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Sarcoidosis in the National Veteran Population

Association of Ocular Inflammation and Mortality

Andrea D. Birnbaum, MD, PhD,[1,2] Dustin D. French, PhD,[1,2] Mehdi Mirsaeidi, MD, MPH,[3] Sarah Wehrli, MD[1]

Purpose: To describe the distribution of ocular sarcoidosis in the veteran population and to determine the association between ocular disease and all-cause mortality.

Design: Retrospective review.

Methods: The Veterans Health Administration National Patient Care Database information on medical diagnoses, date of diagnosis, age, race, gender, and Veterans Administration medical center station number for site-specific calculations for fiscal years 2010 through 2012 was collected. Mortality data were obtained from the Beneficiary Identification Records Locator Subsystem. The patient cohort was identified with a primary diagnosis of sarcoidosis using International Classification of Disease, ninth edition, code of 135 in outpatient treatment files for the study period. The sarcoidosis patients were divided into those with uveitis or orbital inflammation (defined as ocular inflammation for this study) and those without uveitis or orbital inflammation. Survival analysis was performed using the Cox proportional hazard method.

Main Outcome Measure: Association between ocular inflammation and 1-year mortality.

Results: Of 15 130 subjects with sarcoidosis, 3364 (22.2%) were evaluated in an eye clinic within a Veterans Administration Medical Center. Most patients were diagnosed with anterior uveitis (n = 1013; 80.7% of ocular inflammation), and the least common diagnosis was orbital granuloma (n = 28; 2.2% of ocular inflammation). Male gender was protective to the development of uveitis (estimate, 0.76; 95% confidence interval, 0.65−0.88; $P = 0.0005$). The overall 1-year all-cause mortality for all patients with a diagnosis of sarcoidosis was 2.0%. Ocular inflammation was associated with a decrease in 1-year all-cause mortality (simple model: hazard ratio, 0.36; $P = 0.0015$; complex model: hazard ratio, 0.35; $P = 0.013$).

Conclusions: Veterans with ocular inflammation had significantly lower 1-year all-cause mortality than those without documented ocular inflammation. The reason for this finding remains to be established. *Ophthalmology 2015;122:934-938 © 2015 by the American Academy of Ophthalmology.*

Sarcoidosis is a multisystem inflammatory disease of unknown origin that often involves the lungs, skin, and eyes. The lungs and mediastinal lymph nodes are involved in up to 95% of patients with sarcoidosis,[1] and lung biopsy often is used to make a diagnosis even in patients with ocular disease.[1,2] Diagnosis is made in patients with a clinical presentation consistent with sarcoidosis after exclusion of other causes of granulomatous disease and histologic confirmation of noncaseating granulomas.[3] The clinical presentation of ocular disease can range from lacrimal gland involvement to severe vision-threatening uveitis. Two large prospective studies of patients with biopsy-confirmed sarcoidosis in the United States report rates of ocular involvement of 11.8% and 23%.[1,3] Some patients with ocular disease consistent with sarcoidosis are unable to undergo biopsy or do not have an appropriate site for biopsy. In these cases, a diagnosis of probable or presumed ocular sarcoidosis is made based on clinical findings, laboratory testing, and chest imaging results. These diagnostic criteria have been formalized[4] and validated[5] previously.

Mortality resulting from sarcoidosis most often is related to respiratory, cardiac, and neurologic involvement.[6] The relationship between mortality and inflammation of other organ systems is unclear. Patients with ocular disease often require higher doses of immunosuppression to achieve remission,[7] and those treated with topical corticosteroids for sarcoid uveitis may be less likely to achieve spontaneous remission.[8] This suggests a possible association between chronic disease and ocular involvement. The purpose of this study was to describe sarcoidosis in the predominantly male veteran population treated at Veterans Health Administration (VHA) medical centers across the country and to examine the association of ocular involvement with mortality.

