Systemic Lupus Erythematosus Developed Under The Brucellosis Therapy

Bruselloz Tedavisi Altında Gelişen Sistemik Lupus Eritematozus

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ABSTRACT

Drug-induced lupus erythematosus is a disorder which is temporally related to continuous drug exposure and clinical findings resolve upon discontinuation of the offending drug. Its clinical and laboratory findings are similar to systemic lupus erythematosus (SLE). SLE induced by doxycycline, rifampicin or streptomycin are extremely rare. We present the case of a patient who developed arthralgia, leucopenia, lymphopenia and pleural effusion due to the doxycycline, rifampicin or streptomycin drugs treatment.

Keywords: Brucellosis, Doxycycline, Rifampicin, Streptomycin

ÖZET

İlaca bağlı lupus eritematozus, ilaç kullanımına bağlı ortaya çıkan ve ilacın kesilmesi sonrasında klinik bulguların gerilemesi ile karakterize bir bozukluktur. İlaç kaynaklı lupus eritematozusun klinik ve laboratuar bulguları sistemik lupus eritematozusun (SLE) bulguları ile benzerdir. Doksisiklin, rifampisin veya streptomisin ile tetiklenen SLE son derece nadirdir. Bu yazıda doksisiklin, rifampisin veya streptomisin tedavisine bağlı artralji, lökopeni, lenfopeni ve plevral efüzyon gelişen bir olgu sunulmuştur.

Anahtar kelimeler: Bruselloz, Doksisiklin, Rifampisin, Streptomisin

Introduction

Systemic lupus erythematosus (SLE) is a prototypical autoimmune disease characterized by presence of autoantibodies and immune complexes (1,2). It is estimated that up to 10 % of SLE cases are drug-induced lupus erythematosus (DILE) (3). DILE is a syndrome with clinical manifestations and laboratory findings similar to SLE. It is temporarily related to continuous drug exposure which resolves after the offending drug is ceased. The drugs most commonly caused in the development of DILE are hydralazine, procainamide, quinidine, isoniazid, hydralazine, carbamazepine and chlorpromazine (4,5).

We present a case of a young male of DILE developed under the doxycycline, rifampicin and streptomycin drugs used for the treatment of brucellosis.

Case

An 18-year-old man was admitted to the infectious diseases outpatient clinic with complaints of fatigue, malaise, arthralgia and sweating. The diagnosis of brucellosis was made based on positive Brucella standard tube agglutination (STA) test results (titer>1/640) in the presence of clinical signs and symptoms suggestive of brucellosis. Antimicrobial therapy was initiated for brucellosis with doxycycline (200 mg/day), rifampicin (600 mg/day) for 6 weeks and streptomycin (1000mg/day) for 2 weeks.

The patient showed partial improvement of his arthralgia with the treatment however he complained of dyspnea. Symptoms have been developed at the third week of treatment. Chest radiograph showed bilateral pleural effusions, with more pleural fluid in the right side (picture 1). Pleural fluid was analyzed by polymerase chain reaction (PCR) for detecting Mycobacterium tuberculosis and it has been found negative. Adenosine deaminase (ADA) activity was measured at normal levels. Pleural biopsy showed nonspecific pleuritis and fibrosis. The patient was referred to our rheumatology outpatient clinic to investigate the etiology of serositis. At the admission the white blood cell 3400/mm^3, lymphocytes 1200/mm^3, C-reactive protein (CRP) 1.99 mg/dl (normal range 0.1-0.82), erythrocyte sedimentation rate (ESR) 5 mm/h, serum complement protein 3 (c3) level 85.1 mg/dl (normal range: 90-180), serum complement protein 4 (c4) 11.6 mg/dl (normal range: 10-40) were detected. The antinuclear antibody (ANA) was positive at a titer of 1:320 with homogenous pattern. Anti-double-stranded DNA (anti-dsDNA) antibody was positive and anti-histone core antibody was negative. These parameters measured by indirect immunofluorescence. Blood biochemistry and urine analysis were within normal limits. As a result of clinical and laboratory findings, the patient was diagnosed with DILE. The medicaments for Brucellosis treatment were discontinued after DILE diagnosis and the treatment of methylprednisolone was started with a dose of 0.5mg/kg/day. Steroid dose was reduced to 5mg/day and hydroxychloroquine in dose of 200 mg/day was added at the 4 weeks of the treatment. Patient's symptoms were improved.

