

Review article

## Sarcoidosis: benefits of a multidisciplinary approach

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### Abstract

It is well established that sarcoidosis is a multisystem disorder of unknown cause(s). Practically no organ is immune to sarcoidosis. It subsides in most cases, but it may worsen and become chronic in others. Pulmonary problems may persist, but also devastating extrapulmonary complications may become apparent. Appropriate management of sarcoidosis is mandatory as it predominantly affects fairly young adults. This requires the attention of pulmonologists as well as specialists from other medical disciplines. Accordingly, when treating sarcoidosis patients, a multidisciplinary approach is recommended that focuses attention on somatic as well as psychosocial aspects of this erratic disorder. Specialists from all participating medical disciplines—including respiratory diseases—may benefit from a multidisciplinary approach and be stimulated to enhance their professional interest and knowledge of sarcoidosis. The benefit of such an approach should be explored in the near future.

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### 1. Introduction

Sarcoidosis is a disseminated, granulomatous disease of unknown etiology that occurs throughout the world. Various infectious, organic, and anorganic agents are considered to cause a granulomatous reaction in susceptible hosts [1,2]. Some genetic factors alter expression of the disease. Estimates of prevalence range from 1 to 40 per 100,000 individuals, varying among ethnic and racial groups [1]. The clinical course of sarcoidosis is highly variable, and virtually every organ can be involved. The lungs are affected in over 90% of patients with sarcoidosis [1]. It also frequently affects the lymph nodes, skin, and eyes. Notably, the clinical presentation of sarcoidosis is highly variable and the course of the disease is unpredictable. Spontaneous recovery may occur, but the disease can also become chronic and progressive, estimated in up to 25% of the cases. Overall, mortality from sarcoidosis is 1–5%. To

date, it is the second most common respiratory disease in young adults after asthma. In addition, many sarcoidosis patients report non-specific symptoms such as fatigue and pain [1,3–9]. These non-specific symptoms are disabling for the patient, cause an impaired quality of life [9–13], and may become chronic. Especially for patients with chronic sarcoidosis, proper management of their disease is important. In several other disorders such as sleep apnea syndrome, in trauma patients, and in patients with severe functional deficits, early initiation of multidisciplinary treatment appears to be promising and encouraging. In the present paper, the benefits of a multidisciplinary approach for both patients and physicians are discussed.

### 2. Sarcoidosis management and care

#### 2.1. Diagnostic work-up

The management of sarcoidosis is generally coordinated by a pulmonary physician. However, sarcoidosis can

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involve any organ. Sarcoidosis patients not only suffer from symptoms related to the lungs (e.g. cough, breathlessness), but they may also suffer from a wide spectrum of other symptoms [1,3]. These symptoms include persistent fatigue, arthralgias, muscle pain, weight loss, skin lesions, eye problems, and neurological as well as cardiological problems [1,3,9]. In our experience [4,7,9] and that of others [1,3,5,7], these extrapulmonary symptoms appear to be a considerable problem in chronic sarcoidosis. Fatigue, as an integral part of the clinical picture of sarcoidosis, has gained some attention in the literature [3–8], although the exact mechanism is still unknown. Because of these diverse manifestations, patients may consult other specialists too. The diagnostic work-up includes attention to the medical history, relevant exposures, imaging procedures, laboratory tests, bronchoalveolar lavage [14] and, if appropriate, evaluation of biopsy specimens [1]. The course of the disease is mainly monitored by assessing clinical features and by using auxiliary diagnostic procedures. However, an objective system for the assessment of disease activity and severity is still lacking. Unlike other disorders, activity in sarcoidosis does not necessarily indicate a progressive course, a fatal prognosis, or the need for medical treatment. Moreover, test results do not always accurately reflect the disability of the patient, and non-specific symptoms are often hard to objectify.

## 2.2. Therapeutic approach

Longitudinal surveillance of sarcoidosis should be most intensive during the first 2 years after presentation in order to assess prognosis properly and determine the need, if any, for therapy. However, the therapeutic approach is mainly symptomatic as a causative treatment is not yet available [1,15]. The value of corticosteroids—usually the first treatment of choice—is still rather controversial [1,15–17]. Systemic therapy is clearly indicated for respiratory impairment, cardiac involvement, neurosarcoidosis, eye disease, lack of response to topical therapy, and hypercalcemia. In addition, several cytotoxic agents, such as methotrexate, have been used to treat sarcoidosis [1]. Tumor necrosis factor alpha [1,18,19] and, more recently, the involvement of oxidative stress, have been considered in the pathogenesis of sarcoidosis [20,21]. These may very well have therapeutic consequences for the future.

