Case Report / Olgu Sunumu
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Treatment of Subcutaneous Sarcoidosis with Hydroxychloroquine in a Hepatitis B Carrier Patient: A Case Report

Hepatit B Taşıyıcısı Bir Hastada Subkutan Sarkoidozun Hidroksiklorokin ile Tedavisi: Olgu Sunumu

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ABSTRACT

Sarcoidosis is a disorder of unknown etiology affecting many systems and characterized by non-caseating granulomas. Subcutaneous sarcoidosis is the rarest form of specific lesions in cutaneous sarcoidosis. It occurs more frequently in the fourth decade of life and is more common in females than in males. Multiple asymptomatic to slightly painful, firm, mobile, round to oval, skin-colored, or erythematous nodules frequently occur in a bilateral and asymmetric pattern on the extremities. In the differential diagnosis, other diseases presenting with subcutaneous nodules should be excluded. Here, a case of subcutaneous sarcoidosis in a 51-year-old female hepatitis B carrier patient who partially responded to topical steroid treatment and was successfully treated with hydroxychloroquine was presented. In subcutaneous sarcoidosis, patients should be evaluated for systemic involvement. Hydroxychloroquine should be considered among the treatment options.
Keywords: Sarcoidosis; subcutaneous; hydroxychloroquine.

ÖZ

Sarkoidoz, etiyolojisi tam olarak bilinmeyen, birçok sistemi tutan, non-kazeifiye granülomlarla karakterize bir hastalıktır. Deri sarkoidozunda spesifik lezyonların en nadir görülen formu subkutan sarkoidozdur. Subkutan sarkoidoz genellikle yaşamın dördüncü dekadında daha sık görülür ve kadınlarda erkeklerden daha yaygındır. Çoğunlukla ekstremitelerde, bilateral ve asimetrik bir şekilde yerleşen, çoklu asemptomatikten hafif ağrılıya kadar değişebilen, sert, hareketli, yuvarlak ila oval, deri renginde veya eritemli nodüller şeklinde görülür. Ayırıcı tanıda subkutan nodül ile seyreden diğer hastalıklar dışlanmalıdır. Bu çalışmada, topikal steroid tedavisine kısmen yanıt veren ve hidroksiklorokin ile başarılı bir şekilde tedavi edilen, hepatit B taşıyıcısı olan 51 yaşında bir kadın hastada görülen bir subkutan sarkoidoz olgusu sunulmaktadır. Subkutan sarkoidozda hastalar sistemik tutulum açısından da değerlendirilmelidir. Tedavi seçenekleri arasında hidroksiklorokin düşünülmelidir.
Anahtar kelimeler: Sarkoidoz; subkutan; hidroksiklorokin.

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INTRODUCTION

Sarcoidosis, with skin involvement as the second most common manifestation after pulmonary involvement, can present with different morphologies and has been referred to as the "great imitator" (1,2). Subcutaneous sarcoidosis, also known as Darier-Rousy sarcoidosis, is a rare form of cutaneous sarcoidosis. The incidence of subcutaneous sarcoidosis increases in the 4th decade of life and it is more common in

females (1,2). In the treatment of cutaneous sarcoidosis, the extent of lesions and systemic involvement are important and treatment plans should be created accordingly (3).

This case report aimed to present a case of subcutaneous sarcoidosis in a hepatitis B carrier patient who partially responded to topical steroid treatment and was successfully treated with hydroxychloroquine.

CASE REPORT

A 51-year-old female patient applied to our clinic with a complaint of painless swelling in her arms for approximately 1.5 years. Lesions initially appeared as small nodules on both arms and gradually enlarged over time. The patient had a history of hepatitis B carrier status and cholecystectomy. Dermatological examination revealed numerous painless, firm, erythematous subcutaneous nodules ranging from 1 to 3 cm in diameter on the extensor surfaces of both arms (Figure 1).

