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Coexistence of Axial Spondyloarthritis, Systemic Lupus Erythematosus, Sjögren's Syndrome and Secondary Antiphospholipid Syndrome: Case Report

Aksiyel Spondiloartrit, Sistemik Lupus Eritematozus, Sjögren Sendromu ve Sekonder Antifosfolipid Sendromunun Birlikte Görüldüğü Olgu Sunumu

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Öz

Non-Radyografik aksiyel spondiloartrit (nr-axSpA), sistemik lupus eritematozus (SLE), sekonder antifosfolipid antikor sendromu (APS) ve Sjögren Sendromu (SjS) birlikteliğine sahip 55 yaşında bir kadın hastayı sunuyoruz. Nr-AxSpA tanısı enflamatuar bel ağrısı, insan lökosit antijeni B27 pozitifliği ve manyetik rezonans görüntülemede sakroileit varlığına dayanılarak yapıldı. SLE tanısı yanaklarında kelebek şeklinde döküntü, enflamatuar artrit, fotosensitivite, el parmaklarının dorsal eklemler arası alanı tutan eritem, antinükleer antikor (ANA) ve anti-dsDNA pozitifliği, alopesi, düşük serum kompleman seviyeleri, lökopeni ve trombositopeni varlığı ile konuldu. Pozitif labiyal tükürük bezi biyopsisi ile desteklenen sicca semptomları, düşük Schirmer testi, Anti SSA/Ro ve anti-SSB/La pozitifliği ile SjS tanısı konuldu. Ayrıca bu hastada 16. haftada düşük ve 33 yaşında serebrovasküler olay öyküsü vardı. IgG ve IgM antikardiolipin antikorlarının iki kez pozitif olduğu bulundu. Bu nedenle, kendisine sekonder APS tanısı konuldu. Hasta Ax-SpA, SLE, SjS ve APS için sınıflandırma kriterleri doldurmaktadır. Bilindiği üzere farklı genetik, etiyopatogenetik ve klinik özellikleri olan bu dört hastalığın bir arada bulunduğu ilk vaka sunumudur.

Anahtar Kelimeler: Antifosfolipit Antikor Sendromu, Radyolojik Olmayan Aksiyel Spondilartrit, Sistemik Lupus Eritamatozus, Sjögren Sendromu

Abstract

Hereby we report a 55-year-old female patient having the association of non-radiographic axial spondyloarthritis (nr-AxSpA), systemic lupus erythematosus (SLE), secondary antiphospholipid antibody syndrome (APS), and Sjögren's Syndrome (SjS). Diagnosis of nr-AxSpA was made based upon the presence inflammatory low-back pain, human leukocyte antigen B27 positivity, and presence of sacroiliitis only in magnetic resonance imaging (MRI). SLE was diagnosed with butterfly-shaped rash on her cheeks, inflammatory arthritis, photosensitivity, erythema involving dorsal inter-joint area of hand fingers, alopecia together with antinuclear antibody (ANA) and anti-dsDNA positivity, low serum complement levels, leucopenia and thrombocytopenia. Additional presence of sicca symptoms, low Schirmer I test, anti SSA/Ro and anti-SSB/La positivity, supported by positive labial salivary gland biopsy led to the diagnosis of SjS. Furthermore, this patient also had miscarriage at 16th week and cerebral vascular disease at 33 years. Besides, IgG and IgM anticardiolipin antibodies were found to be positive twice. Therefore, she was also diagnosed as secondary APS. She fulfilled the relevant classification criteria for AxSpA, SLE, SjS and APS. To our knowledge, this is the first case report showing the association of these four diseases, with different genetic, etiopathogenetic and clinical systemic inflammatory diseases.

Keywords: Antiphospholipid Antibody Syndrome, Non-Radiographic Axial Spondyloarthritis, Systemic Lupus Erythematosus, Sjögren Syndrome

Introduction

Axial spondyloarthritis (AxSpA) is a chronic inflammatory disease of the axial skeleton which manifests as inflammatory back pain and progressive stiffness of the spine. Patients with axial disease and other features of SpA but no unequivocal sacroiliitis in conventional X-ray now termed as non-radiographic axial spondyloarthritis (nr-AxSpA) (1). Those patients can be diagnosed on the basis of the presence of active inflammation in magnetic resonance imaging (MRI) or human leukocyte antigen B27 (HLA-B27). Systemic lupus erythematosus (SLE) is a chronic inflammatory disease of unknown etiology that may affect the skin, joints, kidneys, lungs, nervous system, sereous membranes, and/or other organs of the body (2). Sjögren's syndrome (SS) is the second most common autoimmune rheumatic condition characterized by lymphocytic infiltrate of the exocrine glands, resulting in dysfunction and destruction of them (3). Antiphospholipid syndrome (APS) is the association of thrombosis and/or pregnancy morbidity with antiphospholipid antibodies (aPL) (lupus anticoagulant (LA), anticardiolipin antibodies (aCL), and/or anti-β2-glycoprotein-I antibodies (aβ2 GPI) (4).