The multidisciplinary approach is aimed at improving patient care and avoiding miscommunication between various participants as much as possible. Moreover, patients may benefit from rehabilitation programs. In some refractory cases, transplantation has even been performed because of organ failure [1]. In pre-transplant screening and follow-up, a multidisciplinary approach is also mandatory.

The fact that many symptoms and disabilities are not related to the lungs and that other organs are often

involved makes a multidisciplinary and central approach to sarcoidosis necessary.

## 3. Central multidisciplinary approach

### 3.1. Patient care

During the past few years, there has been an increase in the number of requests for second opinions by chronic sarcoidosis patients from all over The Netherlands who have come to the outpatient clinic of the University Hospital in Maastricht. To be eligible for a second opinion, patients had to have been referred by their specialist or general practitioner. To improve the management of this chronic patient population and to better meet the increasing demand for these second opinions, a sarcoidosis management center (SMC) was started in January 2000. The most important goal of this center was to focus attention on the multidimensional character of sarcoidosis in order to guide and improve the efficiency of patient care and to increase the cost-effectiveness so as to benefit the health service financially. Another goal was to allow specialists in fields other than lung disease to benefit from a more centralized approach. Finally, it was thought that broadly based research projects initiated by various disciplines could improve knowledge regarding many aspects of this intriguing disease. A multidisciplinary team was thus formed with representatives of various medical and paramedical disciplines, namely, a pulmonary physician, cardiologist, rheumatologist, internist, dermatologist, radiologist, pathologist, ophthalmologist, neurologist, immunologist, ear, nose, and throat physician, toxicologist, and a clinical genetic counsellor.

The approach taken by the SMC is as follows. All medical records of newly referred sarcoidosis patients are reviewed. The diagnosis sarcoidosis is established according to the international guidelines [1]. Referred patients suffer from severe, chronic sarcoidosis. After an intake by the coordinator (M.D.), the patient's complaints are noted carefully. Depending on the nature of the complaints, appropriate members of the SMC are involved in the patient's care (Fig. 1). If no ophthalmologic consultation has been performed prior to the referral, it is done at this time. All relevant medical problems are documented and, if necessary, additional diagnostic procedures are performed. Subsequently, after discussion in the multidisciplinary team, therapeutic advice is given. The patient has a central position in this process, and appointments are carefully planned, avoiding unnecessary delays. The number of chronic sarcoidosis patients referred to the SMC is still increasing: from 41 in 2000, to 72 in 2001, to 83 in 2002. The demographic and clinical data of the population of sarcoidosis patients referred to the SMC between 2000 and 2002 ( $n=196$ ) are summarized in Table 1. The organ most often affected is the lung, although the majority of

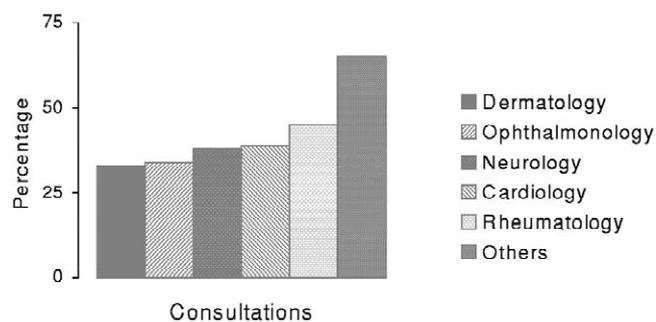


Fig. 1. Percentage of consultations per new sarcoidosis patient visiting the Sarcoidosis Management Center (SMC) Maastricht, The Netherlands.

patients recall suffering from symptoms involving other organs as well (Fig. 1). The mean percentage of specialists involved in the care of patients referred to the SMC is also given in Fig. 1. The mean number of visits per patient each per is seven.