In the histopathological examination, hyperkeratosis, hypergranulosis, and acanthosis were observed in the epidermis; epithelioid histiocytes, multinucleated giant cells, and granuloma structures consisting of lymphocytes and intense inflammation were observed in the deep dermis and subcutaneous fatty tissue; and no staining with Ziehl-Neelsen or periodic acid-Schiff was observed (Figure 2). The patient was diagnosed with subcutaneous sarcoidosis and referred to the pulmonology and ophthalmology departments for examinations of systemic involvement. A chest X-ray revealed hilar fullness (Figure 3), while thorax computed tomography detected millimetric nodules and hilar lymph nodes consistent with sarcoidosis. Serum angiotensin-converting enzyme and calcium levels were normal, as were the results of liver function tests, blood counts, thyroid function tests, and sedimentation rate. Anti-streptolysin O was negative and no ocular pathology was detected. HBsAg, anti-HBe, HBV-DNA, and anti-HBc IgG (+) were present. Due to the patient's status as a carrier of hepatitis B, clobetasol 17-propionate was started instead of systemic corticosteroids. A partial response was achieved after 2 months of treatment. Since the patient's ophthalmological examination and laboratory tests were normal, hydroxychloroquine 400 mg/day was initiated. After 5 months, the lesions disappeared completely.

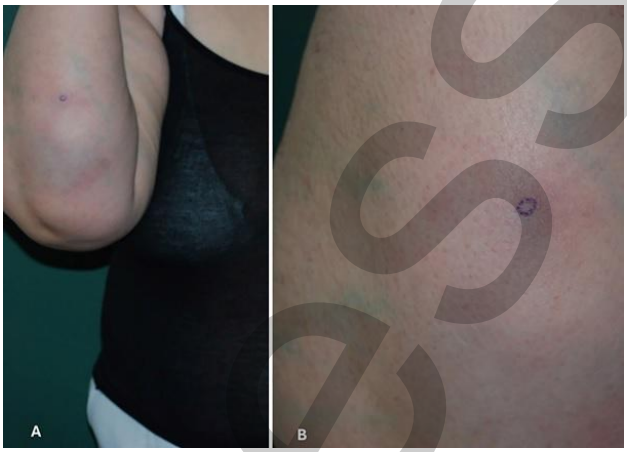

Figure 1. A) Firm, erythematous subcutaneous nodules on right forearm, **B)** Closer view of picture A

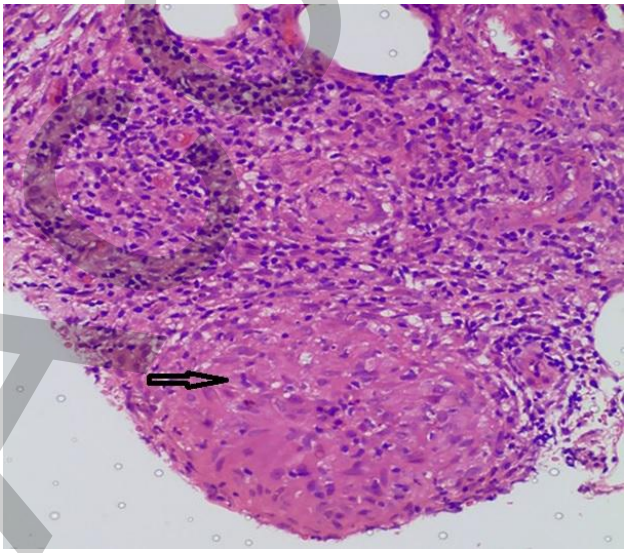

Figure 2. Epithelioid histiocytes and granuloma structures in the deep dermis and subcutaneous fatty tissue (black arrow)

