTC TNM staging system[13]) initial staging results and follow-up data. Race and ethnicity were reported by the patient or their representative upon admission/registration in accordance with the US Census Bureau's race and ethnicity categories.

All demographic and clinical parameters were compared using

descriptive statistics, T-test, and Chi-square/Fisher's exact test. Statistical analysis was performed using the SPSS software.

RESULTS

Of the 288 patients with CMZL or CFCL, 92.4% (n=266) were white, 3.5% (n=10) were AA (9 non-Hispanic black, 1 unknown ethnicity), 1.7% (n=5) Asian, and 0.7% (n=2) "Other" race. Five patients (1.7%) stated unknown race or didn't answer. Of the 183 patients with CMZL, 92.9% were white (n=170), 2.7% AA (n=5), and 2.2% Asian (n=4), while of the 105 CFCL patients, 91.4% were white (n=96), 4.8% AA (n=5), and 1.0% Asian (n=1).

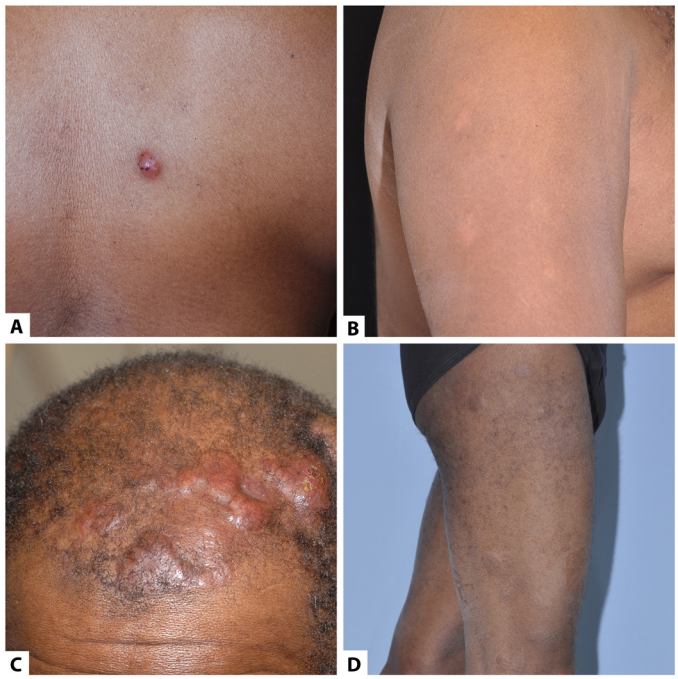
Comparing the demographic and clinical characteristics of the AA versus the white patients revealed younger age at diagnosis in the former group regardless of the lymphoma subtype (median age, 41 vs 54 years; *P*=0.07). Equal numbers of males and females were found among AA patients compared to a slight male predominance among white patients. 55% of the white patients (146/266) presented with a single lesion (T1), while 70% of AA patients (7/10) presented with regional or generalized disease (T2-3).[13] Head and neck involvement was more prevalent in AA compared to white patients (60% vs 31%) with half of the AA patients presenting with lesions localized to the head and neck alone. Disease involvement of three or more body regions (T3b) was found in 20% of the AA patients and in 12% of the white patients. Clinical presentation in AA patients was heterogeneous as described in Table 1 and Figure 1.

Initial staging was completed in all cases as per our inclusion criteria. Overall, 7.3% (21/288 patients) were found to have systemic disease with secondary cutaneous involvement, including 19 white patients (12 with CFCL and 7 with CMZL), 1 AA CFCL patient, and one CFCL patient who didn't provide his race. The rate of concurrent systemic disease diagnosed at initial staging was not significantly different between the ethnic groups (7% in white (19/266) vs 10% in AA patients (1/10)). Five AA patients were lost to follow-up after 1-7 months. In the AA group, 1 patient with PCMZL developed systemic MZL with dural involvement. None of the AA patients with PCFCL developed systemic involvement. According to our institutional records, none of the AA CMZL/CFCL patients died (Table 1). In the white patient's group, 2 patients with PCMZL and 5 patients with PCFCL were subsequently diagnosed with systemic involvement and 13 patients with CMZL/CFCL died.

DISCUSSION

Unlike CTCL, the incidence of CBCL is low in AA patients. A study of the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) database for the years 2004–2008 revealed CBCL incidence rates of 3.6 per 1 million white persons and 1.8 per 1 million AA persons.[3] In the same study, the mean age at diagnosis was significantly lower in AAs (56.7 vs. 63.7 in white patients).[3] The low rate of AA patients with CMZL and CFCL that we identified in our institute, and the younger age at diagnosis are consistent with the SEER data.[10] However, clinical features and prognosis have not been described in AA patients.

FIGURE 1. Clinical presentation in four African American patients with cutaneous B-Cell lymphomas: primary cutaneous marginal zone lymphoma (PCMZL), primary cutaneous follicle center lymphoma (PCFCL) and systemic follicle center lymphoma (SFCL). **A.** PCMZL presenting with an erythematous violaceous nodule on the back (patient 4). **B.** PCMZL presenting with hypopigmented patches on the arms (patient 2). **C.** PCFCL presenting with clustered erythematous nodules on the anterior scalp in (patient 6). **D.** SFCL presenting on the skin as plaques on the lower extremities (patient 10).



