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The clinical course of sarcoidosis: presentation, diagnosis, and treatment in a large white and black cohort in the United States

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Abstract. *Background:* Although numerous reports have described the clinical features of sarcoidosis in various ethnic and racial groups, many have been limited by small size, homogenous populations, and relatively short follow-up periods. We report the clinical characteristics of a large, race-sex-age diverse cohort of sarcoidosis clinic patients followed in a large university medical center for an extended period of time. *Methods:* This study included clinical data for sarcoidosis patients followed over a 12-year period at a sarcoidosis clinic at the Medical University of South Carolina. *Results:* 1774 sarcoidosis patients were identified. Black females were more common (44%) than other race/gender combinations ($p = 0.01$). The diagnosis of sarcoidosis occurred > 3 months after the onset of symptoms in 48% of the cohort and > 1 year after the onset of symptoms in 25%. Anti-sarcoidosis treatment was required in 61% of the patients. Pulmonary function improved over time and the median corticosteroid requirement lessened. Compared to whites, blacks had more advanced radiographic stages of sarcoidosis ($p < 0.0001$), more organ involvement ($p < 0.0001$), and more frequently required anti-sarcoidosis medication ($p < 0.0001$). Compared to women, men had more advanced radiographic stages of sarcoidosis ($p < 0.0001$). *Conclusions:* The analysis indicates that sarcoidosis tends to improve over time in terms of pulmonary function and medication requirements. The disease was found to be more severe in blacks than whites. Treatment was not necessarily required. These results provide a comprehensive model of the course and treatment of sarcoidosis in the clinical setting. *(Sarcoidosis Vasc Diffuse Lung Dis 2012; 29: 119-127)*

Key words: sarcoidosis, phenotype, treatment, corticosteroids, diagnosis

Introduction

Sarcoidosis is a multisystem granulomatous disease of unknown cause. It occurs worldwide although the phenotypic expression of the disease appears to vary in different populations. Numerous reports have been published describing the clinical features of sarcoidosis in specific ethnic or racial groups (1-4). Many of the reports are limited by the short follow-up period. These limitations reduce the level of external validity for consideration in other clinical settings.

In this paper, we report the clinical characteristics of sarcoidosis patients cared for at a US university medical center. The clinic population was large, age-race-sex diverse, and the cohort was followed for an extended period of time. Such a comprehensive report should provide clinical insights into the phenotypic expression of sarcoidosis in the United

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States and has implications concerning the diagnosis, treatment, and prognosis of the disease.

Methods

This study was a retrospective analysis of patients cared for at the Medical University of South Carolina (MUSC) Sarcoidosis Clinic from January 1, 1999 through December 31, 2010. Patients were identified from a MUSC approved clinical database that captured clinical information from patients cared for in this clinic. Patients were analyzed if they met standard criteria for the diagnosis of sarcoidosis (5, 6). This routinely included questioning concerning potential alternate causes of granulomatous inflammation including a history of tuberculosis, family history of tuberculosis, history of tuberculin skin test results, occupational history of beryllium exposure, and history of exposure to agents associated with hypersensitivity pneumonitis.

The data concerning these patients was entered into the database in real time by one of the study investigators (MAJ). The data collected included a) dosing information concerning sarcoidosis medications; b) laboratory data that included the results of pulmonary function tests; c) determination of sarcoidosis organ involvement using *either* the sarcoidosis three-dimensional assessment instrument (SATI) (7) which is a variation of a standard instrument (ACCESS assessment instrument) (8) that incorporates newer diagnostic tests for sarcoidosis (e.g. magnetic resonance and positron emission tomography) *or*, the investigators' judgment in situations when the investigator believed that an organ was involved but the SATI did not incorporate recent technology into sarcoidosis organ assessment; d) findings from the last chest radiograph that was available for review; e) demographic information, date of sarcoidosis symptom onset; and f) the date and site of a confirmatory biopsy if one was performed as determined by one investigator (MAJ). The organs that were specifically being treated for sarcoidosis involvement were also described in the database. Resolution of organ involvement was also documented. For the purposes of this analysis, an organ was defined as being involved with sarcoidosis if it met the criteria for "definite" or "probable" involvement according to ACCESS organ assessment instrument and the SATI (7, 8). Radiographs were interpreted in terms of five "Scadding stages" (Stage 0 to IV) as defined in the Amercian thoracic Society/European Respiratory Society/World Association of Sarcoidosis and other Granulomoatous Disorders consensus statement (6).