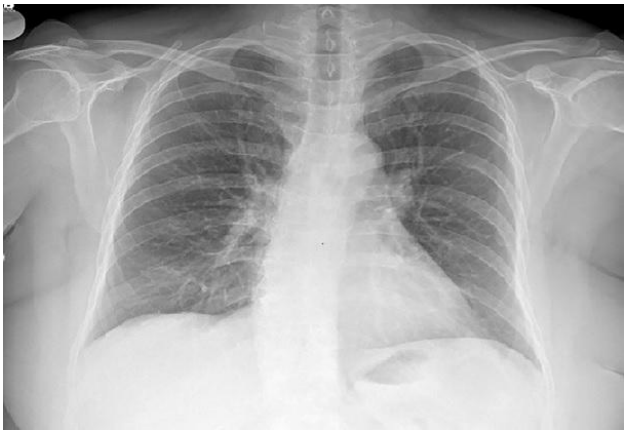

Figure 3. Bilateral hilar lymphadenopathy

DISCUSSION

Sarcoidosis is a systemic disease affecting the lungs, skin, lymph nodes, and eyes. Skin involvement is seen in about 25% of sarcoidosis patients. The etiology remains unknown, but a combination of genetic predisposition and environmental factors are thought to play a role. The disease typically begins before the age of 50 and is more common in females, with an estimated prevalence of 2.17-160 per 100,000 population (2-4).

Skin lesions in sarcoidosis, which are referred to as the "great imitator" and present in different clinical forms, are categorized as specific or nonspecific. Subcutaneous sarcoidosis entails specific skin lesions and constitutes the least common lesion type of that category. These lesions range from 0.5 to 2 cm in size, can vary in number, and are firm, mobile, erythematous, violaceous, skin-colored, or hyperpigmented. They are asymptomatic or mildly painful and typically bilateral and asymmetrically located on the extremities. Differential diagnoses include lipomas, cysts, subcutaneous granuloma annulare, foreign body granulomas, lupus profundus, and cutaneous manifestations of lymphoproliferative malignancies (1,2,5).

The typical histopathological finding for sarcoidosis is non-caseating granuloma (naked granuloma) consisting of epithelioid cells and multinuclear giant cells (3). Three major criteria are required to diagnose sarcoidosis: sufficient clinical findings, demonstration of non-caseating granulomas in one or more tissue samples, and exclusion of other granulomatous diseases (6).

Systemic involvement may occur in subcutaneous sarcoidosis, and bilateral hilar lymphadenopathy was most frequently reported in a previous case series. Uveitis, parotitis, arthritis, mucositis, dactylitis, neurological and renal involvement, and hepatosplenomegaly occur in about 15% of patients, in descending order of frequency There have also been reports of subcutaneous sarcoidosis cases with systemic involvement (5,7). Our patient was also examined for systemic involvement and millimetric nodules were detected in the lungs along with bilateral hilar lymphadenopathy.

In cutaneous sarcoidosis, treatment should be planned according to the extent of the disease, its severity, and its impact on quality of life. Topical steroids, topical calcineurin inhibitors, or intralesional steroids are preferred for localized lesions. If the disease is widespread, slowly progressing, stable, or persistent localized disease, tetracycline or antimalarials can be added to topical treatments. For cosmetically disfiguring, rapidly progressive, or refractory cutaneous sarcoidosis, combination immunosuppressive therapy (topical steroids plus systemic steroids), JAK inhibitors, methotrexate, infliximab, or adalimumab may be used (3). A case of sarcoidosis accompanied by Hepatitis C infection and treated with adalimumab has been reported in the literature (8).

In a retrospective multicentric study by Cohen et al. (4), the use of hydroxychloroquine combined with topical steroids was recommended as the first step in the treatment of cutaneous sarcoidosis. Marchetti et al. (9) treated two cases of subcutaneous sarcoidosis with hydroxychloroquine and proposed it as a first-line treatment option for patients for whom steroids are contraindicated. Youn et al. (10) also treated a patient with subcutaneous sarcoidosis with hydroxychloroquine at 400 mg/day for 5 months and reported improvement in the lesions. Since our patient was a hepatitis B carrier, systemic steroid treatment was not given. Our patient, who did not benefit from topical steroids, received hydroxychloroquine at 400 mg/day and all lesions had healed after 5 months.

In cases of subcutaneous sarcoidosis, patients should be investigated for systemic involvement. As in our case, hydroxychloroquine should be considered among the treatment options.

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