A Case of Isolated Cutaneous Sarcoidosis Accompanied by Rheumatoid Arthritis and Psoriasis

Romatoid Artrit ve Psöriasise Eşlik Eden Izole Deri Sarkoidozlu Bir Olgu

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ABSTRACT We report a 62-year-old woman with skin lesions which had been present for 55 years, and several arthritic deformities of hands and feet for 25 years. The annular, centrally atrophic, erythematous plaques located on the face and extremities were histologically consistent with sarcoidosis, while the biopsy specimens taken from the scaly, erythematous papules and plaques on the trunk revealed psoriasis. Clinical and radiological evaluations of the deformed joints led to the diagnosis of rheumatoid arthritis. Up to date, there have been a few reports on the association of rheumatoid arthritis with sarcoidosis and of psoriasis with sarcoidosis. The presented case is the first one, who demonstrates the coexistence of these three entities. We believe that the concurrence of these three inflammatory-immunological diseases has a meaning far from coincidence. Although the cause for this concurrence is not clear, it may be suggested that immunological processes triggered by unknown common antigens or common pathogenetic pathways led by different antigenic stimuli cause different clinical pictures in the same patient.

Key Words: Arthritis, rheumatoid; psoriasis; sarcoidosis

ÖZET Altmış iki yaşındaki kadın olgu, el ve ayak eklemlerinde 25 yıldır deformitelere ve 55 yaşından beri süregelen cilt lezyonlarına sahipti. Yüz ve ekstremitelerdeki deri lezyonları anüler, ortası atrofik, eritemli plaklar şeklinde olup histolojisi sarkoidozla uyumlu iken, gövdedeki eritemli ve kepekli papül ve plakların histolojisi psöriazisle uyumluydu. Eklemlerdeki bozulmalar, klinik ve laboratuar incelemeleri sonucunda romatoid artrit tanısı aldı. Bugüne dek romatoid artrit-sarkoidoz ve sarkoidoz-psöriazis birlikteliğine ait az sayıda olgu rapor edilmiştir. Sonuç olarak, sarkoidoz- romatoid artrit ve psöriazis beraberliği literatürde ilk kez bildirilmektedir. Bu immünolojik ve inflamatuar hastalıkların birarada olmasının rastlantısal olmadığını düşünmekteyiz. Birlikteliğin nedeni açık olmamakla birlikte, bilinmeyen ortak bir antijenin uyarılmasının ya da farklı antijenik uyarılarla ortak bir patogenetik yola girilmesinin aynı hastada farklı klinik tablolarla karşımıza çıkabileceğini düşünmekteyiz.

Anahtar Kelimeler: Romatoid artrit; psöriazis vulgaris; sarkoidoz

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Sarcoidosis is an idiopathic multisystemic disease defined by Hutchinson in 1877 characterized by non-caseified epitheloid granulomas.[1] Although the etiology is not fully understood, immunological, genetic, infectious and other exogenous factors are accounted for the disease, mediated by CD4+ T helper lymphocytes and cells originating from mononuclear phagocytes.[2] Sarcoidosis may accompany several autoimmune disorders.[2] In the literature there are few case reports on the concurrence of sarcoidosis and rheumatoid arthritis (RA). Here, we present a case with iso-

lated cutaneous sarcoidosis characterized by atrophic and nodular lesions, in addition to the presence of RA and psoriasis.