This investigator made all treatment decision concerning patients at each clinic visit. Treatment was not standardized in terms of a protocol. However, the general approach to treatment included that a) asymptomatic patients were rarely treated (9); b) corticosteroids were the initial drug of choice (9, 10); c) pulmonary sarcoidosis was usually treated with 20 mg of daily prednisone equivalent (11) and tapered to ≤10 mg/day within 3 months; d) methotrexate was often used as a second line agent when a corticosteroid sparing drug was required (10, 12).

Measurements of the percent of predicted forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) were race, age, and gender adjusted according to the criteria of Hankinson and colleagues (13).

Statistical analysis

The data were analyzed using descriptive statistics with stratification by age, race and sex. Categorical variables were compared using Mantel-Haenszel Chi-square's test; and continuous variables were compared using two-tailed t-test and Wilcoxon Rank Sum non-parametric statistics. Odds ratios and 95% confidence intervals were determined using multivariate logistic regression for patients with organ involvement. Cochran-Armitage trend test was used to compare chest radiographic distribution of the Scadding staging between strata. All statistical tests were performed using SAS 9.3 (Cary, NC) software at significance levels of 0.05. Patients with missing data for specific parameters were excluded only for those analyses. Thus the denominations varied for different assessments.

This study was approved by the Medical University of South Carolina (MUSC) Institutional Review Board.

Results

During the 12-year study period, data on 1774 sarcoidosis patients were identified. Table 1 shows the basic demographics of the cohort. Approximate-

Table 1. Baseline characteristics of study cohort

Characteristics	Male	Female	Total
Cohort, n (%)			
White	177 (13.6)	273 (21.0)	450 (34.6)
Black	269 (20.7)	578 (44.5)	847 (65.2)
Other	2 (0.2)	1 (0.1)	3 (0.2)
Total	448 (34.5)	852 (65.5)	1300
Age at onset, μ (sd)			
White	43.1 (12.8)	46.3 (13.0)	45.0 (13.0)
Black	35.2 (10.6)	37.1 (11.1)	36.5 (11.0)
Other	34.5 (6.4)	54.0	41.0 (12.1)
Total	38.4 (12.1)	40.2 (12.6)	39.6 (12.4)
Age at biopsy, μ (sd)			
White	44.4 (12.6)	47.4 (12.7)	46.2 (12.7)
Black	36.5 (10.5)	38.5 (11.0)	37.9 (10.9)
Other	34.5 (6.4)	55.0	41.3 (12.7)
Total	39.6 (12.0)	41.6 (12.3)	40.9 (12.2)

ly two-thirds were black and two-thirds were female. Three of the 1300 patients with racial information were not black or white. The subjects were followed for a mean of 42.2 months (±39.3, median = 28). There were significantly more black females (44%) compared to other race/gender combinations ($p = 0.01$). Males developed their first symptom related to sarcoidosis ($p < 0.03$) and had a diagnostic biopsy ($p < 0.02$) approximately two years earlier than females (Table 1). Blacks developed their first symptom related to sarcoidosis ($p < 0.0001$) and had a diagnostic biopsy ($p < 0.0001$) approximately ten years earlier than whites (Table 1).

Biopsy findings

Of the 1298 patients where biopsy information was available, 1176 (91%) had biopsy proof of granulomatous inflammation in at least one organ. Of these 1298 patients, 441 (39%) had a biopsy of the lung parenchyma and 673 (60%) had a biopsy in an extrapulmonary location (this total exceeds the 1176 that had a confirmatory biopsy as some patients had confirmatory biopsies from multiple organs). Slightly less than half (48%) of the cohort had a diagnostic biopsy within 3 months of symptom onset. However, 25% of patients were not diagnosed with sarcoidosis for at least 1 year after the onset of symptoms attributed to the disease.

Chest radiograph findings

The analysis of chest radiographs of this cohort used the last chest radiograph that was available for review. The chest radiographic distribution in terms of the Scadding stage (N=947) showed a fairly even distribution of all the stages except of an excess of patients with stage 0 (normal) chest radiographs: Stage 0: 313/947, 33%; Stage I: 186/947, 20%, Stage II: 183/947, 19%; Stage III: 102/947 (11%), Stage IV: 163/947, 17%. Blacks demonstrated more advanced Scadding radiographic stages than whites ($p < 0.0001$, $N = 947$) and males demonstrated more advanced radiographic stages than females ($p < 0.0001$, $N = 947$) (Figure 1). Thirty-six of 1332 (2.7%) patients who had chest radiographs had evidence of a mycetoma.

