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Anxiety, its relation to symptoms severity and anxiety sensitivity in sarcoidosis

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Abstract. *Background.* Sarcoidosis is a chronic systemic granulomatous disease of unknown etiology. Previ-ous studies demonstrated that patients with sarcoidosis had high rates of depression and anxiety, and high magnitude of stressful life events. To date, however, studies have not examined the anxi-ety sensitivity in sarcoid patients and the relationship between psychopathology and symptom se-verity of sarcoidosis. The aims of this study were to evaluate prevalence of depression and anxiety in sarcoid patients, to assess their relationship with the disease symptom severity, and to investigate the relationship between sarcoidosis and anxiety sensitivity. *Methods:* Thirty three sarcoid patients and thirty three control subjects completed the following: Hospital Anxiety and Depression Scale, Anxiety Sensitivity Index-3. *Results:* The prevalence of depression (29%) and anxiety (31%) was high among patients and comparable to results from other research groups. Anxiety was significantly correlated with symptom severity and was the main covariate of physical symptoms reported by sarcoid patients. Patients exhibited an increase of their to-tal anxiety sensitivity index and had an increased number of physical concerns. *Conclusions:* These data confirmed earlier reports that anxiety and depression are common in patients with sarcoidosis and expanded on the previous results by showing that patients exhibited increased anxiety sensitivity and a fear of physical sensations. These results, together with the findings that anxiety was associated with sarcoidosis symptom severity, suggest that targeting anxiety and the physical health concerns may be important in the diagnosis and management of this disease. *(Sarcoidosis Vasc Diffuse Lung Dis 2013; 30: 282-288)*

Key words: Sarcoidosis, anxiety sensitivity, anxiety

Introduction

Sarcoidosis is a chronic, multisystem disease of unknown etiology that impairs the functioning and quality of life of afflicted individuals. It occurs throughout the world and affects people in their most productive years of life (1). Its etiology is poorly understood. Although, both genetic and environmental factors have an important role in the development of sarcoidosis, it is plausible that psychosocial factors also play a role (2). The clinical course of sarcoidosis is variable, and even though virtually every organ can be involved, the lungs are affected most often (3). The symptoms often reported by sarcoidosis patients are cough, night sweats, dyspnea, chest pain, and reduced

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exercise capacity. The burden of such a chronic illness as sarcoidosis is related to physical symptoms, but also to non-specific ones, such as fatigue and emotional complaints. These symptoms are disabling for the patient and impair the quality of life (3;4). Many authors suggested an association between sarcoidosis and some psychiatric problems, namely depression and anxiety (5;6). Not only do sarcoid patents exhibit psychiatric symptoms, but there is also some preliminary evidence that these symptoms are related to decreased lung function (5;7).

Although the link between sarcoidosis and psychiatric morbidity has been tentatively established, there is a lack of studies evaluating possible cognitive vulnerability factors for the development of emotional disturbances in sarcoidosis. One such factor could be anxiety sensitivity (AS, fear of anxiety-related symptoms; (8)), which has been shown to be a risk factor for anxiety problems (9;10). Anxiety sensitivity increases the risk of developing anxiety symptoms as well as panic psychopathology (11). Although its elevation in patients with sarcoidosis seems plausible, to our knowledge, it has not yet been examined.

The aim of the present paper is threefold. The first is to assess the prevalence of depression and anxiety in the population of patients suffering from sarcoidosis. Similar to findings in other countries (12), we predicted that the tested group of patients would exhibit elevated scores of depression and anxiety. The second aim is to evaluate a potential relationship between disturbed emotions and sarcoidosis symptoms. Lastly, we would like to evaluate the relationship of sarcoidosis and anxiety sensitivity. The previous studies have reported an increased number of anxiety disorders (5), elevated anxiety levels (6;12), and increased agoraphobic symptomatology in sarcoid patients (7). Therefore, we expected an increase in total anxiety sensitivity along with its subscale, which regards the concerns about physical symptoms, particularly in individuals with an elevated anxiety level.

