Unexpectedly high prevalence of sarcoidosis in a representative U.S. Metropolitan population

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Summary
The prevalence of sarcoidosis in the United States is unknown, with estimates ranging widely from 1 to 40 per 100,000. We sought to determine the prevalence of sarcoidosis in our health system compared to other rare lung diseases and to further establish if the prevalence was changing over time. We interrogated the electronic medical records of all patients treated in our health system from 1995 to 2010 (1.48 million patients) using the common ICD9 codes for sarcoidosis (135), lung cancer (162), and several other lung diseases characterized, like sarcoidosis, as "rare lung diseases". The patient demographic information (race, gender, age) was further analyzed to identify signature data patterns. The prevalence of sarcoidosis in our health system increased steadily from 164/100,000 in 1995 to 330/100,000 in 2010, and this trend could not be ascribed simply to changes in patient demographics or patient referral patterns. We further estimate that the prevalence of sarcoidosis exceeds 48 per 100,000 in Franklin County, Ohio, the demographic profile of which is nearly identical to that of the U.S. Sarcoidosis prevalence increased over time relative to lung cancer, a benchmark disease with stable disease prevalence, and exceeded that of other rare lung diseases. We postulate that the observed 2-fold increase in sarcoidosis disease prevalence in our health system is primarily related to improved detection and diagnostic approaches, and we conclude that the actual prevalence of sarcoidosis in central Ohio greatly exceeds current U.S. estimates.

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Introduction

Sarcoidosis is a chronic systemic disease, most commonly affecting the lungs, that afflicts adults in the primes of their lives. Based upon the ACCESS trial, the largest epidemiological study on sarcoidosis to date, the annual incidence of the disease varies from 5/100,000 in whites to 39/100,000 in African Americans,[1] with an overall prevalence estimated to be 15/100,000 in the USA (www. orpha.net/orphacom/cahiers/docs/GB/Prevalence_of_rare_ diseases_by_alphabetical_list.pdf). As such, sarcoidosis is characterized as a "rare lung disease" (i.e., prevalence <200,000 cases) in the USA. However, firm data relating to the true prevalence of sarcoidosis is lacking and it is unclear if the prevalence of disease is changing over time.

Several features of sarcoidosis tend to obscure the diagnosis, leading to an under-appreciation of the potential impact of the disease on the health care system and society as a whole. Sarcoidosis frequently presents with non-specific complaints, ranging from fatigue and depression, "asthma symptoms" (wheezing, cough), to arthritis and muscle pain or weakness. As such, sarcoidosis can mimic other diseases, leading to misdiagnosis and inappropriate treatments. When these non-specific disease manifestations prevail, or when symptoms are absent,[2] the underlying diagnosis of sarcoidosis may be overlooked. In support of this concept, a review of 9324 forensic autopsies cases in Cuyahoga County (Cleveland), Ohio, indicated that 31 exhibited histopathological evidence of sarcoidosis, which conforms to a population risk of 300/100,000, an order of magnitude higher than suspected based upon death certificate reporting.[3] While it is not possible from the information available from these forensic cases to confirm that all cases were properly classified as sarcoidosis, the study suggests that the true prevalence of sarcoidosis is underestimated.

Several recent developments could contribute to an apparent and/or actual increase in the prevalence of sarcoidosis over the past 15 years. There is reason to believe that the detection of sarcoidosis has improved as clinical standards have shifted toward high-resolution imaging techniques (e.g., CT scanning) and with the development of novel sampling techniques [e.g., endobronchial ultrasound-guided biopsy[4]]. And to the extent that exposure to various environmental antigens promotes sarcoidosis,[5] it follows that acute or chronic exposures to inhaled[6] and perhaps ingested antigens[7] could contribute to more cases of sarcoidosis. The objective of this study was to determine if the prevalence of sarcoidosis is changing over time in our health system and in our community.

Methods

Patient population

The Ohio State University Medical Center's institutional Information Warehouse (IW) was interrogated from 1995 to 2010 by means of Structured Query Language (SQL) queries. The census data for Franklin County was obtained from the US Census Bureau's online resources (http://quickfacts. census.gov/qfd/states/39/39049.html), and was uploaded into the IW in the form of database tables. The patient demographic information (race, gender, age) was gathered for patient groups using specific ICD9 diagnosis codes for sarcoidosis (135), idiopathic pulmonary fibrosis (IPF; 516.3), hypersensitivity pneumonitis (HSP, 495), alpha-1 antitrypsin deficiency (AAT, 273.4), and lung cancer (162); demographics on all patients within our system were collected as well. In this regard, The Ohio State University Medical Center is a regional referral center for all of these rare lung diseases. For the purposes of these analyses each patient was counted once for a given year.

Statistical approach

Data were analyzed by using SAS version 9.2. Line plots were presented to show the trend and the relationship between variables. Cochran-Armitage[8] trend test was used to analyze the proportional trend in years and association between variables. Significance was accepted if $p \leq 0.05$.

Results

Demographics of the regional population

The demographic profile of Columbus, Ohio closely approximates that of the USA (Table 1; and 2010 census results: http://quickfacts.census.gov/qfd/states/00000. html).

Comparison of sarcoidosis prevalence to that of other rare lung diseases

Ohio State University Medical Center (OSUMC) is a regional referral center for all types of lung disease, including sub-specialty clinics for rare lung diseases (IPF, HSP, AAT, sarcoidosis), as well as lung cancer. A total of 1.48 million patients were encountered at OSUMC from 1995 to 2010, and were included in the analysis. The overall disease prevalence and the number of patient encounters attributed to the diagnosis of sarcoidosis was significantly higher than for any of the other rare lung diseases (Table 2).

Given that sarcoidosis prevalence is influenced by race and gender, we further analyzed the contribution of these variables in the observed changes in sarcoidosis prevalence over time within the OSUMC cohort. There was no statistically significant linear trend in proportion of males and females within the OSUMC study population or based on the diagnosis of sarcoidosis (Fig. 2). There was a statistically significant linear trend in proportion between whites and African Americans in the study population (Fig. 3A). The expected increasing trend in proportion of African Americans over the 15-year span changes from 18% to 21.4% while expected decreasing trend in the proportion of whites in years changes from 81.5% to 78.5%. However, there is no statistically significant linear trend in proportion of African American and whites based on the diagnosis of sarcoidosis (Fig. 3B). There was statistically significant linear trend in proportion between sarcoidosis and Lung cancer (Fig. 4). The expected increasing trend in the proportion of