CASE REPORT

A 62-year-old female patient admitted to our outpatient clinic with lesions on her face, body and extremities, developed during her childhood and gradually increased in number. The patient also complained of pain, swelling and morning stiffness at her hand and foot joints for the last 25 years. Severe deformities of these joints had been developed during the last 25 years. Her past medical and family histories were unremarkable except that her sister had type 2 diabetes. Informed constent was obtained from patient, for both the physical and laboratory examinations, and photograph taking. Dermatological examination revealed centrally atrophic, hypopigmented, slightly squamous, peripherally livedoid and erythematous annular plaques which were confluent in some parts, with diameters varying between 0.5 and 5 cm, located at face, bilaterally on the extensor surfaces of the forearms, and over the anterior aspects of tibia (Figure 1 A, B). Three erythematous, nodular and elevated lesions with 0.5-1 cm of diameter were found over the nose (Figure 1 A). Papules and plaques on an erythematous base with easily removable yellowish-orange colored scales were present over the back, anterior aspect of the body and on the proximal surfaces of the upper and lower extremities (Figure 1 C). None of the lesions had sensory loss. Both wrists, metacarpophalangeal, proximal and distal interphalangeal joints had limited extension; there was boutonniere deformity at the first fingers of both hands and swan neck deformity was present at the right index finger (Figure 1 B). There were lateral deviation deformities on metatarsophalangeal joints and flexion deformities on interphalangeal joints of the feet. Laboratory evaluations revealed the following: white blood cells 3.35 x 10^3/μL (4.5-11 x 10^3/μL), hemoglobin 10.4 g/dL (11.5-16 g/dL) , hematocrit 30.7% (36-46%), erythrocyte sedimentation rate 63 mm/hour, glucose: 258 mg/dL (76-100 mg/dL), triglycerides 358 mg/dL (< 150), serum urea nitrogene, creatinine, lactate dehidrogenase, hepatic transaminases, alkaline phosphatase, calcium, complement 3 and complement 4 levels were normal; anti nuclear antibody was negative and romatoid factor was 20 IU/ml (normal value < 20IU/L). Anergic response was obtained to the PPD test. Total protein and calcium were normal in 24-hour urine sample. Chest X-ray revealed increased bronchovascular impressions

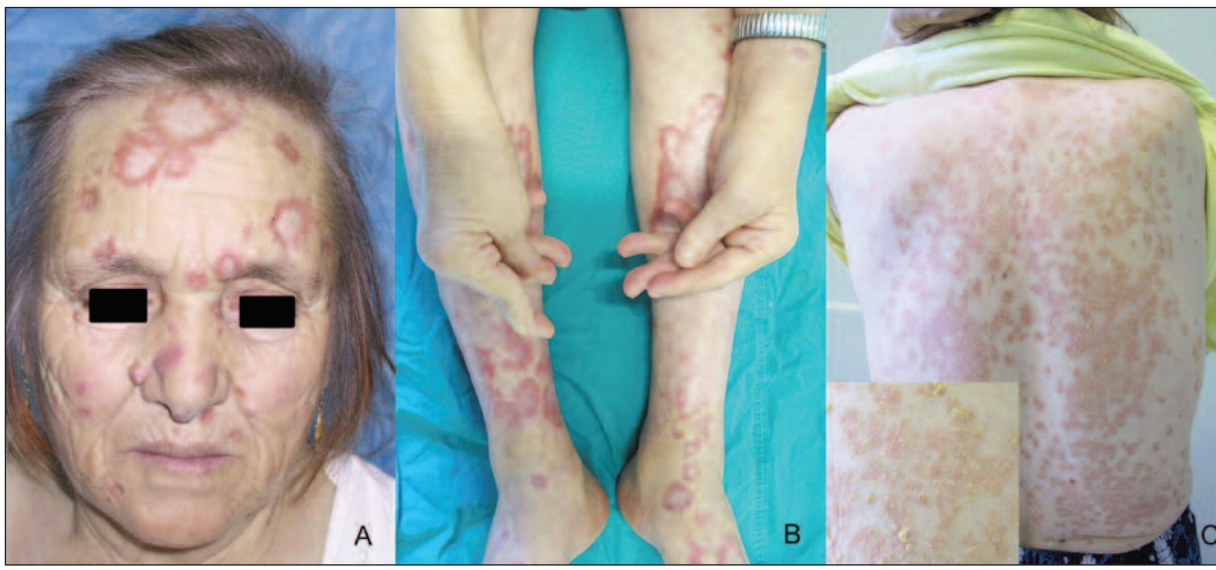

FIGURE 1: (A) Centrally atrophic, hypopigmented, erythematous annular plaque on the face, and nodular lesions on the nose. **(B)** Hand deformities of RA and sarcoid lesions on the anterior aspect of the tibia. **(C)** Yellowish-orange colored, scaly psoriasis lesions located on the back of the patient.