Methods

Subjects

Two groups of participants volunteered to take part in this study. The clinical subjects were 33 consecutive patients with sarcoidosis (according to guidelines of the American Thoracic Society/European Respiratory Society/World Association of Sarcoidosis and Other Granulomatous Disorders) observed in the Department of Pneumonology in the Medical University of Warsaw (N=20), the Institute of Tuberculosis and Lung Diseases in Warsaw (N=6), and the Pulmonology Hospital in Zakopane (N=7). The subjects were hospitalized for diagnostic procedures or for routine observation of the disease progression. Only patients with sarcoidosis that had been confirmed according to international standards were included in the study, and under the condition that these individuals agreed to fill out the questionnaires. Patients with severe comorbidities (confirmed neoplastic diseases, ischemic heart disease, uncontrolled heart failure, chronic obstructive pulmonary disease) or those receiving any types of antidepressants were excluded from the study. The group comprised of 17 women and 16 men. Both sex groups were comparable in terms of age (mean age was 45 years, range: 26-72years). Non-sarcoid control participants were recruited using a snowball procedure. The control group consisted of 21 women and 12 men. These were all healthy volunteers with no record of physical and/or mental illness. The patients and control subjects did not differ in age; furthermore, there was no significant difference in age between the men and women in the control group $t < 1$.

The study was approved by the Ethics Committee of Warsaw Medical University. All subjects gave informed consent to take part in the study.

Measures

The patient questionnaire included items assessing age, sex, education, social situation, history of the disease, smoking history, and the undergoing treatment. Patients were additionally asked to report the presence of the following symptoms: dyspnea, cough, fever, asthenia, myalgia, sweating, weight loss, arthralgia, and erythema. All subjects were given psychological questionnaires including: The Hospital Anxiety and Depression Scale and The Anxiety Sensitivity Index-3. If the participant had vision or language problems, the coordinator read the questionnaire to him.

The Hospital Anxiety and Depression Scale (HADS) (13) is a one-dimensional measure of anxiety and depression designed for use in non-psychi-

atric settings. The scale consisted of 7 anxiety and 7 depression items presented in an alternating order with a 4 point response format. A high score indicated a depression or an anxiety case. This scale has demonstrated satisfactory reliability and validity, including in studies of sarcoidosis patients (14). In our study the HADS scale also reached a high reliability, *Cronbach's alpha* =.86

Anxiety Sensitivity Index-3 (ASI-3) (15;16) is an 18-item self-reported measure of anxiety sensitivity, a fear of anxiety-related symptoms based on beliefs about their potential harmful consequences (e.g., "Unusual body sensations scare me"). Responses are provided on a 5-point scale, ranging from *very little* (scored as 0) to *very much* (scored as 4). ASI-3 is made up of one higher-order factor (ASI Total Score) and three lower-order factors: Physical, Cognitive, and Social Concerns. This questionnaire has shown good reliability and validity (16). The Polish version of the ASI-3 has recently been validated by Michałowski, Holas, and Zvolensky. (in prep.) For our sample, the *Cronbach's alpha* =.85

Statistical analysis.

The analyses were performed using IBM SPSS Statistics, version 19 for Windows software. Descriptive statistics were reported as mean±standard deviation (M±SD) for continuous variables. Group differences were tested with the t-test for independent samples, whereas a one-sample t-test was used when comparing both of the samples to the ASI questionnaire validation sample (16). We also examined relationships between all of the measured variables by relying on Pearson correlation coefficients.

Results

Demographic and clinical characteristics

The demographic and clinical characteristics of both the sarcoid patients and the control group are shown in Table 1. Subsequent percentages of patients reporting various physical symptoms of sarcoidosis are presented in Table 2. At the time of investigation the duration of illness at entry in our study was 9±12.2 years (*median* = 4 years), with 54.5% of the patients having a duration of disease less than 1 year. No one had acute sarcoidosis during current hospitalization but 8 patients reported an acute episode in the past.

Most patients were diagnosed with sarcoidosis less than 5 years ago. Only 5 patients were diagnosed

Table 1. Characteristics of the study group.

