Cutaneous involvement in sarcoidosis: analysis of the features in 170 patients

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Summary In our study, we retrospectively evaluated the clinical features of patients diagnosed as sarcoidosis at our center within the last 36 years and who had skin involvement. Cutaneous involvement was observed in 170 patients (32.9%, 136 females, 34 males). The most frequent skin lesion was erythema nodosum (EN) (106 subjects, 20.5%). In addition, skin plaques and subcutaneous nodules were observed in 22 cases (4.3%), maculopapular eruptions in 19 cases (3.7%), scar lesions in 15 cases (2.9%), lupus pernio (LP) in 14 cases (2.7%) and psoriasiform plaques in five cases (0.9%). Among patients with LP (64.3%) and scar lesions (40%), pulmonary parenchymal involvement was more frequent than patients with other skin lesions. Parenchymal involvement present in 10.4% of patients with EN was significantly less than in patients with LP and scar lesions (P values, respectively, <0.001, 0.002). When patients with skin involvement were compared to other sarcoidosis patients, it was seen that the frequency of females among those with skin involvement was significantly higher than the frequency among other sarcoidosis patients (P<0.001). Parenchymal involvement in sarcoidosis patients without skin involvement was less frequent than in patients with LP; however, more frequent than in patients with EN (both P values=0.002). As a conclusion, skin involvement was diagnosed in approximately one-third of our sarcoidosis patients with a generally female predominance. EN was the most frequent skin lesion encountered. Parenchymal involvement was more frequent in patients with LP and scar lesions and less frequent in patients with EN.

KEYWORDS Sarcoidosis; Cutaneous involvement; Erythema nodosum; Lupus pernio; Scar lesions; Maculopapular eruptions

Introduction

Sarcoidosis is a multisystem disease of unknown etiology characterized by the formation of non-caseating granulomas in the affected organs. Although different series report variable incidences of skin involvement during the course of the disease, nearly one-fourth of sarcoidosis patients have skin involvement.1-3 Different skin lesions associated with sarcoidosis have been reported.4,5 These lesions are divided into two as: specific skin lesions where histologic examination shows the typical sarcoid granulomas and nonspecific skin lesions.3-5 Specific lesions are lupus pernio (LP), infiltrated plaques, maculopapular eruptions, subcutaneous nodules and scars. The most important nonspecific skin lesion seen in sarcoidosis is erythema nodosum (EN).3

In this study, we retrospectively aimed to evaluate the general clinical and demographic features of patients followed up as sarcoidosis at our center who had specific and nonspecific skin lesions. Also, we compared the features of subjects with and without skin involvement.
Materials and methods

Five hundred and sixteen patients (341 females, 175 males) attending the Lung Diseases Department of Cerrahpaşa Medical Faculty, Istanbul, fulfilled clinical or radiologic or both features of sarcoidosis, also supported by the histologic evidence of noncaseating granulomas. Patients with clinical and radiologic features of sarcoidosis have been excluded if there was no histologic confirmation. However, patients with acute disease onset with EN and a radiograph with BHL were considered to have sarcoidosis even though they did not have any histologic confirmation. As a result, 170 of these subjects (32.9%) who had skin involvement of sarcoidosis were included into the study. Other 346 patients with sarcoidosis were taken as the control group.

When diagnosing specific skin lesions, histologic findings were considered. During the study period, the patients had not been whole body screened for skin lesions. The skin changes reported by the patients and noted in the medical charts were taken into account. Patients were included in this study on the basis of clinical data typical of EN: new-onset nodular hypodermitis of <2 months duration, discoloration varying from red to yellow-brown, and localization usually on the legs. In the presence of atypical hypodermitis, skin biopsy was performed to confirm EN.

The medical charts were used to obtain data about the patients’ age, sex, disease stage according to chest X-ray and biopsy results. According to the classification of chest X-rays by De Remee:6 stage I, meant bilateral hilar lymphadenopathy (BHL); stage II, BHL plus pulmonary parenchymal infiltration; and stage III, parenchymal involvement infiltration without BHL.

For statistical evaluation of the data, chi-square and student’s t tests were used.

