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EDİTÖRE MEKTUP / LETTER TO THE EDITOR

Two diseases that mimic each other: Behçet disease and sarcoidosis

Birbirini taklit eden iki hastalık: Behçet hastalığı ve sarkoidoz

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To the Editor,

Behçet disease (BD) is a type of vasculitis affecting both sexes during their young adulthood and has the potential to result in premature death as well as severe morbidity. Its manifestations include oral ulcers, genital ulcers, mucocutaneous lesions (e.g., papulopustular and nodular lesions), joint involvement (e.g., monoarthritis and arthralgia), eye manifestations presenting with panuveitis that may lead to blindness if left untreated, vascular involvement causing potentially lethal arterial aneurysms, deep venous thrombosis, neurologic involvement leading to permanent disability, and gastrointestinal manifestations mimicking those of inflammatory bowel disease[1].

Sarcoidosis is a disease of unknown etiology mostly affecting young adults characterized by noncaseating granulomas in the involved organs. Lung is the mostly involved organ. Manifestations include bilateral hilar adenopathy, pulmonary reticular opacities, skin, joint, and/or eye lesions. Here we present a 41-year-old female sarcoidosis patient who had been followed up with a diagnosis of BD.

A 41-year-old woman was admitted to the ophthalmology department with the complaint of impaired vision. Since panuveitis was detected on ophthalmological examination, the patient was consulted with a rheumatology department in another center. She was diagnosed with BD in the ophthalmology department based on The International Study Group (ISG) criteria since she had the following findings: oral ulcers, papulopustular lesions, arthralgia, and panuveitis. Treatment with colchicine, azathioprine, and prednisolone was initiated. Since she had recurrent uveitis attacks despite this treatment, infliximab treatment was started, after which oral aphthous lesions and uveitis resolved. Infliximab treatment was discontinued after nine years; then, five months later the patient was admitted to the rheumatology department with dyspnea, fatigue, and weakness. Laboratory findings were as follows: hemoglobin 11 g/dl, white blood cell count 6400/mm3, platelet count 414000/mm3, erythrocyte sedimentation rate 81 mm/h, serum C-reactive protein 29 mg/dl, anti-nuclear antibody was negative, and calcium 8,9 mg/dl (normal range: 9-11 mg/dl). The serum angiotensin-converting enzyme (ACE) level was increased to 155 UI/l (normal range<67 U/l).

Pericardial effusion was found on transthoracic echocardiography. Tomography was performed to identify any pulmonary lesions and effusion, and a subpleural nodule of 4 mm in diameter was found in the middle lobe of the right lung and a well-defined solid pulmonary nodule of 12 mm in diameter was found in the posterior part of upper lobe of the right lung (Figure 1). Since malignant lesion was suspected, Positron Emission Tomography Computerized Tomography (PET-CT) was performed. An approximately 11 mm conglomerated lymphadenopathy showed increased fluoro-2

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deoxyglucose (FDG) uptake in the left axillary area (SUV max:9). A 14 x11 mm nodular parenchymal lesion in the posterior segment with SUV max 3.3 and a 17x 13 mm nodular parenchymal lesion in the rear part of the right lung upper lobe with SUV max 6.5 were observed. Increased FDG uptake was present in a mass lesion of approximately 27x22 mm and a high FDG uptake was evident in the right adnexal area of the pelvis. The patient was consulted with the department of obstetrics, and she was operated and the mass in the adnexal area was excised. On pathological examination, mostly non-necrotizing granuloma structures were seen in the peritoneum and omentum. Necrosis foci were mostly fibrinoid. Granulomas were not surrounded by lymphocytes and had a sarcoid appearance. Pathological examination and imaging findings confirmed the diagnosis of sarcoidosis.

