



Retrospective analysis of the frequency and variety of skin lesions in patients diagnosed with sarcoidosis and examined by dermatology in a tertiary health care facility

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Abstract

ARTICLE INFO

Keywords:

Cutaneous sarcoidosis
Systemic sarcoidosis
Non-caseating granuloma
Skin
Erythema nodosum

Received: Dec 29, 2022

Accepted: Jun 01, 2023

Available Online: 23.06.2023

DOI:

[10.5455/annalsmedres.2022.12.397](https://doi.org/10.5455/annalsmedres.2022.12.397)

Aim: The aim of this retrospective study is to examine the frequency and clinical features of skin lesions in patients with sarcoidosis and to compare them with the literature.

Materials and Methods: The files of patients diagnosed with sarcoidosis in the last 10 years in our hospital were reviewed retrospectively. Age, gender, age at diagnosis, dermatology consultation or dermatological examination findings were recorded for all patients.

Results: Thirty (69.8%) of the patients diagnosed with sarcoidosis were female and 13 (30.2%) were male. The mean age was 49.7 ± 12.2 . When the patients are grouped according to the age ranges at which they are diagnosed, there are 1 (%2.3) patient between the ages of 10-19, 4 (%9.3) patients between the ages of 20-29, 6 (%13.9) patients between the ages of 30-39, 16 (%37.2) patients between the ages of 40-49, 8 (%18.6) patients between the ages of 50-59 and 8 (%18.6) patients over the age of 60. The mean age at which female patients were diagnosed with sarcoidosis was 47.56 ± 12.85 , and the mean age at which male patients were diagnosed with sarcoidosis was 41.86 ± 13.81 years. The mean follow-up period of the patients was 4.0 ± 3.1 years. Thirty-one (72.1%) of all patients were examined in dermatology. Dermatological findings including erythema nodosum were detected in 8 (18.6%) patients.

Conclusion: Sarcoidosis is a multisystemic disease that can progress with various clinical findings and should be considered in the differential diagnosis with its frequent or rare findings. In this study, in which the data of patients diagnosed with sarcoidosis in the last 10 years in our hospital were evaluated, our findings were generally similar to the literature data.



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Introduction

Sarcoidosis is a non-caseating granulomatous disease of unknown origin, usually involving the lungs, peripheral and mediastinal lymph nodes, spleen, liver, eyes, skin, and parotid gland. It is a multisystemic disease characterized by inflammation [1-3]. The incidence, prevalence and burden of disease of sarcoidosis vary widely by geographic region, gender, ethnicity and age groups [4]. The reason of sarcoidosis remains unclear, but various factors, including infection, genetic predisposition, and environmental conditions, may play a role [5]. The most important feature of the disease is that the rate of spontaneous remission is 60-70% and the chronic course is observed only in 10-30%

of the disease. Therefore, sarcoidosis is generally evaluated in the group of diseases with a benign course and good prognosis. Mortality rates range from 1-5%, often due to respiratory failure, neurosarcoidosis, and cardiac involvement [6,7].

According to studies, skin is the second or third most commonly affected organ in sarcoidosis, present in up to one-third of the patients. Cutaneous sarcoidosis lesions are frequently the initial signs of the disease and sarcoidosis can stay an isolated dermatological situation in more than 30% of cases. In patients with cutaneous and systemic sarcoidosis, skin findings rise before or at the time of diagnosis in 80% of patients [8]. Skin manifestations are typically multiple erythematous macules, papules, plaques, or subcutaneous nodules. They usually do not cause symptoms, but may have aesthetic significance when localized to the face, as in classic lupus pernio. Specific cutaneous sar-

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coidosis can also occur in scar tissue, traumatized areas, and around embedded foreign objects such as tattoos. Cutaneous sarcoidosis is generally considered a great mimic. Psoriasis, lichenoid, verrucous, and angiolupoid are less common variants of papular or plaque sarcoidosis, which may be confused with psoriasis, lichen planus, warts, or lupus erythematosus, respectively. Erythema nodosum is the most common nonspecific lesion, developing in 25% of cases [8,9]. Other non-specific cutaneous manifestations of sarcoidosis include calcinosis cutis, clubbing, and prurigo [10].

The diagnosis of sarcoidosis is made by demonstrating a non-caseating granuloma structure in one or more tissues in addition to compatible clinical and radiological findings and excluding other granulomatous causes [11]. Since skin symptoms are included in the differential diagnosis with many dermatological diseases, it should be first considered for diagnosis. The aim of this retrospective study is to examine the frequency and clinical features of skin lesions in patients with sarcoidosis and to compare them with the literature.