and increased cardiothoracic ratio. Bilateral hand radiographies revealed narrowing of joint spaces, erosions in some parts, sclerosis and irregularity on the radioulnar joint surfaces, more prominent at the right side, boutonniere deformity of the first fingers of both hands, and flexion contractures of the proximal interphalangeal joints (Figure 2 A). Bilateral feet radiographies revealed subluxations and erosions of the metatarsophalangeal joints, flexion contractures and medial deviation of the interphalangeal joints (Figure 2 B). The joint deformities of the patient were considered as RA due to clinical and radiological findings and according to the criteria of 1988 American College of Rheumatology (ACR). The histopathological examination of nodular and annular lesions was consistent with non-caseified granuloma structures seen in sarcoidosis (Figure 3 A). No mycobacterial DNA was detected by PCR in the specimen obtained from the nodular lesion of the nose. Slit-smear prepared from the skin lesions and normal skin did not reveal any lepromatous bacilli. The biopsy taken from the psoriasiform lesions revealed hyperkeratosis, parakeratosis in cornified layer, clusters of polymorphonuclear cells, irregular psoriasiform acanthosis, loss of granular layer, and suprapapillary thinning (Figure 3 B). Vascular dilatation and perivascular lymphocyte infiltration were seen in superficial dermis. The ophthalmological and neurological examinations were normal. Respiratory function tests revealed mild restrictive and obstructive findings inconsistent with sarcoidosis. Based on these findings, the patient was considered as a case of isolated cutaneous sarcoidosis accompanied by RA and psoriasis. Methotrexate10 mg per week was commenced, but was stopped shortly after the first week of treatment, because of leucopenia (2550 μL) (normal value 4.5-11 x 10^3/μL) . The patient was given 300 mg dose of allopurinol per day, but we did not evaluate the effect of this therapy because she lost to follow-up.