Pulmonary function

Table 2 shows the mean percent predicted FVC and FEV_1 of the cohort analyzed in terms of the

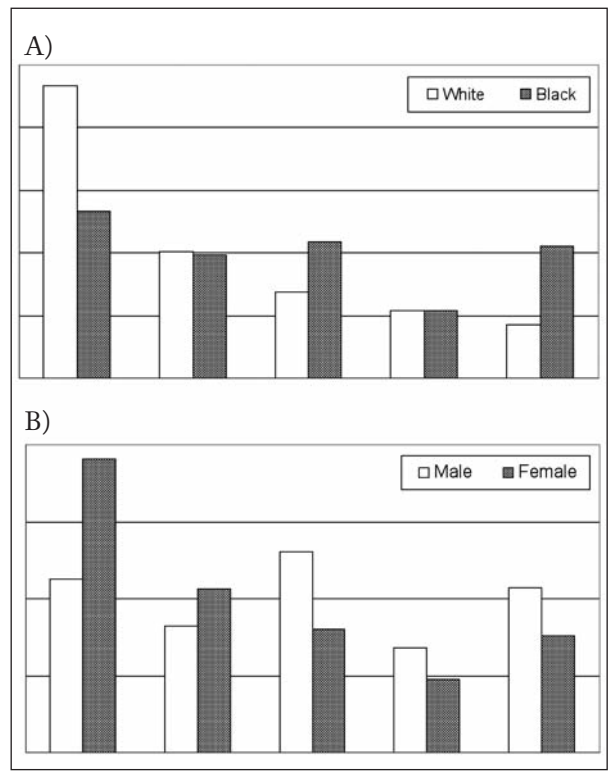

Fig. 1. (A) Proportion of patients per chest x-ray Scadding stage by race. The ratio of black to white patients increases at higher chest x-ray stages and decreases at lower x-ray stages: Cochran-Armitage trend test p-value = <.0001. (B) Proportion of patients per chest x-ray Scadding stage by gender. The ratio of male to female patients increases at higher chest x-ray stages and decreases at lower x-ray stages: Cochran-Armitage trend test p-value <.0001

Table 2. Mean percent predicted FEV_1 and FVC by number of years of follow-up

	Time followed (years)										
	< 1	1	2	3	4	5	6	7	8	9	10+
Cumulative n	718	603	450	349	282	229	189	164	127	97	62
Percent Predicted FEV_1	84.1	85.9	87.1	88.5	89.7	91.1	91.8	91.6	92.8	95.2	93.5
Percent Predicted FVC	88.6	89.9	90.9	92.7	93.2	94.2	95.2	95.3	95.6	97.3	96.5

number of years of follow up. The percent predicted FVC increased from 89% to 97% over 10 years of follow up. The improvement in FVC was relatively continuous over the entire period of follow up. The improvement in FVC was not significantly different in subgroups when examined by race, gender, the use versus non-use of anti-sarcoidosis medication, or the presence versus absence of pulmonary involvement (data not shown). Changes in FEV_1 percent predicted showed a similar continuous improvement (Table 2) with no appreciable differences in the aforementioned subgroups (data not shown).

Organ involvement

Figure 2 shows the organs that were involved with sarcoidosis in this cohort (N=1582). The lung was the most common organ involved (89%, 1403/1582) followed by the skin (26%, 522/1582), eye (23%, 363/1582), and liver (20%, 323/1582). There were major differences between the frequency of sarcoidosis organ involvement and the requirement for treatment of specific organ involvement (Figure 3). Although involvement of the heart with sarcoidosis was relatively rare (5%, 74/1582), it was the organ that was most often treated (62%, 46/74). Other organs that were treated in more than half of the patients included muscle (58%, 11/18), neurologic (56%, 78/139), and lung (51%, 712/1403). Specific organ involvement was more common in blacks than in whites (Table 3). Organ involvement of the lungs, neurologic, skin, eye, and liver was significantly higher in blacks whereas splenic involvement and hypercalcemia was more likely in whites. Certain combinations of organs were more frequently involved in specific races. In terms of examining racial differences concerning the need for treatment, the lung was the only organ in which treatment was required more frequently in blacks than whites (Table 3).