	Clinical		Control	
Variable	N or *mean	% or * SD	N or *mean	% or * SD
Age	45*	12.7*	46*	12.6*
		Gender		
Male	16	48%	12	45.5%
Female	17	52%	20	54.5%
Smokers/	4/	12/	16/	50
exsmokers/	12/	36/	0/	0/
never smokers	17	51%	16	50%
		Pulmonary function tests		
FEV1% predicted	93.4%	14.7%	NA	NA
FVC% predicted	105%	19.9%	NA	NA
		Disease stage *		
group1 / group 2	60/40%		NA	NA
		Education		
University	6	18.2%	25	76%
High school	11	33.3%	8	24 %
Secondary school	4	12%	0	0

*NA- not applicable; * according to Scadding CXR stage*

Table 2. Physical symptoms presented by patients with sarcoidosis.

Variable	N or *mean	% or *SD
Illness duration [years]	9* (median 4)	12.2*
below 10 years	18	54.5
over 10 years	6	18.2
BMI	29.3*	8.4*
Sweating	22	66.7%
Dyspnea	19	57.6%
Cough	19	57.6%
Asthenia	19	57.6%
Arthralgia	12	36.4%
Myalgia	12	36.4%
Weight loss	8	24.2%
Erythema	8	24.2%
Fever	6	18.2%
No symptoms	3	9%

more than 20 years ago. The pulmonary function tests were within normal range in most of the patients. Features of obstruction defined as FEV1%VC<70% were found in three patients – the FEV1% median predicted for these patients was 63%. Eight patients (24%) reported Löfgren syndrome in the past. Three patients were on corticosteroid treatment at the time of study. The reported sarcoidosis symptoms were unspecific, with sweating, general weakness, and those related to respiration complaints being most frequent. Three patients (9%) reported no sarcoid symptoms. Only 2 patients (6%) reported unspecific respiratory system symptoms. Nearly sixty-seven percent of the patients reported elevated sweating. Fifty-seven percent of the subjects reported asthenia, cough, and dyspnea, while 36% reported myalgia and arthralgia. Weight loss and erythema were each reported by 24% of the patients. Nearly 20% of the patients experienced high temperature. For further analyses we calculated the sum of the physical symptoms reported by participants (M = 4.25, SD = 32.4) and considered this variable as an indicator of symptom severity.

Anxiety and depression

The scores from the HADS were separated into subscale scores. Zigmond and Snaith (13) suggested a cutoff score of ≥ 8 for both scales to include all possible cases. Of 33 patients, 9 (29%) patients scored above cutoff range on the depression subscale and 9 (31%) on the anxiety subscale.

Similarly, out of 33 subjects from the control group, 10 (29.4%) of the participants scored above the cutoff range on the anxiety scale and 8 (23.5 %) on the depression scale. In order to assess if depression and anxiety were correlated either with the length of time since the diagnosis, the undergoing treatment, or with the severity of symptoms, we calculated Pearson correlation coefficients. Symptom severity was defined here as the total amount of sarcodosis symptoms reported by patients.

Scores of anxiety and depression were not related to length of time since diagnosis (r (N= 21) = .31, p > .05, r (N = 22) = .10, p > .05, respectively) or being on current treatment (r (N= 29) = .12, p > .05, r (N = 30) = .08, p > .05, respectively). However, anxiety was significantly correlated with symptom severity (r (N= 30) = .47, p < .001). Anxiety level proved to be the main covariate of physical symptoms reported by sarcoidosis patients. This finding led us to a more detailed analysis between low and high anxiety sarcoidosis patients (median split, Me = 5.50, M = 6.16, SD = 2.57) in terms of their anxiety sensitivity.

Anxiety sensitivity and its relation to anxiety

We compared the average scores for total ASI-3 score and for each of the ASI subscale obtained by our patients to our control group and to the control group that was tested during validation of the scale (16). The results of the comparison are presented in Table 3. Sarcoid patients obtained higher scores of total anxiety sensitivity than the comparable reference groups. Further analysis of the differences confirmed our predictions that sarcoid patients have significantly more concerns about their physical symptoms than the control reference groups.

We hypothesized that anxious sarcoid patients would have an elevated total anxiety sensitivity index. To verify this prediction, a series of one way ANOVAs was carried out. Table 4 presents the results of these comparisons.

As expected, there were significant differences in the anxiety sensitivity index between patients with relatively low and high anxiety. Highly anxious patients were more sensitive to anxiety (M = 22.53, SD = 9.05) than the non-anxious patients (M = 13.86, SD = 9.52). A closer look at the ASI subscales revealed that the observed difference is responsible mainly for the social concern subscale. Anxious individuals have elevated sensitivity to social anxiety (M = 8.93 SD = 4.11) compared to relatively low anxious patients (M = 5.60, SD = 4.01).

