Abstract

Background

Sarcoidosis is a chronic disease of unknown aetiology. While it involves various organs, the most common sites of involvement include hilar and mediastinal lymph nodes and the pulmonary parenchyma. Sarcoidosis is a rare disease. Its prevalence varies depending on the part of the world. Sarcoidosis is mainly a disease of young adults, with a slight female-to male predominance. The aetiology of sarcoidosis is unclear and may be associated with bacterial infection or immune-mediated mechanisms. In many patients, the clinical course of sarcoidosis is mild and does not require treatment. However, In about 10% of the cases, the disease leads to pulmonary dysfunction and involvement of extrapulmonary organs, including the heart and the central nervous system. Treatments for sarcoidosis include systemie glucocorticosteroids, immunosuppressant drugs and biologicals.

Aims of the study

The principal aim of the study was to assess the clinical course of sarcoidosis in patients hospitalised at the Department of Respiratory Medicine, University of Warmia and Mazury, Olsztyn, Poland, in 2013–2017, focusing, in particular, on population characteristics and prognostic factors.

The specific aims of the study were as follows:

1. To characterise the group of patients in terms of sex, age, BMI, occupational status, smoking status, and co-morbidities.
2. To analyse the onset of the disease with the accompanying erythema nodosum (Löfgren syndrome) or without this syndrome, and to assess whether the presence of this syndrome affects the course of the disease. To analyse the subjective symptoms reported by the patients. To analyse the diagnostic methods used in the patients in the study population. To analyse the laboratory test results and the respiratory tract microflora determined by microbiological investigation of bronchoalveolar lavage fluid (BALF). To assess the correlations between radiographic (chest radiography, CT) changes in the mediastinal and hilar lymph nodes, changes in the pulmonary parenchyma, and abnormalities in lung function. To analyse the extrapulmonary changes.
3. To analyse the group of patients who experienced complete radiological remission in the pulmonary parenchyma and the mediastinal and hilar lymph nodes Turing the follow-up.
4. To assess the disease course in patients requiring systemic treatment for sarcoidosis, to analyse the factors that could contribute to a severe course of the disease, and to assess the treatment outcomes.
5. To assess the usefulness of ^{67}Ga scintigraphy in selected patients.

Material and methods

We retrospectively analysed medical records of patients hospitalised at the Department of Respiratory Medicine, University of Warmia and Mazury, Olsztyn, Poland, from 1 January 2013 to 31 December 2017, with a diagnosis of sarcoidosis. The study population consisted of

158 patients (82 women and 76 men) aged 23-73 years. We analysed BMI, smoking history, occupational status, subjective symptoms, and co-morbidities. We investigated the impact of Löfgren syndrome occurring at the onset of the disease on the further course of sarcoidosis. We analysed which methods were used to establish the pathological diagnosis of sarcoidosis. We analysed chest radiographs and CT scans and assessed the correlation between the stage of sarcoidosis and the results of lung function tests (TLC, RV, FVC, TL_{CO}, 6MWT). We assessed laboratory test results (lymphocyte and platelet counts, blood calcium levels, transaminase levels, eGFR, results of microbiological investigation of BALF) and the extrapulmonary changes in the course of sarcoidosis. We analysed the course of the disease in 20 subjects who achieved complete radiological remission in the chest, and a group of 26 patients with severe sarcoidosis who required systemic treatment. We also evaluated the usefulness of ^{67}Ga scintigraphy which had been performed in 85 patients from the study population. Statistical analysis of the results was carried out using STATISTICA 13 PL.

Results

There was a slight female-to-male predominance in the study population (F:M ratio was 1.07:1), and the mean age of onset was 43.8±11.3 years and was significantly high er In women. Most of the study subjects were never or former smokers. Only 21.5% of the subjects had normal BMI values, and the remaining subjects were overweight or obese. Most subjects performed physical labour. The most common complaints were cough, shortness of breath, and joint pain. A total of 65.2% of the study population had chronic co-morbidities, the most common ones being hypertension, cholelithiasis, nephrolithiasis and hypothyroidism. In 34.2% of the study population (i.e. significantly more commonly than in individuals aged below 40 years), sarcoidosis first manifested as Löfgren syndrome. In these patients, TL_{CO} improvement, no airway obstruction on spirometry, and normalisation of serum calcium levels were observed on treatment. In 92.4% of the study population a pathological diagnosis of sarcoidosis had been obtained. In more than a half of the subjects, the diagnosis had been established based on the examination of a mediastinal lymph node collected during a mediastinoscopy. Methicillin-susceptible *Staphylococcus aureus* (MSSA) was the most common pathogen cultured from BALF. In patients with severe disease who required systemic treatment with glucocorticosteroids, a decreased FVC at the onset of the disease was more commonly observed. In smokers, a reduced TL_{CO} was significantly more common. In most subjects, a positive correlation was observed between improved lung function test results and radiological remission. Hypercalcaemia was observed in 26.5% of the subjects and a significantly reduced Eger was seen in 7%. In some patients, these abnormalities required treatment. The subgroup of patients treated for renal impairment was predominated by males. Other laboratory abnormalities (lymphopenia, thrombocytopenia, elevated transaminases) were mild and did not require treatment. Extrapulmonary changes were detected in 25.9% of the subjects. The most common extrapulmonary organ involved was the spleen. In a total of 12.7% of the subjects, within 25.3±16.1 months after diagnosis, a complete regression of radiographic changes in the chest was observed. In spite of the complete radiological remission, some of the patients continued to have abnormal lung function test results (particularly TL_{CO}). A total of 16.5% of the study population required systemic treatment for

their sarcoidosis, with the most common reason for initiating such treatment being a deterioration in lung function test results. A severe clinical course of sarcoidosis was more commonly observed in current and former smokers. A considerable proportion of subjects required second- and third-line treatment. Eighty-five subjects underwent ^{67}Ga scintigraphy, which revealed, in most of the patients, articular changes in the course of sarcoidosis. This imaging modality proved useful in the diagnosis of muscular and renal involvement and in the assessment of disease activity in the pulmonary parenchyma and hilar and mediastinal lymph nodes.

Conclusions

1. There was a slight female-to-male predominance in the study population of subjects with sarcoidosis. Most patients were overweight or obese and had co-morbidities, with hypertension being the most common one. Only a small proportion of the subjects were current smokers. The occurrence of Löfgren syndrome at the onset of the disease was associated with a higher rate of improvement in some of the lung function parameters (TL_{CO}, spirometry) and with the normalisation of serum calcium in patients on treatment.

2. In 12.7% of the study population, most commonly in females, a complete radiological remission was observed. Despite complete regression of the changes in the chest, lung function abnormalities, including impaired TL_{CO}, persisted.

3. The clinical course of sarcoidosis in most of the patients was mild. Systemic treatment was required by 16.5% of the patients in the study population, more commonly by patients with co-morbidities, current smokers and former smokers. A decreased FVC at the onset of the disease was an adverse prognostic factor. Deterioration of lung function was the most common indication for initiating systemic treatment.

4. ^{67}Ga scintigraphy is very effective in visualising joint and bone lesions in sarcoidosis, and can also be useful in assessing renal and ocular involvement. It is the Orly modality that enables the assessment of lesions in skeletal muscles. As far as chan ges in the pulmonary parenchyma and lymph nodes are concerned, ^{67}Ga scintigraphy is particularly useful for the assessment of disease activity.