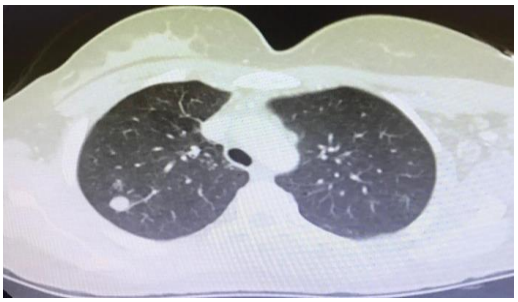

Figure 1. A subpleural nodule of 4 mm in diameter in the middle lobe of the right lung and a well-defined solid pulmonary nodule of 12 mm diameter in the posterior part of the upper lobe of the right lung are seen.

This case initially presented with clinical findings consistent with BD; however, she was finally diagnosed with sarcoidosis. This represents a very rare situation. The patient meets relevant diagnostic criteria for both diseases. Tumor necrosis factor-alpha (TNF-α) inhibitors may paradoxically induce pulmonary and peritoneal sarcoidosis. It should be born in mind by the clinician that anti-TNF-α inhibitors may have paradoxical side effects and patients using such agents should be evaluated accordingly.

Histocompatibility leukocyte antigen (HLA)-B*51 is the most important genetic risk factor for BD, which was initially reported in Japanese studies and further studies reported in other ethnic groups. A meta-analysis reported an overall odds ratio of 5.78 (95% CI=5.00–6.67) for *HLA-B*51* carriers to develop BD. Similar results were obtained in two different genome-wide association studies (GWAS) in Japanese and Turkish BD patients[2].

Sarcoidosis patients have high blood IL-17, IL-23, and IFN-gamma levels and high CD4 T lymphocyte subgroup Th17 has been found in sarcoidosis granuloma, suggesting that inhibition of the Th1/Th17 pathway is necessary to achieve therapeutic efficacy in sarcoidosis[3]. To diagnose BD based on ISG criteria, presence of recurrent oral ulcers and at least two of the following factors are required: eye lesions, recurrent genital ulcers, skin lesions, and a positive pathergy test. We diagnosed our patient with BD based on ISG criteria.

Uveitis is the most common ocular manifestation of BD and may involve the anterior, intermediate, or posterior uveal tract in isolation, or in combination in the form of panuveitis. Uveitis in BD typically presents with acute onset hypopyon and occlusive retinal vasculitis, with predominant inflammation of retinal veins rather than arterioles. While BD uveitis is generally bilateral, exacerbations usually occur unilaterally and alternate between eyes. Uveitis is associated with a worse visual outcome in males. Uveitis affects between 50% and 90% of BD patients, depending on the geographical location. Up to 30% of patients with BD uveitis experience significant visual impairment or blindness. Visual acuity deteriorates with decreased contrast sensitivity, light sensitivity may develop, depth and color perception loss and floaters may occur, and visual field loss may develop. Uveitis has a significant and negative impact on quality of life[4].

Clinically, it is challenging to diagnose sarcoidosis in a patient with BD. Both diseases have the same clinical features: oral aphthae, genital aphthae, ocular disease, skin lesions, gastrointestinal involvement, neurological disease, vascular disease, or arthritis. BD uveitis has several distinctive clinical features that distinguish it from other systemic autoimmune diseases. Recurrent flares of intraocular inflammation characterize uveitis. Anterior uveitis occurs in less than 15% of the patients. The condition manifests itself with sudden acute onset of visual acuity decrease, ocular redness, periorbital pain, photophobia, and tearing. Posterior synechiae may occur. Presence of hypopyon indicates more severe uveitis. The incidence of hypopyon in BD uveitis ranges from 5.4 to 32.4%. Anterior uveitis attacks may accelerate the development of glaucoma[5]. Due to the presence of uveitis findings consistent with

uveitis in our patient, the BD diagnosis was made by the ophthalmology department. Since both diseases have the same clinical features, BD has the potential to be misdiagnosed as sarcoidosis (or vice versa). The present case report shows the development of sarcoidosis in preexisting BD, suggesting that the two diseases have similar pathological pathways. Case reports have emerged demonstrating the seemingly paradoxical induction of sarcoidosis in patients on TNF-α inhibitor therapy[6]. In our case, infliximab might have induced pulmonary and peritoneal sarcoidosis paradoxically. That was why we needed to change the treatment.

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