Finally, we observed an intra-group difference in symptoms severity. On average, low anxious patients reported fewer symptoms (M = 3.2 , SD = 2.36) than anxious individuals (M = 5.0, SD = 2.45), $F_{(1, 28)}$ = 4.2, p = .05.

Discussion

One of the main findings was that sarcoid patients exhibited elevated levels of psychopathology, namely anxiety and depression. Of 33 patients, 9 (29%) scored above cutoff range indicating depres-

Table 3. Descriptive statistics of ASI concerns for men (N= 16), women (N = 17) and the entire sample (N = 33) in comparison to the sample control group (N = 32, t test for independent samples) and the Taylor et al (2007) validation group (N = 4720, women = 3153, and men = 1567, t tests for one sample).

Sample	Physical M (SD)	Cognitive M (SD)	Social M (SD)	Total score M (SD)
Men				
Control (N = 12)	3.92 (2.4)	1.50 (1.68)*	5.16 (2.76)	10.58 (4.87)
Control	3.9 (4.2)	2.8 (3.8)	6.0 (4.8)	12.8 (10.8)
Sarcoidosis	6.63 (5.3)†	2.93 (3.00)	6.94 (4.43)	16.58 (9.61)*
Women				
Control (N = 20)	3.15 (3.32)	3.25 (4.56)	6.05 (5.01)	12.45 (11.34)
Control	4.3 (4.2)	2.6 (3.8)	5.9 (4.7)	12.8 (10.5)
Sarcoidosis	7.65 (4.6)**, **	3.94 (4.9)	6.71 (4.54)	18.29 (10.90) †
Total sample				
Control (N = 32)	3.44 (3.00)	2.59 (3.81)	5.72 (4.27)	11.75 (9.38)
Control	4.2 (4.2)	2.7 (3.8)	5.9 (4.7)	12.8 (10.6)
Sarcoidosis	7.15(4.9)**,**	3.45 (4.06)	6.81 (4.41)	17.42 (10.17)*,*

*Note. The bold values (in grey) were used in t-tests for one sample as the criterion values (16), † p < .06, *p < .05, ** p < .01 , grey asterisks refer to one sample t test comparisons, black asterisks refer to the comparisons between patients and the sample group.*

Table 4. Summary of One Way Analysis of Variance for anxiety sensitivity depending on HADS anxiety level.

Variable	Low Anxiety M (SD)	High Anxiety M (SD)	F
ASI total	13.86 (9.52)	22.53 (9.05)	6.53*
Physical	6.06 (4.95)	8.80 (4.82)	2.34
Cognitive	2.20 (3.21)	4.80 (4.67)	3.15†
Social	5.60 (4.01)	8.93 (4.11)	5.05*

*Note. † p < .09, *p < .05, ** p < .01 *** p < .001*

sion and 9 (31%) exhibited anxiety. Even though control participants exhibited unusually increased levels of depression and anxiety compared to typical findings, current data confirm the previously published studies showing that anxiety and depression are common in the sarcoid population. For example, Ireland and Wilsher, also using HADS, found in their sample of 77 New Zealand sarcoid patients a prevalence of depression of 23% and anxiety of 33% (12). Drent and colleagues (1998) used the Beck Depression Inventory and found the prevalence of depression to be 18% (17). Confirmation of the prevalence of depression and anxiety was not limited to only with self-reporting assessment tools. Goracci et al, based on a structured diagnostic interview, the Mini International Neuropsychiatric Interview (MINI-PLUS), found that among 80 outpatients with sarcoidosis, 44% percent of the subjects endorsed at least one psychiatric DSM-IV axis I diagnosis (5). In this study, 25% of the subjects met the criteria for Major Depressive Disorder, 6.3% for Panic Disorder, 6.3% for Bipolar Disorder, 5% for Generalized Anxiety Disorder and 1.3% for Obsessive Compulsive Disorder. We extended the data related to prevalence of psychopathology by evaluating if anxiety and depression were associated with the sarcoidosis symptom severity. A strong association between anxiety and symptom severity was found. Furthermore, we found that patients who were highly anxious complained of more clinical symptoms of sarcoidosis than those lowly anxious. As far as we know this is the first study which has explored this relationship. In our sample, amongst the highest occurring symptoms were related to respiration, such as dyspnea. There is some indication in the literature that psychoemotional factors are associated with impairment in lung function and dyspnea (18). For example, Klonoff and Kleinhenz found the relationship between increased life stress and impairment of lung function (7). Yeager et al evaluated the association of psychosocial factors with respiratory health in 736 sarcoid individuals and found that 46% of them