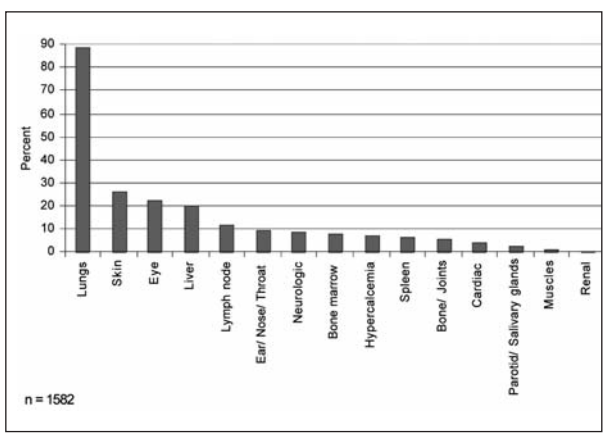

Fig. 2. Percent of patients with organ involvement

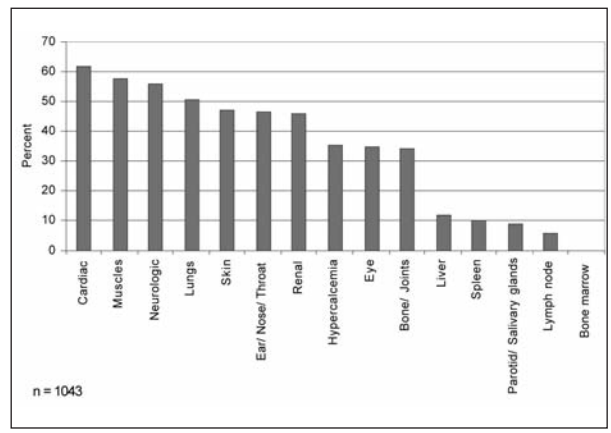

Fig. 3. Percent of patient treatment of specific organ involvement

Blacks tended to had more organs involved than whites (Table 4). The number of organs involved per patient increased over time from 2.19 organs/patient at the first clinic visit to 2.99 organs/patient in those followed for more than 6 years (Table 5A). Although blacks had more new organs involved during follow-up than whites (blacks: mean = 0.31 ± 0.86 versus whites: mean 0.19 ± 0.77), this did not reach statistical significance (Table 5B).

Table 3. Organ involvement by race (n=1248)

	White (n=429)		Black (n=819)		Organ involvement** OR (95%CI)
Organs, n (%)	Involved	Treated*	Involved	Treated*	
Lungs	363 (84.6)	129 (35.5)	749 (91.5)	442 (59.0)	2.05 (1.43, 2.94)†
Neurologic	28 (6.5)	15 (53.6)	85 (10.4)	48 (56.5)	1.67 (1.07, 2.61)‡
Lymph nodes	52 (12.1)	1 (1.9)	102 (12.5)	7 (6.9)	1.00 (0.70, 1.43)
Renal	3 (0.7)	2 (66.7)	8 (1.0)	3 (37.5)	1.46 (0.38, 5.53)
Cardiac	17 (4.0)	11 (64.7)	39 (4.8)	22 (56.4)	1.29 (0.72, 2.31)
Skin	97 (22.6)	41 (42.3)	305 (37.2)	150 (49.2)	1.97 (1.51, 2.58)†
Eye	62 (14.5)	25 (40.3)	225 (27.5)	74 (32.9)	2.19 (1.61, 2.99)†
Liver	68 (15.9)	7 (10.3)	182 (22.2)	23 (12.6)	1.48 (1.09, 2.01)‡
Bone marrow	29 (6.8)	0	66 (8.1)	0	1.22 (0.78, 1.92)
Spleen	41 (9.6)	5 (12.2)	52 (6.4)	5 (9.6)	0.63 (0.41, 0.97)‡
Bone/ Joint	30 (7.0)	9 (30.0)	53 (6.5)	17 (32.1)	0.91 (0.57, 1.44)
Ear, Nose, Throat	33 (7.7)	16 (48.5)	87 (10.6)	40 (46.0)	1.39 (0.91, 2.11)
Parotid/Salivary glands	13 (3.0)	1 (7.7)	21 (2.6)	3 (14.3)	0.85 (0.42, 1.72)
Muscle	5 (1.2)	3 (60.0)	7 (0.9)	5 (71.4)	0.75 (0.24, 2.38)
Hypercalcemia	42 (9.8)	16 (38.1)	47 (5.7)	17 (36.2)	0.58 (0.37, 0.89)‡
Multiple Organs					
Spleen and Liver	27 (6.3)	0	29 (3.5)	3 (10.3)	0.53 (0.31, 0.91)‡
Eye and Neurologic	3 (0.7)	0	29 (3.5)	4 (13.8)	5.31 (1.60, 17.5)‡
Ear, Nose, Throat and Skin	11 (2.6)	7 (63.6)	55 (6.7)	21 (38.2)	2.65 (1.37, 5.12)‡

* The n (%) reported in the Treated columns represents the proportion of treated patients among those with each specific organ involved.
** Adjusted odds ratios (95% confidence intervals) for organ involvement in black patients (white = reference group) adjusted for gender. Lung treatment was significant for black patients (OR 2.68 (2.06, 3.48; p <.0001)).
† p <.001
‡ p <.05

Table 4. Average organs involved for population

	n	Mean (sd)
Total	1582*	2.33 (1.30)
White	429	2.06 (1.19)
Black	819	2.48 (1.36)**

* Total n was higher than the sum of the white and black patients (1248) because organ data was available on 334 patients who did not have racial data.
** Blacks have significantly higher number of organs involved as compared to whites, difference of 0.42: T-test p-value <.0001.

