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Case Report

Coexistence of systemic lupus erythematosus and ankylosing spondylitis: another case report and review of the literature

Figen Tarhan[1], Mehmet Argın[2], Gerçek Can[1], Mustafa Özmen[1], Gökhan Keser[3]

Abstract

The coexistence of systemic lupus erythematosus (SLE) and ankylosing spondylitis (AS) is very rare, and, to the best of our knowledge, there are only 8 reported cases in the English literature. Here, we present another case with the coexistence of these two diseases, and review the clinical and laboratory features of the previously reported cases. A 55 year-old female patient, with a diagnosis of SLE with locomotor, skin, renal and hematopoietic system involvement, which had been confirmed by relevant autoantibody positivity, and hypocomplementemia and biopsy-proven membranous lupus nephritis, was referred to our clinic suffered from typical inflammatory low-back pain after eight years of follow-up. Sacroiliac magnetic resonance imaging (MRI) confirmed the presence of bilateral active sacroiliitis with bone marrow oedema. HLA-B27 was positive and bilateral calcaneal spurs were also detected by conventional radiography. Therefore, the additional diagnosis of AS was made, eight years after the diagnosis of SLE. Inflammatory low-back pain typically responded to treatment with non-steroidal anti-inflammatory drugs.

Including the present case, most of the reported cases of the coexistence of SLE and AS are female, and SLE generally precedes the occurrence of AS. The present case is also notable as the patient had both MRI confirmation of bilateral active sacroiliitis and HLA-B27 positivity. The coexistence of these two diseases with different genetic backgrounds in the same patient is much lower than expected based upon their prevalence in the general population. Although it has been suggested that the very rare combination of the susceptibility genes of each disease may explain the rarity of coexistence, epidemiological data concerning the genetic risks for the coexistence of SLE and AS are not available.

Key words: Systemic lupus erythematosus, ankylosing spondylitis, HLA-B27, double-stranded DNA antibody

Introduction

Systemic lupus erythematosus (SLE) is a chronic inflammatory disease of unknown aetiology that may affect the skin, joints, kidneys, lungs, nervous system, serous membranes, and/or other organs of the body. Ankylosing spondylitis (AS) is a chronic inflammatory disease of the axial skeleton which manifests as inflammatory back pain and progressive stiffness of the spine (1, 2). These two autoimmune rheumatologic diseases, which have a different aetiopathogenesis as well as diverse clinical and genetic characteristics, are rarely seen together. To the best of our knowledge, there are only 8 reported cases of the coexistence of SLE and AS in the English literature (3-10). Here, we report another case with the coexistence of these two diseases. The present patient is a 55 year-old female who was being followed-up due to the diagnosis of SLE, and later received the additional diagnosis of AS. We also intend to review the clinical and laboratory features of the previously reported cases.

Case Presentation

In 2003, the present case referred to the rheumatology outpatient clinic with 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. At that time, she was 47 years-old. Her laboratory test results were as follows: erythrocyte sedimentation rate (ESR) 45 mm/hr, C-reactive protein (CRP) 0.4 mg/dL (0.001-0.82), rheumatoid factor negative, white blood cell (WBC) count 3.85/µL (4.60-10.2), haemoglobin 10.4 g/dL (12.2-18.1), serum ferritin 18.3 ng/mL (20-300), antinuclear antibody (ANA) test 1/320 peripheral and speckled, anti-double-stranded DNA (Crithidia test) was positive (2+), complement 3 (C3): 65 mg/dL (83-193) and complement 4 (C4): 3 mg/dL (15-57). Liver and renal function tests, serum protein and creatinine phosphokinase levels, platelet count, urine analysis and thyroid function tests were within the normal limits. Bilateral anteroposterior hand x-rays were normal. The diagnosis of SLE was made based upon the presence of inflammatory arthritis, malar rash and photosensitivity, together with high ESR, low CRP, antinuclear antibody (ANA) and anti-dsDNA positivity, along with low serum complement levels. Since there was only joint

1 Department of Internal Medicine, İzmir Atatürk Research and Training Hospital, İzmir, Turkey

2 Department of Radiology, Ege University Faculty of Medicine, İzmir, Turkey

3 Department of Rheumatology, Ege University Faculty of Medicine, İzmir, Turkey

Address for Correspondence: Figen Tarhan, Clinic of Internal Medicine, İzmir Atatürk Research and Training Hospital, İzmir, Turkey

E-mail: eminefigentarhan@hotmail.com

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and skin involvement, the initial treatment included hydroxychloroquine (200 mg/day) and moderate to low doses of methylprednisolone. She responded well to this treatment. Unfortunately, she did not return for regular visits, and was lost to follow-up for six years.