PCFCL and PCMZL present classically as non-painful, often pruritic, erythematous to violaceous papules, plaques, or nodules.[2] PCFCL has a predilection for the head, neck, and trunk, and PCMZL tends to appear on the trunk and upper extremities.[2] While the anatomic distribution in AA patients followed the classical distribution, these patients overall presented with more regional or generalized disease compared to white individuals, who mostly presented with solitary lesions. Interestingly, all five AA patients with CFCL had involvement of their head and neck compared to about a half of the white patients. While some of the AA patients presented with a typical clinical appearance of indolent CBCL (Figure 1A, 1C), some of the patients had an unusual presentation, such as hypopigmented patches (Figure 1B) and scattered flat plaques (Figure 1D). Secondary skin involvement by systemic MZL or FCL was rare regardless of race. Our study shows no clear evidence of prognostic implications for AA race in CMZL/CFCL.

TABLE 1.

Characteristics and Outcome of the African American Patients With Cutaneous Marginal Zone lymphoma and Follicle Center Lymphoma

Patient No.	Diagnosis	Sex/Age	ISCL/ EORTC T-Classification[13]	Clinical Presentation	Initial Clinical Differential Diagnosis	Initial Treatment and Response	Follow-up Period	Long-term Outcome
1	PCMZL	F/ 24y	T2	Violaceous patches and papules on the back and chest.	-	Observation, PR	16y, 10m	Developed systemic MZL disease involving the dura 16 years post diagnosis.
2	PCMZL	M/ 31y	T3	Hypopigmented patches on bilateral arms and back. (Figure 1B)	Granuloma annulare, sarcoidosis mycosis fungoides	Observation, SD	5m	-
3	PCMZL	F/ 28y	T3	Nodules with overlying hyperpigmentation on bilateral arms.	Cyst, Lipoma, dermato-fibroma.	Observation, lost to F/U	1m	-
4	PCMZL	F/ 55y	T2	Erythematous violaceous nodules on the back. (Figure 1A)	Papular urticaria, Sarcoidosis, Lupus erythematosus	Topical steroids, SD	7m	-
5	PCMZL	F/ 57y	T1	A single nodule on the eyelid	-	Excision, CR	5m	-
6	PCFCL	M/ 60y	T2	Clustered erythematous nodules on the anterior scalp. (Figure 1C)	DFSP, scalp tumor	Involved field radiotherapy, CR	9y, 3m	No recurrence no POD.
7	PCFCL	M/ 40y	T1	Single nodule on the scalp.	-	Excision and Involved field radiotherapy, CR	7y, 8m	Multiple skin recurrences.
8	PCFCL	M/ 42y	T2	Skin-colored nodules on the forehead and cheek.	Angiolipoma	Topical steroids, lost to F/U	3m	-
9	PCFCL	F/ 35y	T1	Single erythematous nodule on the nose.	-	Involved field radiotherapy, CR	13y, 10m	No recurrence no POD.
10	SFCL with cutaneus involvement*	M/ 57y	T3	Plaques on the head, neck, and lower extremities. (Figure 1D)	Sarcoidosis	Observation, POD (transformation to Cutaneous DLBCL 6months after diagnosis)	5y, 6m	Systemic disease was histologically-confirmed by a testicular biopsy 1y after initial diagnosis.

*Disease presented initially on the skin. Initial PET scan suggested systemic lymphoma; however histologic confirmation and treatment were declined at first by the patient.
PCFCL=Primary cutaneous follicle center lymphoma; PCMZL=Primary cutaneous marginal zone lymphoma; SFCL=systemic follicle center lymphoma; DLBCL=cutaneous diffuse large cell lymphoma, CR=complete response; PR=partial response; POD=progression of disease; SD=stable disease;F/U=follow-up.
ISCL/EORTC=International Society for Cutaneous Lymphomas/cutaneous lymphoma task force of the European Organization of Research and Treatment of Cancer.

Higher T classification at diagnosis in AAs could imply delay in diagnosis — possibly due to socioeconomic factors or heterogenous clinical presentation. However, the younger age at the onset of disease argues against this hypothesis and may suggest difference in pathophysiology between races. Hence, it becomes critical to evaluate prognosis in this group, which was excellent in our small case-series despite two cases with extracutaneous disease. However, this should be evaluated in larger cohorts of AA patients with longer follow- up periods.

Limitations of this study include sample size and possible referral bias; this is a retrospective case-series from a single tertiary cancer center. Our non-white patients' rate of disease is comparable to similar PCBCL cohorts supporting the significance of our findings.[14] Due to the low number of patients, we were unable to evaluate other race groups. Our findings should be validated prospectively in larger cohorts with longer follow-up.

In conclusion, the present study highlights the heterogenous clinical presentation of CMZL/CFCL in AA patients. Unlike the poor prognosis in AA patients with MF, our case-series suggests an indolent course and excellent prognosis despite more advanced T classification at presentation in AA patients compared to white patients with low-grade CBCL.

DISCLOSURES

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