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Research Article

Cutaneous Sarcoidosis in African Americans

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Abstract

Background: Though African Americans are known to be at greater risk of acquiring sarcoidosis and developing more severe disease, few studies have analyzed the racial differences in cutaneous sarcoidosis.

Aim: Our study sought to characterize patients' cutaneous disease in terms of color and morphology, and to establish whether race, presence of cutaneous sarcoidosis, or specific lesion characteristics were associated with the age at diagnosis.

Methods: Sarcoidosis patients' charts were reviewed retrospectively for sex, race, and age at diagnosis. If present, cutaneous lesions were further characterized by color and morphology.

Results: 491 patients had sarcoidosis, and 122 (25.3%) patients had cutaneous involvement. Black patients were more likely to have cutaneous involvement than white patients (p<0.001). There was no difference in color or morphology of cutaneous lesions between black and white patients.

Conclusions: Blacks are at higher risk for developing cutaneous disease, but, aside from lupus pernio, color and morphology of cutaneous sarcoidosis lesions are no different between black and white patients.

Keywords: Sarcoidosis; Epidemiology; Cutaneous Sarcoidosis; Race; Ethnic Skin

Introduction

Despite being discovered over a hundred years ago, sarcoidosis remains an enigmatic disease; currently, the etiology remains unknown and every organ system is vulnerable. Originally described as a cutaneous disease, sarcoidosis is now known as a multi-system granulomatous disorder [1,2]. The pulmonary system is most commonly involved, but sarcoidosis may also affect the heart, eyes, central nervous system, liver, bone marrow, lymph nodes, bones, and skin [3]. Cutaneous involvement occurs in up to 25% of patients and has developed in 70-80% of those patients before or at the time of systemic diagnosis [4-7]. Cutaneous lesions of sarcoidosis are categorized as either specific, i.e. containing noncaseating granulomas, or nonspecific, i.e. containing no granulomas [8,9]. The most common nonspecific cutaneous manifestation is Erythema Nodosum (EN) which develops in up to 25% of cases. However, excluding EN, cutaneous sarcoidosis does not have a typical appearance. The lesions of cutaneous sarcoid may appear hyperpigmented, hypopigmented, atrophic, or ulcerated, and may develop as macules/patches, papules/plaques, or as subcutaneous lesions [7]. The most severe form of cutaneous sarcoidosis is lupus pernio, a chronic eruption of violaceous, indurated papules or nodules usually found on the ears, fingers, cheeks, and nose, particularly along the alar rim [10,11]. In addition to its varied appearance on the skin, it is unclear whether sarcoidosis lesions present differently with regard to pigmentation and morphology on black versus white skin.

In the United States, sarcoidosis is more common in young African-American women [12-14]. In African Americans, sarcoidosis tends to present at a younger age, and cutaneous sarcoidosis lesions (except erythema nodosum) are believed to be more common [12,15,16]. It is now well understood that African Americans are at higher risk for more severe pulmonary and cutaneous sarcoidosis [8]. However, aside from lupus pernio, which occurs more frequently in African Americans, it is not clear if morphological presentations of cutaneous disease vary by race [17,18]. Our study retrospectively analyzed data collected from sarcoidosis patients seen at our institution over one year. The aims of the study were to characterize patients' cutaneous disease in terms of color and morphology, and to establish whether race, presence of cutaneous disease, or specific lesion characteristics had any impact on the age at which the diagnosis of sarcoidosis was made.

Methods

An institutional review board-approved, cross sectional, retrospective chart review was conducted at the Johns Hopkins Medical Institutions (JHMI). We reviewed the electronic medical records of patients with the International Classification of Diseases, Ninth Revision (ICD-9) diagnostic code for sarcoidosis, who were seen between January 1 and December 31, 2010 in the Johns Hopkins Sarcoidosis Clinic and the Dermatology Clinics. These charts were individually reviewed to confirm the diagnosis of sarcoidosis. Patients were considered as having sarcoidosis if they had a pathology report showing noncaseating granulomas. However, for the patients who came to JHMI already carrying a biopsy-proven diagnosis of sarcoidosis, repeat biopsies were seldom performed. For these patients, the pathology slides from prior biopsies were reviewed by the consulted physician and documented in the initial consult note. The charts were reviewed for sex, race, and age at diagnosis.

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Age at diagnosis was determined by either the age at which the first diagnosis was made at our institution or by patient report if they were diagnosed prior to being seen at our institution. If there were cutaneous manifestations, the lesions were further characterized by color (hyperpigmented, hypopigmented, or skin colored) and morphology (macular, papular, or nodular). The cutaneous lesions were further categorized as lupus pernio if the patient had biopsy proven sarcoidosis, and the lesion was clinically qualified as lupus pernio.