In terms of organ involvement by gender, males had more sarcoidosis involvement of the lungs and heart than females whereas females had more sarcoidosis involvement of peripheral lymph nodes, skin, eye, and liver (Table 6). In terms of examining racial differences concerning the need for treatment, lung and neurologic involvement required treatment more frequently in males and skin involvement required treatment more frequently in females (Table 6).

Medications

Sixty-one percent (1083/1774) received some anti-sarcoidosis medication at some time during the

Table 5A. Average number of organs involved per years followed (n = 846)

Years followed	n	Mean (sd)*
0	143	2.19 (0.99)
1	182	2.40 (1.24)
2	124	2.62 (1.52)
3	81	2.48 (1.35)
4	67	2.84 (1.52)
5	57	2.88 (1.35)
6+	192	2.99 (1.47)

* There is a significant increase in the number of organs involved by the amount of time followed. For every 1 year increase in time followed there was a 0.13 increase in the number of organs involved (Trend analysis: std error 0.02; p <.0001). However, this relationship is extremely weak, Adjusted R^2 = 0.04. Wilcoxon estimate <.0001.

Table 5B. Average number of new organs after initial visit

Cohort	n	Mean (sd)
Total	862	0.27 (0.84)
White	196	0.19 (0.77)
Black	552	0.31 (0.86)*

* The number of new organs involved since the first visit is not statistically different between blacks and whites (difference of 0.12): T-test p-value = 0.11.

Table 6. Organ involvement by gender (n=1256)

Organs, n (%)	Female (n=826)		Male (n=430)		Organ involvement** OR (95%CI)
	Involved	Treated*	Involved	Treated*	
Lungs	720 (87.2)	358 (49.7)	398 (92.6)	215 (54.0)	1.99 (1.31, 3.04)
Neurologic	73 (8.8)	34 (46.6)	40 (9.3)	29 (72.5)	1.10 (0.73, 1.65)
Lymph nodes	115 (13.9)	7 (6.1)	40 (9.3)	1 (2.5)	0.62 (0.42, 0.91)‡
Renal	6 (0.7)	3 (50.0)	5 (1.2)	2 (40.0)	1.65 (0.50, 5.46)
Cardiac	27 (3.3)	15 (55.6)	29 (6.7)	18 (62.1)	2.18 (1.27, 3.74)‡
Skin	300 (36.3)	152 (50.7)	104 (24.2)	39 (37.5)	0.59 (0.45, 0.76)†
Eye	210 (25.4)	71 (33.8)	77 (17.9)	28 (36.4)	0.67 (0.50, 0.90)‡
Liver	183 (22.2)	25 (13.7)	69 (16.1)	5 (7.3)	0.68 (0.50, 0.93)‡
Bone marrow	60 (7.3)	0	35 (8.1)	0	1.15 (0.74, 1.78)
Spleen	66 (8.0)	8 (12.1)	27 (6.3)	2 (7.4)	0.75 (0.47, 1.19)
Bone/ Joint	58 (7.0)	16 (27.6)	25 (5.8)	10 (40.0)	0.81 (0.50, 1.32)
Ear, Nose, Throat	90 (10.9)	44 (48.9)	31 (7.2)	13 (41.9)	0.66 (0.43, 1.01)
Parotid/Salivary glands	21 (2.5)	3 (14.3)	13 (3.0)	1 (7.7)	1.18 (0.56, 2.39)
Muscle	7 (0.9)	5 (71.4)	5 (1.2)	3 (60.0)	1.35 (0.42, 4.29)
Hypercalcemia	51 (6.2)	15 (29.4)	40 (9.3)	19 (47.5)	1.49 (0.96, 2.31)
Multiple Organs					
Spleen and Liver	41 (5.0)	3 (7.3)	15 (3.5)	0	0.66 (0.36, 1.21)
Eye and Neurologic	20 (2.4)	2 (10.0)	12 (2.8)	2 (16.7)	1.26 (0.61, 2.62)
Ear, Nose, Throat and Skin	52 (6.3)	23 (44.2)	15 (3.5)	5 (33.3)	0.58 (0.32, 1.05)

