

Short Communication

The Epidemiology of Systemic Sarcoidosis in Eastern Hertfordshire, UK

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Abstract

Background: Sarcoidosis is an uncommon multi-system disease characterised by the development of granulomatous inflammation within affected tissues. The purpose of this study was firstly to redefine the incidence of sarcoidosis within a UK population and secondly to identify the potential cost to the National Health Service of provision of optimal treatment for all manifestations of the disease.

Methods: A population of 51566 people living in the eastern Hertfordshire region of the UK was studied prospectively over a three year period in a general practice setting.

Results: Fifteen new cases were identified of whom half showed multi-system disease at onset. The annualised incidence of the disease in this population was 9.69×10^{-5} .

Conclusion: The results show that the prevalence of systemic sarcoidosis in a representative population of the UK is the same as that in other countries. The results have been used to estimate the annual cost of provision of biological therapies in the disease in the UK.

Keywords: Sarcoidosis; Neurosarcoidosis; Epidemiology; Drug prescribing

Summary Box

What is already known on this subject?

The epidemiology of sarcoidosis has been measured before in the UK, but not for 30 years. Most previous papers have measured the rates of incidence but not the various subtypes of the disease, and this paper has set out to do this.

What does this study add?

This paper identifies that the prevalence of multisystem disease in the disorder is 50%, and those with respiratory disease required less treatment than those with multisystem disease. The crude annualised incidence was calculated to be 9.69×10^{-5} .

The data were used to calculate the financial requirement to the UK National Health Service of provision of optimal treatments including biological therapies. These data have not previously been ascertained.

Introduction

Sarcoidosis is a multisystem auto-inflammatory disease which affects any tissue within the body. The lungs and mediastinal lymph nodes are the most commonly involved; the eyes, skin, liver and joints less so. Every tissue has been shown to be involved [1]. In the ACCESS study 736 patients seen over a two year period 95% showed involvement of the respiratory system, 50% had disease isolated to one tissue (97% of whom had thoracic disease), 30% showed involvement of two systems, the remainder having up to 7 tissues involved at the time of diagnosis [2]. Over a two year follow up 80% had resolved or stabilised and 23% showed spread of the disease to other tissues [3]. The nervous system is affected in 5% of cases [4].

In some the disease is acute and self limiting, in others sub acute and relapsing, or chronic and progressive. The immunopathology is of an infiltrative granulomatous inflammation leading to tissue fibrosis.

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Early epidemiological studies revealed varying incidences throughout the US and Scandinavian countries of 15×10^{-5} - 28×10^{-5} , with a recognition that the disease is more prevalent in African Americans than European Americans [5] and much less common in south east Asia than in Scandinavia [6,7]. In the UK there was an early study in the Isle of Man (stimulated by an outbreak of the disease in that area) which defined an annual incidence of 14×10^{-5} between 1977 and 1983 [8], and more recently a study of the respiratory form of the disease in England defined an annual incidence in that country of 5×10^{-5} [9]. No study has yet been undertaken in the UK which defines the incidence of all forms of the disease and to investigate what racial differences may exist. This is increasingly important as a more aggressive approach to the treatment of the disease evolves, in particular with the use of biological agents which have been shown very substantially to improve outcome in those with severe forms of the disease [10]. The cost of such treatments is high, and it is important therefore to identify firstly those who require such therapies and secondly what the cost to the National Health Service would be.

The Royal Free Hospital is a large teaching hospital in north London which acts as a referral centre to the local and regional hospitals of North London, Hertfordshire and Bedfordshire, and has for 50 years been a tertiary referral centre for the treatment and management of Sarcoidosis. The eastern Hertfordshire region is close to London and whose community is predominately town dwelling with some rural parts. The population demographics closely correspond to those of England as a whole. This study was undertaken through general practices whose boundaries overlap and which cover about half the population of this region. The study was approved by the local research ethics committee.

