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Epidemiology of Sarcoidosis 1946-2013: A Population-Based Study

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Abstract

Objective: To characterize the epidemiology of sarcoidosis from 1946 through 2013.

Patients and Methods: An inception cohort of patients with incident sarcoidosis from January 1, 1976, through December 31, 2013, in Olmsted County, Minnesota, was identified based on comprehensive individual medical record review. Inclusion required physician diagnosis supported by histopathologic confirmation, radiologic features of intrathoracic sarcoidosis, and a compatible clinical presentation. Data were collected on demographic characteristics, clinical presentation, laboratory investigations, and mortality. The data were augmented with a previously identified cohort of Olmsted County residents diagnosed as having sarcoidosis in 1946-1975. Incidence rates were age and sex adjusted to the 2010 US white population.

Results: A total of 448 incident cases of sarcoidosis were identified (mean age, 44.2 years; 52% women). The annual incidence of sarcoidosis was 10.0 per 100,000 population. The incidence of sarcoidosis increased in women from 1950 to 1960, but otherwise there were no significant calendar year trends. However, the peak age at incidence for women shifted from 40 to 59 years in 1950 to 50 to 69 years in 2010. Similarly, the peak age at incidence for men shifted from 30 to 49 years in 1950 to 40 to 59 years in 2010. Ninety-seven percent of patients had intrathoracic involvement, but only 43% had respiratory symptoms. The overall mortality of patients with sarcoidosis was not different from that of the general population (standardized mortality ratio=0.90; 95% CI, 0.74-1.08).

Conclusion: Sarcoidosis occurred in approximately 10 persons per 100,000 per year. Most of the patients had intrathoracic involvement, although less than half had respiratory symptoms. Overall mortality was not different from that of the general population.

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Sarcoidosis is a multisystem disorder of unclear etiology typically affecting the lymphatic system and the lungs. The presence of noncaseating granuloma is the histopathologic hallmark of the disease. The clinical course of the disease can range from an acute self-limited process to progressive organ dysfunction with significant morbidity and mortality. Sarcoidosis is generally categorized into 2 subgroups, intrathoracic and extrathoracic, based on the site of involvement.[1]

The epidemiology of sarcoidosis, especially in the United States, is not well described because a limited number of epidemiologic studies have been conducted.[2-5] The first epidemiologic study of sarcoidosis in the United States was published in 1986.[2] This study used the resources of the Rochester Epidemiology Project to identify all the incident cases of sarcoidosis in Olmsted County, Minnesota, from 1946 through 1975. The age- and sex-adjusted incidence of sarcoidosis was 6.1 per 100,000 person-years. Incidence figures from subsequent studies were variable, ranging from 9.6 to 71 per 100,000 person-years.[3,4] Ethnic/racial differences were also observed.[3] Studies on mortality found that age-adjusted mortality rates varied from 1.3 to 28.0 per 1,000,000, depending on sex, ethnicity/race, and calendar year.[5-7]

The objective of this study was to characterize the epidemiology of sarcoidosis, with emphasis on annual incidence and mortality, from 1946 through 2013 in a geographically well-defined population of patients.

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PATIENTS AND METHODS

Data Source and Study Population

Through the resources of the Rochester Epidemiology Project, the population of Olmsted County,

Minnesota, in which resides the city of Rochester, is well suited for investigation of the epidemiology of sarcoidosis because comprehensive and complete medical records for all residents seeking medical care for more than 6 decades are available. A record linkage system allows ready access to the medical records from all health care providers for the local population, including Mayo Clinic and Olmsted Medical Center and their affiliated hospitals, local nursing homes, and the few private practitioners. The potential of this data system for use in population-based studies has previously been described.[8,9] This system ensures virtually complete ascertainment of all clinically recognized cases of sarcoidosis in the residents of Olmsted County.

Approval for this study was obtained from the Mayo Clinic and Olmsted Medical Center institutional review boards, and the need for informed consent was waived.

Study Design

A cohort containing Olmsted County residents diagnosed as having sarcoidosis from January 1, 1976, through December 31, 2013, was identified to augment the previously identified cohort of Olmsted County residents diagnosed as having sarcoidosis from 1946 through 1975.[2] All patients with diagnosis codes related to sarcoid, sarcoidosis, and contextual noncaseating granuloma were screened for inclusion in the cohort based on comprehensive individual medical record review. Inclusion required physician diagnosis supported by histopathologic and radiologic features of intrathoracic sarcoidosis, a compatible clinical presentation, and exclusion of other granulomatous diseases. Tissue samples were considered positive if they demonstrated noncaseating granuloma without evidence of acid-fast bacilli or fungi. The only exception to the requirement for histopathologic confirmation was stage I pulmonary sarcoidosis, which required only radiographic evidence of symmetrical bilateral hilar adenopathy with or without mediastinal lymphadenopathy in the absence of symptoms or identifiable causes. Isolated granulomatous disease of a specific organ except for the skin was also included if there was no better alternative diagnosis. Patients with a diagnosis of sarcoidosis before residency in Olmsted County were not included.[10,11]

A standardized data extraction form was used to record the following information: date of diagnosis, age at diagnosis, sex, self-reported ethnicity, smoking status, date of last follow-up, status at last follow-up (died or alive), cause of death, presence of intrathoracic disease, presence of symptoms related to intrathoracic disease, radiologic findings, presence of extrathoracic disease, angiotensin-converting enzyme level, and calcium level. Data on self-reported ethnicity were collected to investigate the possible racial difference of the incidence of sarcoidosis.

Case verification and data extraction was conducted by the first author (P.U.). To ensure the accuracy of the data, 10% of the medical records were randomly selected and reviewed by the second author (E.M.C.) and the senior author (E.L.M.).

Statistical Analyses

Descriptive statistics (means, percentages, etc) were used to summarize the data. Age- and sex-specific incidence rates were calculated by using the number of incident cases as the numerator and population estimates for adults (age $\geq$18 years) based on decennial census counts as the denominator, with linear interpolation used to estimate population size for intercensal years. Overall incidence rates were adjusted for age, sex, or both to the 2010 white population of the United States. To compute 95% CIs for incidence rates, it was assumed that the number of incident cases followed a Poisson distribution. Trends in incidence rates were examined using Poisson regression methods, with smoothing splines for age and calendar year. The annual incidence rates were graphically illustrated using a 3-year, centered moving average to reduce the random fluctuations over time.

Mortality rates were estimated using the Kaplan-Meier method and were compared with expected mortality rates for persons of the same age, sex, and calendar year estimated using Minnesota population life tables. The standardized mortality ratio (SMR) was estimated as the ratio of the observed and expected number of deaths. The 95% CIs for the SMR were calculated assuming that the expected rates are fixed and the observed rates follow a Poisson distribution. Univariable Cox models adjusted for age, sex, and calendar year of