* The n (%) reported in the Treated columns represents the proportion of treated patients among those with each specific organ involved.
** Adjusted odds ratios (95% confidence intervals) for organ involvement in male patients (female = reference group) adjusted for race. Lung treatment (1.31 (1.01, 1.69), p <0.05) and Neurologic treatment (OR 3.03 (1.32, 6.97), p <0.05) were significant for males; Skin treatment (OR 0.58 (0.37, 0.92); p < 0.05) was significant for females.
† p <.001
‡ p <.05

study period, with 55.3% (981/1774) receiving corticosteroids. Five percent (91/1774) of the cohort received at least one dose of a monoclonal antibody directed against tumor necrosis factor alpha. More black patients received anti-sarcoidosis medications at some time than whites 631/847, 74.5% versus 248/450, 55.1%; p < 0.0001) and, specifically, more blacks also received corticosteroids at some time than whites 592/847, 69.9% versus 207/450, 46%; p < 0.0001). Males received more corticosteroid treatment at some time than females (293/449, 65.3% versus 510/857, 59.5%, p < 0.01) and females received more anti-malarial treatment at some time than males (123/857, 14.4% versus 37/449, 8.2%, p < 0.05). Twelve percent (213/1774) of the cohort received methotrexate at some time, and there were no differences in terms of race or gender in terms of the use of methotrexate. All the statistical analyses concerning medications reported above were adjusted for race, gender, and all organ involvement. The median prednisone daily dose progressively decreased from 10 mg in patients followed for less than 1 year to 5 mg in those followed for 6 years. Those followed for more than 6 years required daily prednisone doses ranging from 5 to 10 mg.

Potential follow-up biases

We examined potential biases in terms of the characteristics of the cohort in terms of the length of follow-up. We did find some biases in that a higher proportion of females than males were followed for 2 years and for 5 years (65.8% of females were followed ≥ 2 years compared to 53.1% of males p = 0.0008 Chi-square; 36.0% of females were followed > 5 years, 21.0% of males followed > 5 years, p < 0.0001 Chi-square). In addition, a higher proportion of blacks than whites were followed for 2 and 5 years (65.5% of blacks followed > 2 years compared to 50.3% of whites, p = 0.0002 Chi-square; 36.1% of blacks were followed > 5 years compared to 17.4% of whites followed > 5 years, p < 0.0001 Chi-square). We also found that patients who were followed ≤ 28 months (the median time of follow-up for the cohort) were statisitically less likely to be receiving anti-sarcoidosis medications than those fol-

lowed for > 28 months (77% versus 90%, p < 0.0001, Chi Square). This suggests that those followed for more than the median follow-up time may have had more severe disease than those followed for a shorter period of time.

Discussion

We have described clinical characteristics of a large cohort of sarcoidosis patients followed in a major US university medical center. These data provide insight into the phenotypic expression, approach to treatment, and outcome of sarcoidosis patients. As this data base included a large number of both black and white patients, the results may be generalizable to other populations. In addition, the database provides insight into racial differences concerning this disease. The diagnosis of sarcoidosis was relatively secure in this cohort as more than 90% of the patients had biopsy confirmed granulomatous disease and the patients were routinely questioned concerning a history for alternative causes of granulomatous inflammation. We believe that these data may serve clinicians and patients in terms of understanding than manifestations of sarcoidosis and course of the disease while undergoing standard treatment.

The lung was clearly the most common organ involved with sarcoidosis followed by the skin, eye, and liver. These results are similar to those reported in the NIH-sponsored A Case Controlled Etiology of Sarcoidosis Study (ACCESS) which included 736 patients (14) In ACCESS, only a small cohort of these patients (215 patients) were followed for a 2-year period (3). Therefore, ACCESS data is limited compared to our analysis with regards to assessing the clinical course of sarcoidosis in terms of length of follow-up and numbers of patients.

Nearly 40 percent of our cohort did not receive anti-sarcoidosis treatment. Blacks were treated more often with anti-sarcoidosis therapies than whites. This finding is consistent with previous reports (15, 16) The average corticosteroid dose was relatively low (<15 mg/day of prednisone equivalent) and was able to be almost halved over the first five years of follow up. These data suggest that sarcoidosis does not require high doses of prednisone and that the doses can typically be successfully lowered over time. These results confirm previous studies using this approach (15, 17). We acknowledge that it is possible that corticosteroids dose was lowered because of the addition of corticosteroid sparing medications and not an improvement in the disease. Although cardiac sarcoidosis and neurosarcoidosis were found in only 5 and 9 percent of our patients respectively, these two organs were treated in the highest percentage of cases when they were involved. This reflects the concern for potential life threatening complications of sarcoidosis involvement in these organs (18-21). Conversely, although the liver and peripheral lymph nodes were organs commonly involved with sarcoidosis, they required treatment in less than 12 percent of cases.