### 3.2. Research changes and challenges

As mentioned before, the cause of sarcoidosis is still unknown. The disease most likely represents an inflammatory response to one or more agents (bacteria, fungi, virus, and/or chemicals). The advantage of a system of central management for sarcoidosis patients appears to be the knowledge gained about this erratic disease. We have been able to identify specific aspects of symptoms, especially fatigue [4,6,10], which influence the quality of life in sarcoidosis [9–13]. Furthermore, an acute phase response appears to be involved [6]. Polymorphonuclear neutrophils in bronchoalveolar lavage fluid obtained from newly diagnosed sarcoidosis patients has been found to be associated with prognosis [22], and this has recently been confirmed by others [23]. Interestingly, the possible involvement of oxidative stress in the pathogenesis of sarcoidosis, as well as the association of exposure to

man-made mineral fibers and the development of sarcoid-like granuloma [24], have also been demonstrated. More recently, based on clinical grounds, a pattern of symptoms consisting of peripheral pain and autonomic dysfunction, highly suggestive of small fiber neuropathy with autonomic involvement, was recognized [25]. Autonomic dysfunction, including rather non-specific symptoms such as pain, appears to be linked to a small fiber neuropathy. It is tempting to speculate that this hitherto unrecognized finding in sarcoidosis may account, at least in part, for the associated life-threatening events. This may have therapeutic and prognostic implications. Moreover, the recognition of an organic basis for peripheral pain and autonomic symptoms in chronic sarcoidosis patients appears to be important, as patients have reported benefiting from knowing the cause of their complaints [3]. Collecting data from larger cohorts may contribute to the exploration of pathophysiological mechanisms, and it offers the opportunity to conduct genetic studies as well [1,2,26]. Future research should address the systemic aspects of sarcoidosis more extensively.

Practically, the significance of the multidisciplinary approach appears to be more balanced patient care, with attention to the different aspects of sarcoidosis. From the patient's point of view, this approach increases the efficiency, as appointments and multidisciplinary consultations are scheduled as much as possible on 1 day. Patients also benefit in another way: their regular check-ups are coordinated, and treatment strategies established, after discussion with members of the multidisciplinary team. To date, the potential benefits to the health systems in terms of long-term care costs that could be saved, and to society in the prevention of working days lost, are considerable. However, we realize that this new approach to patient care, where the patient has a central position, requires changing the organization of patient care and support from health care systems. Ideally, patients with severe sarcoidosis should have easy access to such a center; they should not

Table 1

Demographic and relevant clinical data of the sarcoidosis patient population ( $n=196$ ) referred to the Sarcoidosis Management Center in 2000–2002

Age: mean±S.D. (years)	42.6±11.8
Gender: female/male (%)	45.4/54.6
Race: Caucasian/non-Caucasian (%)	89.3/10.7
Time since diagnosis: mean±S.D. (years)	4.7±6.3
Chest X-ray stage (0/I/II/III/IV; %)	18.9/18.4/24.5/27.6/8.2
Treatment	
Never (%)	35.2
Prednisone/prednisone+MTX/MTX+anti-TNF- $\alpha$ (%)	45.8/16.4/2.6
Painkillers (%)	34.5
Prevailing damage (e.g. initial reason for treatment)	
Lung involvement	82.0
Eye involvement	3.8
Neurosarcoidosis	3.3
Hypercalcemia	2.2
Cardiac involvement	1.6
Other (skin lesions, lupus pernio, arthralgia, etc.)	7.1

$n$ =Number of cases; S.D.=standard deviation; MTX=methotrexate; TNF- $\alpha$ =tumor necrosis factor alpha.

have to travel too much. Therefore, three centers throughout The Netherlands are recommended. Patients suffering from other multisystemic disorders, including other interstitial lung diseases, could also benefit from such a multidisciplinary approach in the future. The next step has to be a qualified assessment of cost-effectiveness of these centers; not only must the benefit to the individual patient be properly assessed, but also the possible financial benefits or limitations for the health service.

In conclusion, the management of sarcoidosis patients should be intensive and not limited to pulmonologists. The complicated, multidimensional nature and the wide range of symptoms of sarcoidosis underlines the need for a multidisciplinary system of management. This approach is strongly encouraged as a substantial number of sarcoidosis patients suffer from extrapulmonary manifestations that necessitate appropriate health care. Moreover, with representatives of diverse clinical disciplines working together as a team, the likelihood of developing new therapeutic strategies, promoting research into the pathophysiological nature of the disease, and including diseases such as sarcoidosis in training programs increases. Future studies should provide a qualified estimation of cost-effectiveness of these structured, multidisciplinary approach centers, and they should focus on assessing the benefits of a more central position of the patient in health care.

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