Discussion

DILE is a reversible disorder related with exposure to several drugs. Diagnosis of DILE is not easy and there are no standard diagnostic criteria for DILE. However, the resolution of both clinical and serological features following drug discontinuation is an important clue for the diagnosis of DILE (6). DILE was initially reported in patients treated with hydralazine. Later procainamide and anticonvulsant drugs were revealed to cause DILE (7). Recently, over 80 drugs have since been associated with

development of DILE. The etiopathogenesis of DILE is not exactly known. The chemical structure of drugs and genetic factors are thought to play a role in the pathogenesis. The symptoms and laboratory findings of DILE are similar to SLE. Myalgia and arthralgia were seen in the majority of cases. Renal and central nervous system involvement and malar rash are generally less frequent in DILE compared to SLE (4). Severe hematological findings are uncommon in DILE as laboratory findings. Anti-histone antibodies were found positive in most of the patients with DILE. Unlike idiopathic SLE, positive anti-dsDNA is rare in patients with DILE (6).

The first step in DILE therapy is to determine the drug causing the disease and cease its usage. In most of the patients the disease is regressed with the cease of the drug, while for some patients additional therapy may be needed. Therapy may differ according to the disease severity and the affected organ. Non-steroidal anti-inflammatory drugs or low-dose corticosteroids are sufficient for patients with musculoskeletal system complaints, while patients with severe renal involvement or vasculitis should be treated like idiopathic SLE (8).

Doxycycline, rifampicin and streptomycin are frequently used in the treatment of brucellosis. Although some of the side effects of these drugs are well known to cause DILE, It has only been demonstrated in a limited number of case reports (9,10).

In our case, development of pleural effusion after Brucellosis therapy and non-existing typical SLE findings such as malar rash and photosensitivity lead us to diagnose DILE.

In conclusion, at the presence of SLE for patients without showing typical symptoms such as malar rash, discoid lesion, renal involvement; it has been of importance to investigate drugs used by the patients and to terminate drug usage causing DILE.

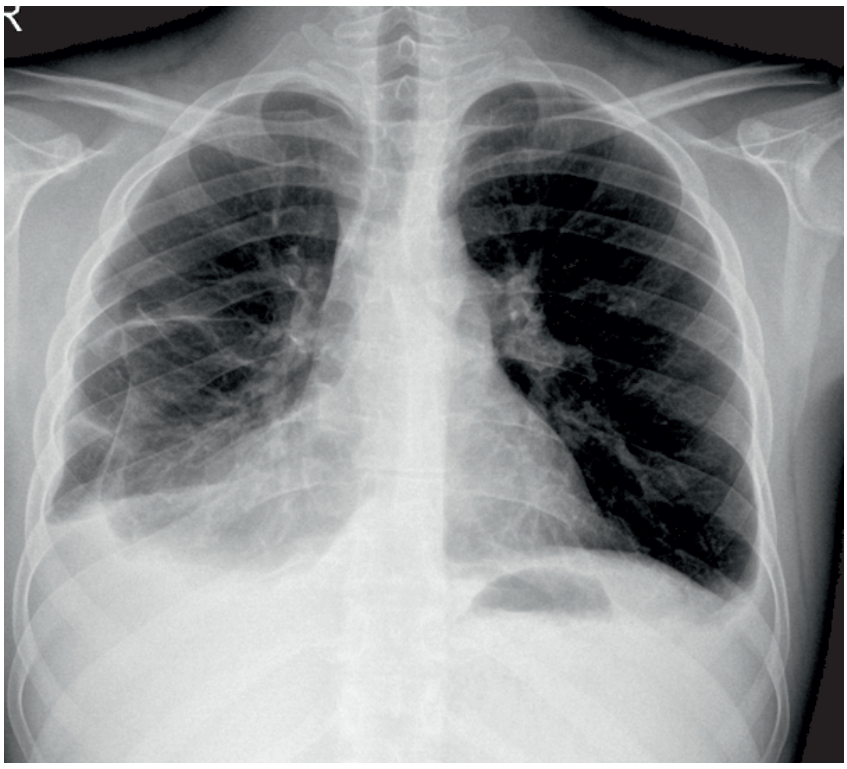

Figure 1. Posterior-anterior (PA) chest X-ray of the patient

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