Although the four most common extrapulmonary organs involved with sarcoidosis were identical in our cohort and the ACCESS patients, the percentages were significantly different (skin – MUSC 26%, ACCESS 16%; eye - MUSC 23%, ACCESS 12%; liver – MUSC 20%, ACCESS 12%; peripheral lymph node – MUSC: 12%, ACCESS 15%. The greater frequency of involvement of extrapulmonary organ involvement might be attributable to differences in the patient populations but also to the fact that our cohort was followed for a longer period of time. The average number of organs involved with sarcoidosis was two and one-third. In patients followed for more than 6 years, the average number of organs involved with sarcoidosis increased by 0.8. ACCESS found that patients developed an average of 0.3 new organs/patient (67 organs/215 patients) over a 2-year period of follow-up[3]. Similarly to our data, ACCESS determined that the development of new organ involvement was more likely in blacks (45/98 = 0.48 new organs/patient over 2 years) than in whites (20/117 = 0.17 new organs/patient over 2 years).

Slightly more than half of the cohort had a diagnostic biopsy within 3 months of symptom onset. However, more than 20% of patients were not diagnosed with sarcoidosis for at least 1 year after the onset of symptoms attributed to the disease. These results are very similar to those previously reported in ACCESS, although our analysis of this issue included 1140 patients whereas ACCESS analyzed 189 (22).

Spirometric values improved in our cohort over the follow up period. This improvement was similar in those patients who were treated with anti-sar-

coidosis medication at some time compared to those who never received treatment. Also, the presence or absence of sarcoid pulmonary involvement did not affect these results. These data suggest that general prognosis of pulmonary sarcoidosis is one of slow improvement. Furthermore, these data support the contention that treatment may not affect the natural course of the disease (23).

We also performed several novel analyses in this sarcoidosis cohort. Although there have been detailed analyses of chest radiographic findings in sarcoidosis including comparing a Scandinavians to a Japanese population (1, 24), to our knowledge, there has been no previous examination of chest radiographic findings in blacks compared to whites. The frequency of mycetoma in sarcoidosis has not been previously reported. The need for anti-sarcoidosis therapy has been described over two years of observation (15) but never over an extended period of time. In addition, several other analyses involving sarcoidosis organ involvement and pulmonary function have not involved a large number of patients followed continuously over many years.

This study has several limitations. First, numerous patients had missing data. Although data were collected in real time during each patient clinic visit, not all tests were obtained on all patients at every visit. Thus our analyses may be subject to potential bias in the results, as the pre-test probability of an abnormal result may be higher in those patients who had a test ordered compared to a patient who did not. We did also identify some biases in terms of race and gender in terms of follow-up. We acknowledge that this might skew the long term follow-up of the cohort in terms of spirometric change. Second, although most of these data were objective, the treatment data was based upon the subjective approach of one clinician (MAJ). Therefore, the decision to use anti-sarcoidosis medication and the dose used was determined by one individual and may not represent ideal nor typical sarcoidosis care. Third, although the number of subjects in this cohort was large, the number followed for more than 6 years was less than 200 so that the analyses concerning more than 6 years of follow-up are circumspect. Fourth, although we collected pulmonary function data and information on new organ involvement, we did not specifically assess the rate of relapse in this cohort. Therefore, we are unable to determine the rate of relapse over time. Fifth, we did not have the capacity to determine each patient's status (e.g., remission, active disease, death) at or after their last follow-up visit. This fact may have particularly affected the data of patients followed for long periods of time as we suspect that those with remission may have been preferentially lost to follow up. Sixth, the evaluation of organ involvement was not standardized and was often generated by the development of symptoms. This may bias the rates of organ involvement, although it could be argued that clinically insignificant organ involvement is unlikely to affect therapeutic decisions or outcome. Finally, this analysis suffers from not being a prospective, randomized trial so that it is unclear whether the results described could have been manipulated by alternative treatment approaches.

Nonetheless, we believe these data provide a framework concerning the clinical characteristics of American sarcoidosis patients as well as their outcome when monitored and treated using the clinical approach of an individual with extensive clinical experience in the field. Furthermore, we propose that these data could be viewed as a metric against which other sarcoidosis patient populations and specific treatment approaches could be measured. Likewise, the size of the cohort may reduce the effects of the potential bias.

In summary, this report describes the clinical findings of a large US cohort of sarcoidosis patients followed for many years in a university medical center. A disproportionate number of patients were female and African American. The disease was more severe in African Americans. Treatment was not required in a large portion of the cohort. The need for treatment was dependent on race as well as the specific organs involved. The diagnosis of sarcoidosis is often delayed for months to years after the development of the initial symptoms attributed to sarcoidosis. There is a small increase in the total number of organs involved with sarcoidosis over time. Pulmonary function slowly improves over time, and this improvement is not related to race, gender, pulmonary involvement with sarcoidosis, or the need for therapy. While these results cannot be generalized to all settings and populations, the descriptive results can be considered a model of the course and treatment of sarcoidosis in the clinical setting.

