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Consequences of Sarcoidosis



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KEYWORDS

- Cognitive impairment Depressive symptoms Exercise limitation Fatigue Pain Rehabilitation
- Sarcoidosis Small fiber neuropathy Quality of life

KEY POINTS

- Consequences of sarcoidosis are wide ranging, and have a great impact on patients' lives.
- Sarcoidosis patients suffer not only from organ-related symptoms, but also from a wide spectrum
 of rather nonspecific disabling symptoms.
- Absence of evidence does not mean evidence of absence.
- Management of sarcoidosis requires a multidisciplinary personalized approach that focuses on somatic as well as psychosocial aspects of the disease.

INTRODUCTION

The clinical expression, natural history, and prognosis of sarcoidosis are highly variable and its course is often unpredictable.¹ Clinical manifestations vary with the organs involved.¹,² The lungs are affected in approximately 90% of patients with sarcoidosis, and the disease frequently also involves the lymph nodes, skin, and eyes. Remission occurs in more than one-half of patients within 3 years of diagnosis, and within 10 years in two-thirds, with few or no remaining consequences.² Unfortunately, up to one-third of patients have persistent disease, leading to significant impairment of their quality of life (QoL).³ Interpretation of the severity of the sarcoidosis can be complicated by its heterogeneity. Several major concerns

of sarcoidosis patients include symptoms that cannot be explained by granulomatous involvement of a particular organ.4 Apart from lungrelated symptoms (eg, coughing, breathlessness, and dyspnea on exertion), patients may suffer from a wide range of rather nonspecific disabling symptoms.^{2,5} These symptoms, such as fatigue, fever, anorexia, arthralgia, muscle pain, general weakness, muscle weakness, exercise limitation, and cognitive failure, often do not correspond with objective physical evidence of disease.^{2,5–9} These issues are often troubling to pulmonologists and other sarcoidologists because they do not relate directly to a physiologic abnormality, are difficult to quantify and hence to monitor, and are challenging to treat.4

The authors have nothing to disclose.

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Symptoms such as fatigue can be nonspecific and difficult to objectify. Moreover, absence of evidence does not mean evidence of absence.5,7 Sarcoidosis-related complaints, including fatigue, may become chronic and affect patients' QoL even after all other signs of disease activity have disappeared.7,10,11 Hence, patients consult their physician not only with organ-specific symptoms-directly related to the organ(s) involved-but also with nonspecific health complaints, such as fatigue, cognitive failure, exercise intolerance, and muscle weakness. 12 These impairments in sarcoidosis are disabling, especially when they become chronic. 13,14 Sarcoidosis consists of several overlapping clinical syndromes ("the sarcoidosis"), each with its own specific pathogenesis. A complete evaluation of sarcoidosis could make use of a panel with 4 disease domains or dimensions: extent of disease, severity, activity, and impact. 15-17 Severity of sarcoidosis in each organ is defined as the degree of organ damage sustained from sarcoidosis. The interpretation of the severity of sarcoidosis can be complicated by its heterogeneity. The organ damage can be estimated subjectively by the intensity of symptoms, objectively as a percentage decline from normal capacity (eg, percentage of the predicted normal value on pulmonary function testing), or by critical location of lesions (eg, cardiac block). However, pulmonary function test results do not always represent changes in the severity of pulmonary sarcoidosis, 18 which illustrates that the demonstration of sarcoid activity remains an enigma. Assessment of inflammatory activity in sarcoidosis patients without deteriorating lung function or radiologic deterioration but with unexplained persistent disabling symptoms is an important and often problematic issue. Historically, evaluation of the various available tools for the assessment of inflammatory activity has been hampered by the lack of a gold standard. This article focuses on the impact of the broad range of sarcoidosis-related problems on patients' lives.

SYMPTOMS

In addition to symptoms related to the organs involved, patients may suffer from all kinds of less specific symptoms. These sarcoidosis-related disabling symptoms can significantly decrease a person's QoL, especially in chronic sarcoidosis. ¹⁹ All these symptoms may have major consequences and impact on the patients' lives and those of their relatives.

Fatigue

Fatigue is the most frequently described and devastating symptom in sarcoidosis, and is

globally recognized as a disabling symptom. The reported prevalence varies from 60% to 90% of sarcoidosis patients,5 and up to 25% of fatigued sarcoidosis patients report extreme fatigue. Physicians generally assess disease severity and progression in sarcoidosis on the basis of clinical tests, such as pulmonary function tests, chest radiographs, and serologic tests. However, these objective clinical parameters correlate poorly with the patients' subjective sense of well-being.8,20 Sarcoidosis patients may suffer from substantial fatigue even in the absence of other symptoms or disease-related abnormalities. For example, fatigue and general weakness may persist even after routine clinical test results have returned to normal.⁵ There is a positive association between symptoms of suspected small fiber neuropathy (SFN) and fatigue, as well as between dyspnea and fatique. 13,21,22 So far, no organic substrate has been found for the symptoms of sarcoidosis-associated fatigue.

To date, no appropriate definition of fatigue exists. Fatigue can be seen and measured as a unidimensional or multidimensional concept. The multidimensional concept of fatigue can be divided into at least 2 categories: physical and mental or passive and active fatigue.^{5,10}

Some sarcoidosis patients are debilitated by the symptoms of their disease and are unable to work; others are underemployed and incapable of achieving their full potential owing to their health issues.23 Individuals affected by the disease frequently seem to be completely healthy, so their symptoms are often not taken seriously by family, friends, employers, and health care professionals. Consequently, some patients lose their desire and ability to socialize with others effectively, causing relationships and family dynamics to ultimately suffer. These combined factors impact on an individual's economic status, interpersonal relationships, and family dynamics, increase their stress levels, and induce depression in patients.

The etiology of this troublesome problem remains elusive and is usually multifactorial. Fatigue can be a consequence of the treatment itself, for instance, as a complication of corticosteroid therapy. The diagnosis of sarcoidosis-associated fatigue requires extensive evaluation to identify and treat potentially reversible causes. ^{5,6} Its etiology may involve granuloma formation and cytokine release. However, despite effective treatment of the sarcoidosis, many patients continue to experience fatigue. ^{5,24} Comorbidities associated with sarcoidosis, including depression, anxiety, hypothyroidism, and altered sleep patterns, may all contribute to fatigue. ^{23,25}

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