Statistics

Statistical analyses were completed using SPSS 19.0 (SPSS Inc, 2001). Consistent with the aims of the study, analyses progressed in three steps. First, characteristics of patients with cutaneous disease were examined using descriptive statistics and chi-square comparisons for color and morphology by race and sex. Next, linear regression models examined age at diagnosis of sarcoidosis with the full sample. For these models, race (white/black), cutaneous involvement (yes/no), color, and morphology were the main predictors with a continuous outcome variable for age at diagnosis. Multivariate models accounted for cutaneous disease, sex, color, morphology, and race (where appropriate). Significance levels for all analyses were set at $p<0.05$.

Results

In total, 491 patients were found to have sarcoidosis diagnosed by tissue biopsy or by historical data from their referring provider. Most of the patients were evaluated in the Johns Hopkins Sarcoidosis Clinic.

Characteristics of patients with cutaneous lesions

One hundred and twenty-two (25.3%) patients had cutaneous involvement. Three of those patients also carried a diagnosis of hepatitis raising the concern for interferon induced sarcoid-like disease. However, two of the three patients never required interferon treatment. The third patient did receive interferon treatment, but not until 2 years after the diagnosis of sarcoidosis was made. Of the patients with cutaneous sarcoidosis, 26 (21.5%) were men, 96 (78.7%) were women, 96 (78.7%) were black, 21 (17.2%) were white, 2 (1.6%) were Hispanic and 3 (2.5%) were of unknown race (Table 1). Because the latter groups had such small sample sizes, data from the black patients and white patients only were analyzed. Based upon these data, black patients are more likely to have cutaneous involvement than white patients (p<0.001) (Table 1).

Nine patients (7.4%) with cutaneous sarcoidosis had hypopigmented lesions, 73 (59%) had hyperpigmented lesions, and 28 (23%) had skin colored lesions. In terms of morphology,

Table 1: Demographics of patients with cutaneous lesions.

	Men n (%)	Women n (%)	Overall n (%)
White n (%)	7 (5.7)	14 (11.5)	21 (17.2)
Black n (%)	19 (15.6)	77 (63.1)	96 (78.7)
Hispanic n (%)	0 (0)	2 (1.6)	2 (1.6)
Unknown n (%)	0 (0)	3 (2.5)	3 (2.5)
Overall n (%)	26 (21.5)	96 (78.7)	122

Table 2: Color and morphology of lesions (cutaneous patients only).

	Overall n (%)	Men n (%)	Women n (%)	Overall n (%)	White n (%)	Black n (%)
Color of lesions						
Hypopigmented	9 (7.4)	1 (4.5)	8 (9.6)	9 (8.6)	0 (0)	9 (10.1)
Hyperpigmented	73 (59)	11 (50)	58 (69.9)	69 (65.7)	11 (68.8)	58 (65.2)
Skin-colored	28 (23)	10 (45.5)	17 (20.5)	27 (25.7)	5 (31.3)	22 (24.7)
Morphology of lesions						
Nonpalpable	11 (9)	3 (13.6)	8 (9.1)	10 (9.5)	1 (6.3)	9 (10.1)
Palpable	70 (57.4)	15 (68.2)	55 (62.5)	66 (62.9)	7 (43.8)	59 (66.3)
Subcutaneous	29 (23.8)	4 (18.2)	25 (28.4)	29 (27.6)	8 (50)	21 (23.6)

11 patients (9%) had nonpalpable lesions (macules or patches), 70 (57.4%) had palpable lesions (papules or plaques), and 29 (23.8%) had subcutaneous lesions (nodules). For 12 of the patients (10%), the lesions were not described (Table 2).

No significant relationship was found between race and the color of cutaneous lesions (i.e. hypopigmented, hyperpigmented, or skin-colored) ($p=0.39$). Additionally, no significant relationship was found between race and the morphology of cutaneous lesions. The data suggest that there is a significant relationship between sex and cutaneous lesion color. Women were more likely to have hyperpigmented lesions (69.9%) while men were more evenly split between hyperpigmented (50%) and skin colored lesions (45.5%) (p<0.05) (Table 2).

In the patients with cutaneous sarcoidosis, 29 (23.8%) were diagnosed specifically with lupus pernio. Three (10.3%) of those patients were black men and 25 (86.2%) were black women (one woman's race was unknown).

Age at diagnosis

For the total cohort, the average age at diagnosis of sarcoidosis in patients without cutaneous disease was 43.1 (SD=12.2) years. However, in patients with cutaneous disease, the average age at diagnosis was 39.6 (SD=10.4) years (β=-0.13, $p<0.01$). There was also a significant effect of race on the age at diagnosis. In our cohort, the mean age at which black patients were first diagnosed with sarcoidosis was 40.5 (SD=11.8) years, compared to 46.1 (SD=11.4) years in white patients (β=-0.22, $p<0.001$).