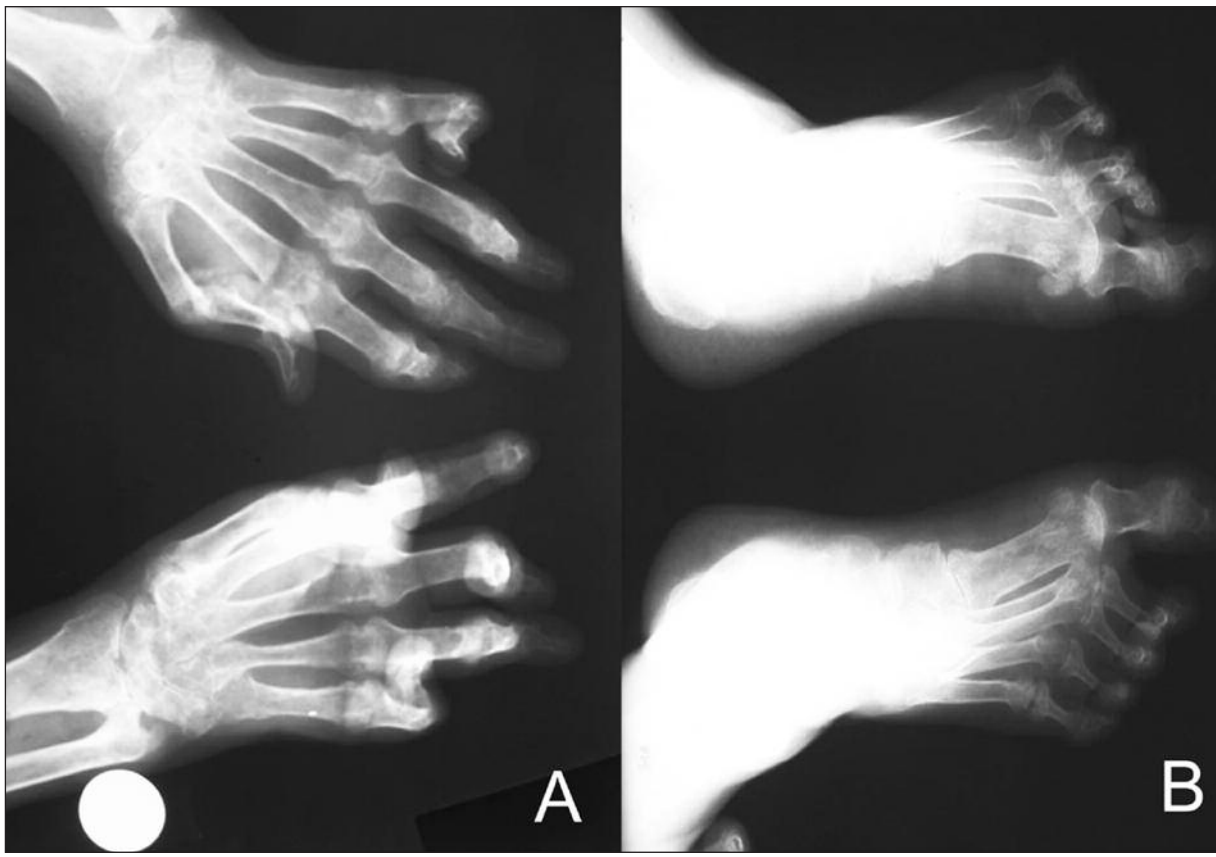

FIGURE 2: (A-B) Radiographic images of the patients hands and feet showing rheumatoid arthritis deformities

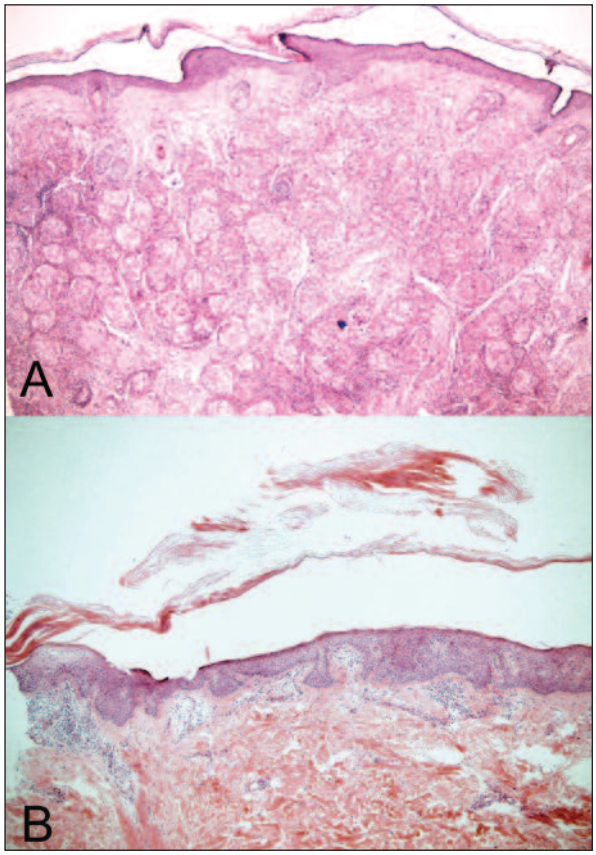

FIGURE 3: (A) Histopathologic image of annular and nodular lesions showing non-caseified granulomas typically seen in sarcoidosis (HE x 100). **(B)** Histopathological appearance of psoriasis lesions demostrates hyperkeratosis, parakeratosis, irregular psoriasiform achantosis and loss of granular layer and perivascular lymphocyte infiltration (HE x 40).

DISCUSSION

Although it is not yet established which antigen or antigens are responsible from sarcoidosis, there are numerous data indicating that granulomas are associated with a cellular immune response developed as a result of the antigenic stimuli.[3,4]

It is reported that sarcoidosis may accompany many autoimmune disorders including systemic lupus erythematosus (SLE), systemic sclerosis, hemolytic anemia and primary biliary cirrhosis.[4] Some immunological findings in sarcoidosis *(suppression of peripheral immune response, hyperactive T cell and macrophage mediated granulomatous inflammation, excess humoral immune reaction)* are similar to the immunological profile seen in animal models of autoimmunity and in patients with SLE,[4] suggesting that sarcoidosis and autoimmune disorders are closely related.