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These four immune rheumatologic diseases, which have different etiopathogenesis, as well as diverse clinical and genetic characteristics, are rarely seen together. Hereby, we report the first case with the co-existence of these four diseases.

Case

In July 2017, 53-year-old female patient referred to our rheumatology outpatient department with the complaints of pain, swelling and morning stiffness in the joints of her fingers and a butterfly-shaped rash on her cheeks, which became prominent after exposure to sunlight. She also complained of inflammatory low-back pain radiating to her buttocks and associated with morning stiffness lasting longer than 1 hour, since she was 30 years old. Additional problems included difficulty in speech and walking, and sicca symptoms. Past medical history revealed that she had intermittent parotid swelling, had a single pregnancy terminating with miscarriage at 16th week, and a cerebral vascular event when she was 33 years old.

Physical examination was notable with arthritis of the right 2nd, 3rd, 4th proximal interphalangeal (PIP), 2nd, 3rd metacarpophalangeal (MCP) and left 2nd, 3rd PIP joints, erythema involving dorsal inter-joint area of hand fingers and alopecia. The sacroiliac joint compression was painful.

Neurological examination revealed dysarthria, right lower extremity muscle strength 3/5, left lower extremity muscle strength 5/5.

Laboratory test result were as follows; white blood cell count (WBC) 3.85/µL (4.60-10.2), hemoglobin 10.4 g/dL (12.2-18.1), platelet count: 64.000 (180-370x10^3), erythrocyte sedimentation rate (ESR) 45 mm/hr, C-reactive protein (CRP):0.4 mg/dL (0.001-0.82), Rheumatoid Factor (RF): positive, Antinuclear Antibody (ANA) test peripheral and speckled positive in 1/320 titre, anti-double-stranded DNA, anti Ro and anti-La antibodies positive. Anticardiolipin antibody (ACA) IgG and IgM were found to be positive in two different occasions. Serum complement 3 (C3) level was 65 mg/dL (83-193) and complement 4 (C4) level was 8 mg/dL (10-40), showing hypocomplementemia. Furthermore HLA-B27 test was also positive. Urine analysis, liver and renal function tests, serum protein and creatinine phosphokinase levels and thyroid function tests, Hepatitis C Virus antibodies were within normal limits.

Conventional radiography of pelvis x- ray was normal. However, magnetic resonance imaging (MRI) showed presence of active sacroiliitis (Figure 1).

Schirmer I test was 4 mm and 5 mm, in 5 minutes, on the right and left eye, respectively. Labial salivary gland biopsy was interpreted as having focus score of 3 (Figure 2).

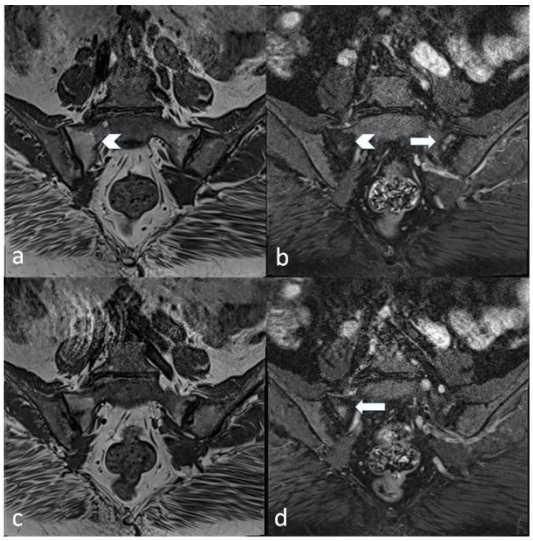

Figure 1: Semicoronal T1-weighted (a, c) and T2-weighted fat saturated (b, d) imaging sequences of sacroiliac joints showed lesions (hypointense on T1-weighted and hyperintense on fat-saturated images) on both sacral wings compatible with active sacroiliitis (arrows). There were also periarticular fat deposition (arrow heads) and sclerosis.

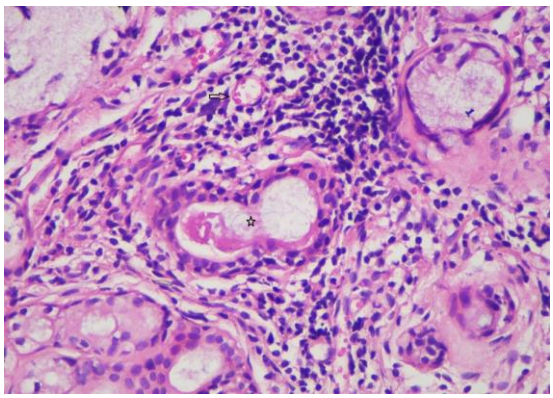

Figure 2: Intensive lymphocytic infiltration is observed around the salivary gland structures (asteriks) and vein (arrow) (hematoxylin-eosin, 400 magnification).