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Table 1. List of International Classification of Disease, Ninth Edition, Codes for Ocular Inflammation Identified

Uveitis Diagnosis	International Classification of Disease, 9th Edition, Code
Panuveitis	360.12
Iritis, acute	362.00
Iritis, uveitis, acute NOS	364.00
Iridocyclitis, recurrent	364.02
Hypopyon	364.05
Uveitis, chronic NOS	364.10
Uveitis, anterior	364.30
Scleritis and episcleritis	379.00
Anterior scleritis	379.03
Scleritis with corneal involvement	379.05
Posterior scleritis	379.07
Focal choroiditis chorioretinitis juxtapapillary	363.01
Focal choroiditis chorioretinitis posterior pole	363.03
Other and unspecified forms of chorioretinitis and retinochoroiditis	363.20
Focal choroiditis chorioretinitis	363.04
Focal retinitis and retinochoroiditis juxtapapillary	363.05
Focal retinitis and retinochoroiditis macular paramacular	363.06
Focal retinitis and retinochoroiditis posterior pole	363.07
Focal retinitis and retinochoroiditis peripheral	363.08
Disseminated chorioretinitis posterior pole	363.11
Disseminated chorioretinitis unspecified	363.10
Disseminated chorioretinitis generalized	363.13
Orbital granuloma	376.00

NOS = not otherwise specified.

Methods

Study Design and Patient Data

The VHA National Patient Care Database was accessed to collect information on medical diagnoses, date of diagnosis, age, race, gender, and Veterans Administration Medical Center station number for site-specific calculations. The clinical database consolidates information from approximately 5.3 million veterans at approximately 1300 sites of care throughout the nation. More than 95% of VHA enrollees are men; approximately 83% are white and 13% are black. Patient-specific clinical information from medical records was not available for review. De-identified, longitudinal, patient-specific data were available for fiscal years 2010 through 2012 (beginning October 1, 2010, and ending September 30, 2012).

Death data were obtained from the Beneficiary Identification Records Locator Subsystem (BIRLS). The BIRLS is a Veterans Benefits Administration database that contains death records of all beneficiaries. The BIRLS file is updated weekly through either a match process with the Social Security Administration Death Master File, or notification from a hospital, cemetery, or relative. The ascertainment of death sensitivity of BIRLS ranges from 80.0% to 94.5% and compares favorably with the 83.0% to 83.6% rate for Social Security Administration files and the 87.0% to 97.9% rate for the National Death Index.[9]

Study Population

The patient cohort was identified with a primary diagnosis of sarcoidosis using International Classification of Disease, ninth edition (ICD-9), of 135 in outpatient treatment files for fiscal years 2010 through 2012. The patients were divided further into those with uveitis or orbital inflammation based on the ICD-9 codes. Using the first 3 digits of the code, similar diagnoses then were grouped together: panuveitis, 360; anterior uveitis, 362 and 364; scleritis and episcleritis, 379; choroiditis and retinitis, 363; and orbital granuloma, 376 (Table 1).

Statistical Analysis

Survival analysis was performed using the Cox proportional hazard method. The dependent variable was death (death = 1; survival = 0) within 1 year or 365 days from the first date of a sarcoidosis diagnosis. Two models were used. The first model, designated the simple model, included age, black race, gender, and uveitis. A second model, designated the complex model, used all the same criteria as the simple model with adjustment for Elixhauser comorbidities. The Elixhauser methodology is a well-established health services research method that uses diagnosis codes to identify common comorbidities related to increased length of stay, hospital charges, and death.[10] The Elixhauser comorbidities were applied to the VHA National Patient Care Data for our cohort as a means of measuring patient comorbidities. All analyses were conducted with Statistical Analysis Software version 9.3 (SAS Inc, Cary, NC). The protocol was approved by the Institutional Review Board and the Veterans Administration Research and Development Committee for Compliance with Human Protection (protocol no. 13-048).

Results

In a VHA population of 5.3 million (based on patients using services in 2010), a total of 15 130 patients were assigned the diagnostic code for sarcoidosis (ICD-9 code 135) between October 1, 2009, and September 30, 2012 (fiscal years 2010 through 2012). The mean age of this population was 55.7 years (standard deviation, 11.4 years), with a range of 21 to 94 years. The sarcoidosis population was 50.8% black and 86.0% male.