RA, which is an autoimmune connective tissue disease, may accompany sarcoidosis. Although the incidences of both diseases are relatively high in the population, up to date, only 14 cases with concurrent RA and sarcoidosis have been reported.[5-7]

The diagnosis of RA is made by detecting 4 of the 7 criteria consisting morning stiffness, arthritis in three or more joint group, arthritis in hand joints, symmetrical arthritis, radiographic changes, presence of rheumatoid nodules and positive serum rheumatoid factor as determined by ACR in 1988.[8] Synovial biopsy findings are not among the diagnostic criteria. As there may be articular changes in patients with sarcoidosis similar to that in RA, the inflammatory characteristics of synovial biopsy may indicate the causative origin of the joint involvement. Nevertheless, in the chronic arthritis due to sarcoidosis, characteristic non-caseified granulomas can be demonstrated with biopsy only in half of the cases.[9] The latter one may be considered in the differential diagnosis of the skin lesions of our patient, due to the relatively similar histopathologic features. However, both the localization of the lesions and the clinical findings are different enough to eliminate this diagnosis for the presented case.

Our patient was diagnosed as RA since she has 5 of the 7 ACR criteria, but synovial biopsy could not be performed due to lack of patient consent. In the biopsy specimens obtained from annular skin lesions, typical sarcoidal granulomas were seen. Although the anergy in our patient supports sarcoidosis, there is no finding favoring sarcoidosis in the auscultation of the lungs, chest radiography and respiratory function tests.

There are still no certain internationally accepted criteria for the diagnosis of sarcoidosis. However, since sarcoidosis is a multisystemic disease, involvement of many systems and tissues with typical histopathological characteristics are usually deemed necessary for the diagnosis.[10] On the other

hand, cutaneous involvement may occur without systemic involvement.[11,12] Therefore, the diagnosis of sarcoidosis was not established in our patient, instead, a definition as "isolated cutaneous sarcoidosis" was found to be more appropriate for the designation of skin lesions.

In recent years, a hypothesis was developed considering that the deviations of the T cell immunity in RA are not limited with inflammatory lesions, on the contrary, it is a basic disorder involving the whole body. Thus, the immune system of RA patients includes many T cells active against the body's own antigens. These auto-reactive T cells are caused by the deviations of the mechanisms that maintain T cell homeostasis and control of the cell proliferation.[13] From this standpoint, the occurrence of other auto-immune diseases in RA patients is not an unexpected finding.

Psoriasis is characterized by keratinocyte hyperproliferation and mononuclear cell infiltration consisting mainly of activated T cells. Although its pathogenesis is not elucidated with all aspects, today it is increasingly accepted as a T cell mediated auto-immune disorder.[14] According to these findings, psoriasis may be considered as one of the autoimmune diseases accompanying sarcoidosis or RA. In the literature there are few case reports on the concurrence of sarcoidosis and psoriasis.[15]

From the aspect of genetic susceptibility, it is reported that HLA groups frequently seen in subjects with sarcoidosis, RA and psoriasis are different from each other.[2,13,14] Also the inflammatory characteristics of these entities have marked differences. However, as seen in sarcoidosis, it has been demonstrated that CD4+ T lymphocytes are activated by a yet unknown antigen in RA and psoriasis. On the other hand, many common cytokines such as IL-2, IFNγ and TNFα are playing a role in the pathogenesis of these three diseases. The benefit of TNFα blockers such as infliximab in the treatment of these diseases indicates that they may have a common pathway in their pathogenesis.[16]

In conclusion, our case is the first case of the concurrent sarcoidosis, RA and psoriasis reported in the literature. These three conditions may have occured coincidentally in our patient, however we believe that it may have a meaning far from coincidence. Although the cause for this concurrence is not clear, it may be suggested that immunological processes triggered by unknown common antigens or common pathogenetic pathways led by different antigenic stimuli cause different clinical pictures in the same patient.

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