Our case was diagnosed with primary SjS based on positive Schirmer's test, positive biopsy result of minor salivary gland and positive anti Ro and anti-La antibodies positive

The initial treatment included methylprednisolone 4 mg/day, hydroxychloroquine 400 mg/day, acetylsalicylic acid 100 mg/day, diclofenac 100 mg/day and lansoprazole 30 mg/day. Rehabilitation was started and regular exercise recommended. Improvement in symptom and laboratory parameters was observed at 3-month control.

The consent of the patient to share his medical information was taken.

Discussion

To our knowledge, this is the first case report showing the association of these four diseases, with different genetic, etiopathogenetic and clinical systemic inflammatory diseases at the same time in

a patient. Although SLE, SjS and APS coexistence may be common, association of additional nr-AxSpA is rare. This patient fulfills the criteria for Lupus International Collaborating Clinics Criteria for SLE (5), American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) Criteria for SjS (6), revised Sapporo criteria for APS (7) and ASAS (Assessment of Spondyloarthritis International Society) classification criteria for AxSpA (1).

AxSpA belongs to a group of inflammatory rheumatic diseases known as spondyloarthritis (SpA). The prototoype of this family is ankylosing spondylitis (AS). nr-AxSpA is, yet another member, recently included in the SpA group. The major difference between these two diseases is the presence or absence of radiographic sacroiliitis in conventional radiographs. Radiographic sacroiliitis is the hallmark of AS, whereas in nr-AxSpA sacroiliitis can only be demonstrated by MRI. The present case with nr-AxSpA was diagnosed as APS based on the presence of both clinical (thrombosis and pregnancy loss history) and laboratory (two recurrent anticardiolipin antibody positivity) findings. Previously there are some case reports of isolated ACA positivity or APS in cases with SpA.

Juanola et al. found that the prevalence of antiphospholipid antibody positivity was significantly higher in patients with AS than in healthy controls (29% vs 5%, $p<0.002$). However, they reported only two patients with AS fulfilling the diagnostic criteria for APS (8). On the other hand, Buchanan et al. found increased titers of ACA in patients with psoriatic arthritis (PsA), which also belongs to the group of SpA, but not in patients with AS (9). Mateo et al. reported ACA positivity in two cases with AS. One of these cases was defined to have infarct in pons and high ACA positivity at 34 years of age. The other case was defined to have deep vein thrombosis and ACA positivity (10). Karter et al. reported a case of leukocytoclastic vasculitis in a patient with AS having inflammatory back pain, anterior uveitis, HLA-B27 positivity, presence of sacroiliitis both in sacroiliac joint conventional radiography and computed tomography. Two weeks after the treatment including corticosteroids and nonsteroidal anti-inflammatory drugs was started, the patient presented with arterial embolism, and ACA IgG was also found to be positive, resulting with the additional diagnosis of APS (11). Blanchard et al. reported a 60-year-old AS patient with leg ulcers and lupus anticoagulant positivity (12).

Aforementioned cases consist of those cases diagnosed with AS.

Association of secondary SjS with SLE and APS is usual, but association of SjS with SpA is rather rare. Brandt et al. reported that 8 (7.6%) of 105 patients with SpA also fulfilled the European criteria for SjS (13). Kobak et al. demonstrated the presence of SjS in 10% of patients with AS, according to the American-European consensus criteria (14). Our case with nr-AxSpA was diagnosed with primary SjS based on positive Schirmer's test, positive biopsy result of minor salivary gland and positive anti-SSA/Ro; she also fulfilled ACR/EULAR criteria for SjS (7).

The association of SpA with SLE is also uncommon. Tarhan et al. reported a female case with coexistence of AS and SLE, as well as they reviewed the literature and found out eight additional cases showing this association. The case which Tarhan et al. reported was diagnosed as SLE, based on presence of type V lupus nephritis, and involvement of musculoskeletal and hematological systems, as well as autoantibody positivity (15). However, the present case was diagnosed as SLE due to musculoskeletal and hematological system involvement and autoantibody positivity.

In conclusion, our case is the first example so far, showing the coexistence of nr-AxSpA, SLE, SjS and APS.

Although coexistence of the last three disorders is not unusual and may be expected in clinical ground, additional diagnosis of nr-AxSpA is interesting and attracts attention.

Written consent: A written patient consent certificate was obtained from the patient (or his legal guardian) that his medical data may be published (06/12/2020).

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