Results

Out of 516 sarcoidosis patients, 170 (32.9%) presented with various skin manifestations and 136 of them were females and 34 were males. EN was observed to be the most frequent skin lesion. In all types of skin lesions, the number of female patients outnumbered males. The distribution of skin lesions and the demographic features of the patients are shown in Table 1. Although the differences were not significant, the LP group had the highest and the subcutaneous nodule group had the lowest mean age (Table 1).

Fifteen patients (14.1%) with EN simultaneously had subcutaneous nodules, eight (7.5%) had maculopapular rash and skin plaques, and one had LP. One of the patients with maculopapular rash also had a cutaneous plaque. In addition, the clinical presentation of 71 (67%) of the 106 patients with EN was in the form of acute sarcoidosis-Löfgren syndrome.

When the clinical and demographic features of patients with skin involvement were compared to other sarcoidosis patients, results as shown in Table 2 were obtained. The prevalence of females among sarcoidosis patients with skin involvement was significantly higher in comparison to those without skin involvement (P<0.001). Although the mean age and the frequency of pulmonary parenchymal involvement was less in the group with skin involvement, the difference was not significant (Table 2).

The distribution of skin lesions in various radiographic stages of sarcoidosis is shown in Table 3. Pulmonary parenchymal involvement was most frequent in subjects with LP (64.3%) and scar lesions (40%) (Table 1). The incidence of parenchymal involvement in patients with EN was significantly less frequent than in patients with LP, scar lesions and those without skin involvement.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>The frequency of various skin lesions in our sarcoidosis patients, the demographic features and the frequency of parenchymal involvement in these different groups.</th>
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<tbody>
<tr>
<td></td>
<td>n (%)</td>
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<tr>
<td>Erythema nodosum</td>
<td>106 (20.5)</td>
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<tr>
<td>Skin plaques</td>
<td>22 (4.3)</td>
</tr>
<tr>
<td>Subcutaneous nodules</td>
<td>22 (4.3)</td>
</tr>
<tr>
<td>Maculopapular rash</td>
<td>19 (3.7)</td>
</tr>
<tr>
<td>Scar lesions</td>
<td>15 (2.9)</td>
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<tr>
<td>Lupus pernio</td>
<td>14 (2.7)</td>
</tr>
<tr>
<td>Psoriasiform lesions</td>
<td>5 (0.9)</td>
</tr>
</tbody>
</table>
The incidence of parenchymal involvement in patients with LP was significantly higher than in patients with maculopapular rash, plaque lesions, subcutaneous nodules and patients without skin involvement (P values, respectively, 0.002, 0.01, 0.01, 0.002).

**Discussion**

Different series report variable frequencies of skin involvement in sarcoidosis. In our study, approximately one-third of the patients had sarcoidosis-related skin lesions. In two different series, skin lesions other than EN were reported to be 11% and 19%. In our study, the frequency of skin lesions other than EN was 18.8%. The frequency of cutaneous involvement and also that of particular types of skin lesions in sarcoidosis vary in different races and geographical regions. Studies from America reported that in addition to sarcoidosis being more frequent in individuals of African-American origin, skin involvement in these subjects also took a more severe form. One study said that black South African sarcoidosis patients had extensive skin involvement. Indian sarcoidosis patients were reported to have skin involvement at a frequency of 42%. Although LP was previously thought to be limited to Northern Europe, patients from other areas of the world have also been reported. Studies from USA, UK and Finland reported that one of the most frequent causes of EN was sarcoidosis.

We observed that females were more frequent in our sarcoidosis patients with skin involvement than in those with no skin involvement. Other series about skin involvement in sarcoidosis similarly reported that skin was more frequently involved in females. This might be because hormones, particularly estrogen, might play a role in the development of skin lesions—especially EN. Another factor which increases the frequency of females in sarcoidosis patients with skin lesions might be not making every patient undergo a routine dermatologic check-up; however, including only the skin lesions reported by the patients. This might be explained by the possibility that females have a greater tendency than males to observe their body for this type of changes.