Materials and Methods

The study was carried out in accordance with the Helsinki declaration. Approval for the study was obtained from the local ethics committee on 29.09.2020 (Inonu University Clinical Research Ethics Committee, decision no: 2020/1029). The files of patients diagnosed with sarcoidosis in the last 10 years in our hospital were reviewed retrospectively. Age, gender, age at diagnosis, dermatology consultation or dermatological examination findings, lung tomography findings, biopsy method, and duration of follow-up of patients were recorded for all patients. The patients were divided into groups according to their age ranges. Age of onset of the disease was compared according to gender.

Statistical analysis

The SPSS v22.0 (IBM corp, released 2013, Armonk, NY) software was used for statistical analysis. Shapiro–Wilk’s test was used to investigate the compliance of continuous variables with normal distribution. Chi-square analyses and Fisher’s Exact Test were used in the analysis of cross tables (distribution of categorical variables). Categorical data were summarized as number (percentage) and continuous data as mean \pm standard deviation (SD). Independent sample t-test was used for the comparison between genders, since the age of onset of the disease fit the normal distribution. P values <0.05 were defined to indicate statistical significance.

Results

Thirty (69.8%) of the patients diagnosed with sarcoidosis were female and 13 (30.2%) were male. The mean age was 49.7 ± 12.2 (minimum: 20, maximum: 73). When the patients are grouped according to the age ranges at which they are diagnosed, there are 1 (%2.3) patient between the ages of 10-19, 4 (%9.3) patients between the ages of 20-29, 6 (%13.9) patients between the ages of 30-39, 16 (%37.2) patients between the ages of 40-49, 8 (%18.6) patients between the ages of 50-59 and 8 (%18.6) patients over the

Table 1. Demographic and clinical characteristics of sarcoidosis patients.

Demographic and clinical characteristics	Mean \pm SD	
Age at diagnosis, mean \pm SD	45.81 \pm 13.25	
Follow-up time (years), mean \pm SD	4.0 \pm 3.1	
	Subgroup	n (%)
Gender	Female	30 (69.8)
	Male	13 (30.2)
Skin findings	Yes	8 (18.6)
	No	35 (81.4)
Lung parenchyma findings	Yes	41 (95.3)
	No	2 (4.7)
Lung mediastinal findings	Yes	41 (95.3)
	No	2 (4.7)
Biopsy method	No	11 (25.6)
	TBB	10 (23.3)
	EBUS	6 (14)
	VATS	9 (20.9)
	Others (skin, ekstratorasik LAP)	5 (11.6)
	Lung + others	2 (4.7)

Table 2. Comparison of sarcoidosis patients by age groups and gender.

Disease age range	Female, n (%)	Male, n (%)	P value
0-39 years	6 (20)	5 (38.5)	0.26
>40 years	24 (80)	8 (61.5)	
Total	30 (100)	13 (100)	

age of 60. The mean age at which female patients were diagnosed with sarcoidosis was 47.56 ± 12.85 , and the mean age at which male patients were diagnosed with sarcoidosis was 41.86 ± 13.81 years. It was determined that the age at diagnosis of female patients was 6 years longer than that of male patients. There was no statistically significant difference between men and women in terms of the mean age of onset of the disease ($p=0.19$). The mean follow-up period of the patients was 4.0 ± 3.1 years. Thirty-one (72.1%) of all patients were examined in dermatology. Dermatological findings including erythema nodosum were detected in 8 (18.6%) patients. When we look at eight patients with dermatological findings, it was seen that respiratory complaints started first in 4 (50%) patients, skin findings developed first in 3 (37.5%) patients, and skin findings and respiratory complaints started together in 1 (12.5%) patient at the time of diagnosis (Table 1).

The patients were divided into two groups according to age, as under 40 years old and over, and compared according to gender. There was no statistically significant difference according to age groups in male and female patients ($p=0.26$) (Table 2).

Discussion

In spite of extensive research over the past several decades, the pathogenesis of sarcoidosis remains incompletely understood. The mostly held view is that the granulomatous process is driven by an exaggerated immune response to the yet unknown antigen [12,13]. Granulomatous inflammation is characterized by a Type-1 helper (Th1)-mediated immune response with accumulation of macrophages, monocytes, and activated T-lymphocytes, and an elevated production of key inflammatory mediators [as tumor necrosis factor (TNF)- α , interleukin (IL)-12, interferon (IFN)- γ , IL-2, Tumor growth factor (TGF)- β , IL-18, and IL-8] [14].