References

1. Pietinalho A, Ohmichi M, Lofroos AB, et al. The prognosis of pulmonary sarcoidosis in Finland and Hokkaido, Japan. A comparative five-year study of biopsy-proven cases. Sarcoidosis Vasc Diffuse Lung Dis 2000; 17: 158-66.
2. Behbehani N, Jayakrishnan B, Khadadah M, et al. Long term prognosis of sarcoidosis in Arabs and Asians: predictors of good outcome. Sarcoidosis Vasc Diffuse Lung Dis 2006; 23: 209-14.
3. Judson MA, Baughman RP, Thompson BW, et al. Two year prognosis of sarcoidosis: the ACCESS experience. Sarcoidosis Vasc Diffuse Lung Dis 2003; 20: 204-11.
4. Nagai S, Shigematsu M, Hamada K, et al. Clinical courses and prognoses of pulmonary sarcoidosis. Curr Opin Pulm Med 1999; 5: 293-8.
5. Judson MA. The diagnosis of sarcoidosis. Clin Chest Med 2008; 29: 415-427, viii.
6. Hunninghake GW, Costabel U, Ando M, et al. ATS/ERS/WASOG statement on sarcoidosis. American Thoracic Society/European Respiratory Society/World Association of Sarcoidosis and other Granulomatous Disorders. Sarcoidosis Vasc Diffuse Lung Dis 1999; 16: 149-73.
7. Judson MA. A proposed solution to the clinical assessment of sarcoidosis: the sarcoidosis three-dimensional assessment instrument (STAI). Med Hypotheses 2007; 68: 1080-7.
8. Judson MA, Baughman RP, Teirstein AS, et al. Defining organ involvement in sarcoidosis: the ACCESS proposed instrument. ACCESS Research Group. A Case Control Etiologic Study of Sarcoidosis. Sarcoidosis Vasc Diffuse Lung Dis 1999; 16: 75-86.
9. Judson MA. An approach to the treatment of pulmonary sarcoidosis with corticosteroids: the six phases of treatment. Chest 1999; 115: 1158-65.
10. Schutt AC, Bullington WM, Judson MA. Pharmacotherapy for pulmonary sarcoidosis: a Delphi consensus study. Respir Med 2010; 104: 717-23.
11. McKinzie BP, Bullington WM, Mazur JE, et al. Efficacy of short-course, low-dose corticosteroid therapy for acute pulmonary sarcoidosis exacerbations. Am J Med Sci 2010; 339: 1-4.
12. Baughman RP, Winget DB, Lower EE. Methotrexate is steroid sparing in acute sarcoidosis: results of a double blind, randomized trial. Sarcoidosis Vasc Diffuse Lung Dis 2000; 17: 60-66.
13. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. Am J Respir Crit Care Med 1999; 159: 179-87.
14. Baughman RP, Teirstein AS, Judson MA, et al. Clinical characteristics of patients in a case control study of sarcoidosis. Am J Respir Crit Care Med 2001; 164: 1885-89.
15. Baughman RP, Judson MA, Teirstein A, et al. Presenting characteristics as predictors of duration of treatment in sarcoidosis. Qjm 2006; 99: 307-15.
16. Gottlieb JE, Israel HL, Steiner RM, et al. Outcome in sarcoidosis. The relationship of relapse to corticosteroid therapy. Chest 1997; 111: 623-31.
17. Johns CJ, Michele TM. The clinical management of sarcoidosis. A 50-year experience at the Johns Hopkins Hospital. Medicine (Baltimore) 1999; 78: 65-111.
18. Judson MA. Cardiac sarcoidosis: there is no instant replay. Chest 2005; 128: 3-6.
19. Kim JS, Judson MA, Donnino R, et al. Cardiac sarcoidosis. Am Heart J 2009; 157: 9-21.
20. Yazaki Y, Isobe M, Hiroe M, et al. Prognostic determinants of long-term survival in Japanese patients with cardiac sarcoidosis treated with prednisone. Am J Cardiol 2001; 88: 1006-10.
21. Huang CT, Heurich AE, Sutton AL, et al. Mortality in sarcoidosis. A changing pattern of the causes of death. Eur J Respir Dis 1981; 62: 231-8.
22. Judson MA, Thompson BW, Rabin DL, et al. The diagnostic pathway to sarcoidosis. Chest 2003; 123: 406-12.
23. Paramothayan S, Jones PW. Corticosteroid therapy in pulmonary sarcoidosis: a systematic review. Jama 2002; 287: 1301-7.
24. Romer FK. Presentation of sarcoidosis and outcome of pulmonary changes. Dan Med Bull 1982; 29: 27-32.