The most frequently encountered skin lesion in our sarcoidosis patients was EN: it is known to be a nonspecific skin lesion of sarcoidosis, points to acute and benign disease and its frequency varies according to geographic regions and in people of different ethnicities. The fact that nearly two-thirds of our patients with EN had acute sarcoidosis...
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(Löfgren syndrome) supports the thought that it is associated with acute, benign disease. It was also suggested that 17% of sarcoidosis patients presented with Löfgren syndrome-EN. In different series of EN, the etiologies are quite variable depending on ethnic background and geographical region; however, sarcoidosis is one of the most frequent causes of EN. A recent large survey on the etiology of EN reported that the most frequent cause of secondary EN was sarcoidosis. In that study, in three-fourths of the patients in whom EN were secondary to sarcoidosis, the clinical presentation was in the form of Löfgren syndrome.

It is known that sarcoidosis patients presenting with EN and Löfgren syndrome are younger and predominantly female when compared to others. EN, like all other types of skin lesions, was more frequent in females. There was no significant difference in the mean age of the groups with different skin lesions. It was said that sarcoidosis patients with EN had a better prognosis than others. In our study, the prognoses of these patients were not evaluated. However, the less-frequent involvement of the pulmonary parenchyma in EN patients than in patients with other skin lesions, and the higher number of early stage patients among those with EN support the hypothesis that EN is associated with benign disease.

Maculopapular eruptions were detected in 3.7% of our patients. Some studies about this subject claim that they are the most frequent form of granulomatous cutaneous involvement in sarcoidosis. Maculopapular lesions—similar to EN—usually accompany acute sarcoidosis and they are a good prognostic parameter. In that study, pulmonary parenchymal involvement was relatively less frequent in patients with maculopapular lesions. It was also reported that maculopapular lesions coexist with especially EN. In our study, EN was present in 42% of the subjects with maculopapular lesions.

LP is the most characteristic skin lesion in sarcoidosis. It was demonstrated that it pointed out to chronic fibrotic disease of long duration. LP was diagnosed in 2.7% of our patients. In different series, LP was reported to occur at a frequency of 2.6% in sarcoidosis. The presence of parenchymal involvement in more than half of our patients with LP confirms that it is the hallmark of chronic fibrotic disease.

Old scar infiltrations and skin plaques are commonly observed skin lesions in generally chronic sarcoidosis. Patients with these lesions usually have extrathoracic involvement. While these lesions were present in 2.9% of our patients, it was important that pulmonary parenchymal involvement was more frequent in such cases. Skin plaques were relatively more frequent skin lesions than scars. However, parenchymal involvement in these cases was not as prominent as in scar lesions. A large series reported that plaques were present in 6.2% and scar lesions in 1.3% of patients.

It is said that subcutaneous nodules are less frequent in sarcoidosis than other skin lesions. Although it was reported that subcutaneous nodules were associated with EN, it was also said that they were skin lesions more frequently accompanying systemic form of sarcoidosis. It was suggested that they were of no prognostic importance. In our study, 68% of patients with subcutaneous nodules had EN and parenchymal involvement in these patients was less frequent than those with chronic lesions like LP; so, we can say that it is a benign form more commonly associated with EN.

Of cutaneous sarcoidosis lesions, only lesions which become chronic and leave scar, like LP and plaque lesions, need to be treated with systemic steroid therapy. However, in most of the cases steroid therapy is needed because of organ involvement other than the skin. The treatment and overall prognosis of cutaneous sarcoidosis is primarily dependent on the degree of systemic involvement. In case of disfiguring skin lesions, local or intralesional steroid therapy might sometimes be effective. It was reported that in addition to steroids hydroxychloroquine and methotrexate might be of help in chronic cutaneous sarcoidosis. It is not generally necessary to administer immunosuppressive therapy for EN, symptomatic therapy is usually enough.

Concluding, we saw that approximately one-third of our sarcoidosis patients were affected by different skin lesions. Females were more frequent among subjects with skin involvement. EN was the most common skin lesion among our sarcoidosis patients. Although pulmonary parenchymal involvement was more frequent in patients with scar lesions and LP, it was less frequently seen in the presence of EN, maculopapular and plaque lesions.

References