Age at diagnosis by lesion color and morphology for patients with cutaneous sarcoidosis

Patients who developed skin-colored lesions were diagnosed on average at the age of 43.89 (SD=9.0) years, those with hyperpigmented lesions at 38.46 (SD=10.4) years, and those with hypopigmented lesions at 36.11 (SD=10.8) years. There was a statistically significant difference for age at diagnosis between patients who developed skin-colored lesions and patients with hyperpigmented lesions (β=0.25, $p<0.05$). There was no such statistical relationship found for age at diagnosis based on the patients' lesion morphology ($p=0.80$).

Multivariate models

To examine the potential associations of race, cutaneous involvement, color and morphology on age at diagnosis in a fully adjusted model, multivariate regression analyses were examined. For the total cohort, race and cutaneous involvement effects with

Table 3: Associations with Age at Diagnosis for Sarcoidosis Patients.

	Unadjusted			Adjusted		
Full Sample	**β**	**B**	**95%CI**	**β**	**B**	**95%CI**
Race	-0.22***	-5.70	-8.03 -3.38	-0.13	-3.90	-9.74 1.95
Cutaneous	-0.13**	-3.42	-5.87 -0.97	0.02	0.79	-9.94 11.52
Cutaneous Sample						
Color	0.25*	4.47	1.02 7.91	0.25*	4.69	0.89 8.48
Morphology	0.03	0.44	-2.95 3.82	-0.08	-1.33	-4.96 2.30

***p<0.001, **p<0.01, *p<0.05

Adjusted models included covariates of sex, race, cutaneous involvement, color, and morphology where appropriate.

age at diagnosis are no longer present after accounting for sex, color, and morphology (Table 3). However, for the cutaneous sarcoidosis sample, the significant difference in age at diagnosis for patients who developed skin-colored lesions versus those patients with hyperpigmented lesions remains (β=0.25, $p<0.05$) even after accounting for sex, race, and morphology.

Discussion

Though not extensively studied, it has been suggested that blacks are more likely to develop cutaneous sarcoidosis [19]. In our study, almost 80% of the patients with cutaneous sarcoidosis were black. When compared to whites, blacks were more likely to have skin manifestations with their sarcoidosis. In this study, skin colored lesions were diagnosed on average 5.43 years later than hyperpigmented lesions, and the difference in age at diagnosis remained significant even after adjusting for sex, race, and morphology in a multivariate model. This data suggests that perhaps patients and physicians may notice hyperpigmented lesions earlier than skin-colored lesions. We also examined the effect of cutaneous involvement on age at diagnosis. Judson et al. found that patients with sarcoidosis were typically diagnosed within 6 months of their symptom onset, thus the age at diagnosis is a reasonable estimate for age of disease onset [20]. When using a univariate model, patients with cutaneous sarcoidosis were diagnosed, on average, 3.5 years earlier than patients who never developed cutaneous lesions. Additionally, our data showed a statistically significant association between race and age at diagnosis for systemic sarcoidosis with blacks being diagnosed 5.6 years earlier than whites when using a univariate model. However, after accounting for sex, color of the lesions, and morphology of the lesions, the statistical significance disappears. This loss of significance may demonstrate that sex or lesion characteristics alone actually account for the difference in age at diagnosis. However, if sex and lesion characteristics are independent of race or cutaneous involvement, i.e., blacks are no more likely to have certain lesion characteristics, then it would be inappropriate to adjust for lesion characteristics when investigating the effect of race on age at diagnosis. As many of these relationships are still unknown, more studies may be required to elucidate the true effect of race and cutaneous involvement on age at diagnosis. The most severe manifestation of cutaneous sarcoidosis that was consistently recorded was lupus pernio. Lupus pernio has been shown to be associated with a worse prognosis both in terms of more severe systemic disease and more chronic cutaneous lesions [21,22]. In our study, there were 29 patients with a diagnosis of lupus pernio and 25 of those patients were black women. The limitations of this study were primarily due to using retrospective data and the lack of long-term follow up data for these patients. Additionally, there is a geographic bias since this data is based on patients in the Northeastern region of the United States and therefore our conclusions may not be generalizable to other areas of the US or to other countries. While the pathophysiology is unclear, both prior research and our findings suggest that not only does sarcoidosis affect blacks more often than whites, blacks are also more likely to develop cutaneous disease. Thus, on routine skin examinations, persistent hyperpigmented and hypopigmented lesions should prompt consideration of sarcoidosis in the differential diagnosis especially in African-American patients.

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