Methods

The general practices of Hertford and Ware were approached and asked to participate. A search of all those patients diagnosed previously with sarcoidosis was made at baseline, then each practice was asked to repeat the search every six months in order to identify all new cases diagnosed within that time. Newly diagnosed patients were asked to consent to their records being examined pseudonymously by the author in order to identify the symptoms, signs and investigations results, to confirm the diagnosis and to observe the treatment recommended, then its outcome. The study began in January 2014 and the last assessment

was made in July 2017. Data were analysed using an Excel data analysis add in programme.

Results

There are four general practices in Hertford and three in Ware. One of the Ware surgeries was unable to provide administrative support and so the study comprised all patients in the remaining six surgeries. The mean total patient population over the study period was therefore 51566. All patients identified provided consent.

Over the 36 month period of case ascertainment 15 new cases were diagnosed (Table 1). Five were female, mean age 47.1 ± 11.6 years. The thorax was involved in 14, and in 7 cases there was multisystem disease at onset. All but one patient was white Caucasian.

Histological confirmation was obtained through mediastinal node biopsy in 11, cervical node biopsy in 3 and skin biopsy in 2 others.

Three received no treatment and were observed. Twelve received steroids and of these three-received immunosuppression (one azathioprine, one methotrexate, and one methotrexate and leflunomide) as well. Those who received no treatment or oral steroids only all had single system intrathoracic disease. At the end of the study period 11 had been adjudged to be well and had been discharged on no treatment and the remainder continued hospital based care. The mortality during the study period was 0.

The crude annualised incidence of the disease over the three year period was 9.69, 5.2 in those with single organ disease and 4.5 in those with multisystem disease.

Discussion

This is the first epidemiological study of multisystem disease in sarcoidosis in the UK for the past 30 years. The annualised incidence is calculated to be 9.69×10^5 , the same as the result of a large population studied over a prolonged period in Olmsted County, Minnesota [11]. There is a predominance of males not seen in other reports, but the clinical features and the prevalence of thoracic and extrapulmonary manifestations are in keeping with previous studies. The low number of non-white patients does not allow for a reasonable estimation of racial differences in the acquisition of the condition, which will need to be addressed by a larger study. The importance of an up to date epidemiological study in the UK lies in the assessment of the provision of funds required to treat the disease by the most efficient and successful means. The UK National Health Service is currently severely underfunded, and provision of new treatments is hugely complicated by a system of service framework agreements which limit provision of funds for treatment and which in the case of uncommon diseases makes it virtually impossible to compose agreements for treatment; at the time of writing it is impossible to be granted funding to prescribe biological therapies to any patient with sarcoidosis requiring them in the UK. And yet immunotherapy with biological agents blocking TNF α receptors has been shown to be highly effective in severe and treatment resistant cases of sarcoidosis within all tissues [10]; it is important to define the need for treatment funding in this patient population. Although no accurate proportions have been published, an examination of large clinical series suggest that around 40% of new cases (predominately those with single tissue and intrathoracic disease) has self-limiting non-recurrent disease requiring either no treatment or low dose oral steroids for a time, a further 40% has relapsing or progressive disease requiring low dose oral immunosuppression which is effective in the majority, and 20% has severe and treatment resistant disease. Those who require such treatment include those with CNS disease (of whom 10% will not respond to steroids and high dose oral immunosuppression alone [12]), refractory skin and bone disease (R Baughmann, personal communication). Only

1% of those treated at Moorfield's eye hospital uveitis unit and 1% of those with respiratory disease attending the sarcoidosis clinic of the Royal Brompton hospital have required immunotherapies over the past 5 years (H Petruskin and T Maher, personal communications). If we extrapolate the results of this small regional study to the whole population of England (53×10^6) it would be expected that there be 5300 new cases of Sarcoidosis per year, half of whom would have thoracic disease alone and half multisystem disease. 1600 would have ophthalmic disease and 265 neurological involvement. 70-80% would require treatment, of whom 30% would receive immunosuppression. If the proportion of cases who require immunotherapies is correct it may be estimated that only 65 new cases require treatment with intravenous medications including immunotherapy per year. The cost of treatment with biological therapies for sarcoidosis in the whole of England would be estimated therefore to be only £520,000 per year, or 0.0000003 % of the total pharmacy budget of the NHS in England [13].

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