reported significant symptoms of depression (vs. 27% of controls), which were associated with decreased FVC and greater dyspnea (18). In the present study we found the association of anxiety and severity of sarcoidosis symptoms, including the most frequent: sweating, dyspnea, cough and asthenia, but not depression. Increased body sensations, or body vigilance, are essential to the experience of anxiety and are common in different anxiety disorders, especially in panic disorder (19). Therefore, it is possible that elevated anxiety through heightened awareness of bodily sensations and increased number of panic symptoms might contribute to the perceived unpleasantness of symptoms such as dyspnea. Psychophysiological research has evidenced that the respiratory rate is increased by physiological arousal, and in people with respiratory disorders (COPD and asthma), the hyperventilation that results from anxiety markedly worsens shortness of breath by causing bronchoconstriction and lung hyperinflation (20;21). There is data indicating that COPD patients have higher prevalence of panic-spectrum psychopathology (22;23), (Holas, Michałowski & Domagala-Kulawik in prep.). For example, Holas et al., (in prep.) found that COPD individuals had an elevated fear of bodily sensations, increased avoidance, and an elevated level of physical concerns subscale of ASI comparing to healthy controls.

As far as we know, there is only one published study on sarcoidosis addressing the issue of panic-spectrum psychopathology. In this study, an increased number of agoraphobic/ panic symptoms were found, similarly as with COPD (7). However, data on anxiety sensitivity (AS) have not been reported yet. AS predisposes to anxiety problems (9;10), is associated with an interoceptive-oriented emotional distress, and the physical concerns subscale of the ASI were found to be uniquely and statistically predictive of bodily vigilance (24). Therefore, to assess cognitive vulnerability to anxiety, panic and bodily vigilance, we decided to examine anxiety sensitivity in sarcoid patients. As expected, they obtained higher scores of total ASI and had significantly more concerns about physical symptoms than the comparable group. The further analysis showed that highly anxious sarcoid patients had higher total ASI than the non-anxious patients, but interestingly, it was the social concern subscale of ASI, that was responsible for this difference. It seems that physical concerns are generally high in sarcoid patients, regardless of the anxiety level, whereas patients with elevated anxiety are more sensitive to negative social evaluations. One might speculate that those individuals might have fear of social scrutiny regarding their symptoms of sarcoidosis, which may further increase their general distress. The future studies should further elucidate the extent to which an anxiety and anxiety sensitivity contribute to the lung impairment, symptom severity, and problems in sarcoidosis management.

In the limitations of the present study, a relatively small number of subjects should be mentioned. The current findings should be interpreted with caution because of the lack of a Polish validation of assessment instruments used (HADS), especially since, as far as we know, there are no current Polish norms for the scale. Similarly, based on our findings, unusually high levels of depression in healthy subjects (28%) were also reported by another group (25). Given that there might be some cultural differences, the generalizability of the present findings is unclear. We did not take into account the stage of sarcoidosis in the analysis. However, in our sample, patients were only in the I or II stage of disease. Furthermore, in our clinical practice we do not observe major correlation between the number and intensity of clinical symptoms and the stage of sarcoidosis based on chest X-ray. There is a possibility that corticosteroid use might cause psychological symptoms. However, in the present study we did not find any relationship between psycho-emotional distress and corticosteroid use.

In conclusion, anxiety and depression were found to be common in patients with sarcoidosis. Anxiety was significantly correlated with symptom severity reported by patients. Patients also showed elevated anxiety sensitivity and had more physical concerns when compared to reference groups. Those who were additionally highly anxious feared more of negative social evaluation. These findings call for including stress and anxiety management interventions into the diagnostic procedures, management and treatment protocol for sarcoidosis and point to including behavioral medicine practitioners or mental health professionals in the management of this disease.

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