Some studies describe that sarcoidosis is more common in women than in men, and others observe no difference between the sexes [15,16]. Women tend to be diagnosed with sarcoidosis at a later age. A later age at diagnosis in women than in men may be associated with reduced lung function associated with menopause [17]. Sarcoidosis is usually diagnosed between the ages of 30-50 [18]. The mean age of the patients in our study at the time of diagnosis was 45.81 ± 13.25 years and the female/male ratio was 2.3, which was consistent with the literature. In the study conducted by Musellim et al. [2] on 293 sarcoidosis patients in Turkey, it was concluded that the disease is more common in women (female/male: 2.08) and the diagnosis age of women is 10 years longer than men. Similarly, in the study of Fernández-Ramón et al. [16], the highest incidence in men was in the 30-39 age range, 10 years earlier than in women. In our study, the mean age at diagnosis was 47.56 ± 12.85 in females and 41.76 ± 13.81 in males. Thus, the mean age at diagnosis of women was 6 years longer than men. Sadi Aykan et al. [7], when grouped according to the age at diagnosis, it was observed that although there was accumulation between the ages of 30-49, the greatest peak was in the group above 50 years of age. In our study, similar to this study, although there was accumulation between the ages of 30-49, the disease was seen at an equal rate in the groups aged 40-49 and over the age of 50. Childhood sarcoidosis is rare; it has 2 different forms, early onset and late onset. Although the prognosis is better in children than in adults, symptomatic multisystem involvements are more severe at very young ages [19]. In our study, there was 1 child patient and he was 15 years old at the time of diagnosis. At the time of diagnosis, he had no skin findings but had symptomatic pulmonary findings.

Cutaneous involvement in all sarcoidosis cases ranges between 9-37% [20]. In our study, this rate was found to be 18.6%, which is consistent with the literature. Maculopapular lesions are the most common specific cutaneous sarcoidosis lesions. Lesions are frequently localized in the head, neck, back, extremities, and rarely in the oral cavity [21]. The papules and papulonodular lesions of sarcoidosis are typically located on the face, particularly in the eyelids and nasolabial folds, but also on the neck, trunk and extremities, or within old wounds. Plaque lesions are localized on the extensor surfaces of the back, buttocks, face and extremities, may occur within scars [8]. In our study, the most common lesion area was the head-neck region with a rate of 33.3%, consistent with the literature.

In studies evaluated according to skin lesion types, Mangas et al. [1] reported the most common noduloplaque form (%31), Güler et al. [22] the most common papule, plaque and nodule forms (33.3%), Collin et al. [23] the most common papule form (44%), Jung et al. [24] reported that the most common noduloplaque form (%41.2). In our study, papule form in 3 (37.5%) patients, erythema nodosum in 2 (25%) patients, nodule form in 1 (12.5%) patient, subcutaneous nodular form in 1 (12.5%) patient, 1 (12.5%) patient had plaque form.

Clinical suspicion and characteristic histological findings are important for diagnosis [21]. The diagnosis of sarcoidosis is based on three main criteria: consistent and adequate clinical presentation; demonstrating the presence of non-caseating granulomas in one or more tissue samples; and exclusion of other causes of granulomatous disorders [25]. The clinical diagnosis of sarcoidosis is difficult due to the polymorphic nature of the lesions and being a mimic disease. Differential diagnosis includes lupus vulgaris (cutaneous tuberculosis), rosacea, lupus erythematosus, eosinophilic granuloma faciei, perniones (frostbite), granuloma annulare, atypical mycobacteriosis, leprosy, leishmaniasis, syphilis, cutaneous lymphoma [26]. Therefore, infectious agents should be excluded in biopsy materials and laboratory tests, and sarcoidal granulomas should be distinguished from other granuloma-causing diseases.

As a result; Sarcoidosis is a multisystemic disease that can progress with various clinical findings and should be considered in the differential diagnosis with its frequent or rare findings. For the diagnosis of cutaneous sarcoidosis, it is necessary to suspect first. A detailed physical examination should be performed for diagnosis; The diagnosis should be made in the presence of clinical, histopathological, radiological and laboratory findings. Patients with cutaneous sarcoidosis should be screened for systemic involvement and followed up.

Ethical approval

Inonu University Clinical Research Ethics Committee approval was obtained (No: 2020/1029).

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