In 2009, six years after the first visit, she was referred to the rheumatology outpatient clinic with malaise and oedema. She reported using hydroxychloroquine and methylprednisolone treatment for almost two years and stated that she remained well during this period. She later confessed that she had stopped the hydroxychloroquine treatment and only used methylprednisolone 4 mg daily irregularly. She pointed out that malaise and oedema had first occurred nearly 3-4 months ago and persisted thereafter. Blood pressure was normal. Her laboratory test results were as follows: ESR 32 mm/hr, WBC count 3.24/μL (4.60-10.2), haemoglobin 12.1 g/dL (12.2-18.1), ANA 1/320 peripheral, anti-double-stranded DNA (Crithidia test) positive, C3: 50 mg/dL (83-193) and C4: 2 mg/dL (15-57). Although urinary analysis was initially normal, proteinuria in the non-nephrotic range (520.41 mg/24 hours) was detected. There was no haematuria, and the remaining laboratory tests were within normal limits (Table 1). Renal biopsy was performed, and histopathological examination showed membranous glomerulonephritis, consistent with class V lupus nephritis. High dose methylprednisolone (48 mg daily) and azathiopirine (AZA) 2 mg/kg/d were commenced. In addition, trandolapril 2 mg/d was added to reduce urinary protein loss. Methylprednisolone dose was later gradually tapered to 4 mg/d. She responded well to this treatment; oedema regressed and proteinuria disappeared.

In the first few months of 2011, she complained of severe inflammatory low-back pain, which was worse in the morning and after resting periods, and improved with daily activity. There was morning stiffness which persisted for 6-7 hours. There was also pain with pressure application on both sacroiliac joints (SIJ); anterior flexion and lateral movements of the lumbar vertebra were limited. Conventional radiography of the pelvis revealed grade 2 bilateral sacroiliitis (Figure 1), while conventional lateral radiography of the feet showed bilateral calcaneal spurs at the insertion of plantar fascias (Figure 2). Magnetic resonance imaging (MRI) revealed bilateral active sacroiliitis, which was more prominent on the right side, based upon bone marrow oedema in T2-weighted STIR sequences and contrast enhancement in T1-weighted sequences (Figure 3, 4). HLA-B27 was also found to be positive. Hence, the additional diagnosis of AS was made eight years

Table 1. Clinical symptoms, findings, laboratory test results and treatment over time

	At the time of SLE diagnosis (2003)	At the time of lupus nephritis diagnosis (2009)	At the time of AS diagnosis (2011)
Prominent clinical symptoms and findings	Inflammatory arthritis of the hand joints, malar rash, photosensitivity	Oedema, malaise	Inflammatory back pain
White blood cell	3.85/μL	3.24/μL	4.25/μL
Haemoglobin	10.4g/dL	12.1g/dL	11.5/g/dL
Platelet	Normal	Normal	Normal
Erythrocyte sedimentation rate	45 mm/hr	32 mm/hr	22 mm/hr
Antinuclear antibody test	1/320 peripheral and granular	1/320peripheral	1/160 peripheral
Anti-dsDNA (Crithidia) test	Positive	Positive	Positive
Complement 3 (N: 83-193)	65 mg/dL	50 mg/dL	70 mg/dL
Complement 4 (N: 15-57)	3 mg/dL	2 mg/dL	15 mg/dL
Proteinuria	Negative	520.41 mg/24 hours	Negative
Haematuria	Negative	Negative	Negative
Liver function tests	Normal	Normal	Normal
Serum creatinine level	Normal	Normal	Normal
Treatment	Hydroxychloroquine, methylprednisolone	Methylprednisolone, azathiopirine, trandolapril	NSAID, methylprednisolone, azathiopirine, trandolapril

SLE: systemic lupus erythematosus; AS: ankylosing spondylitis

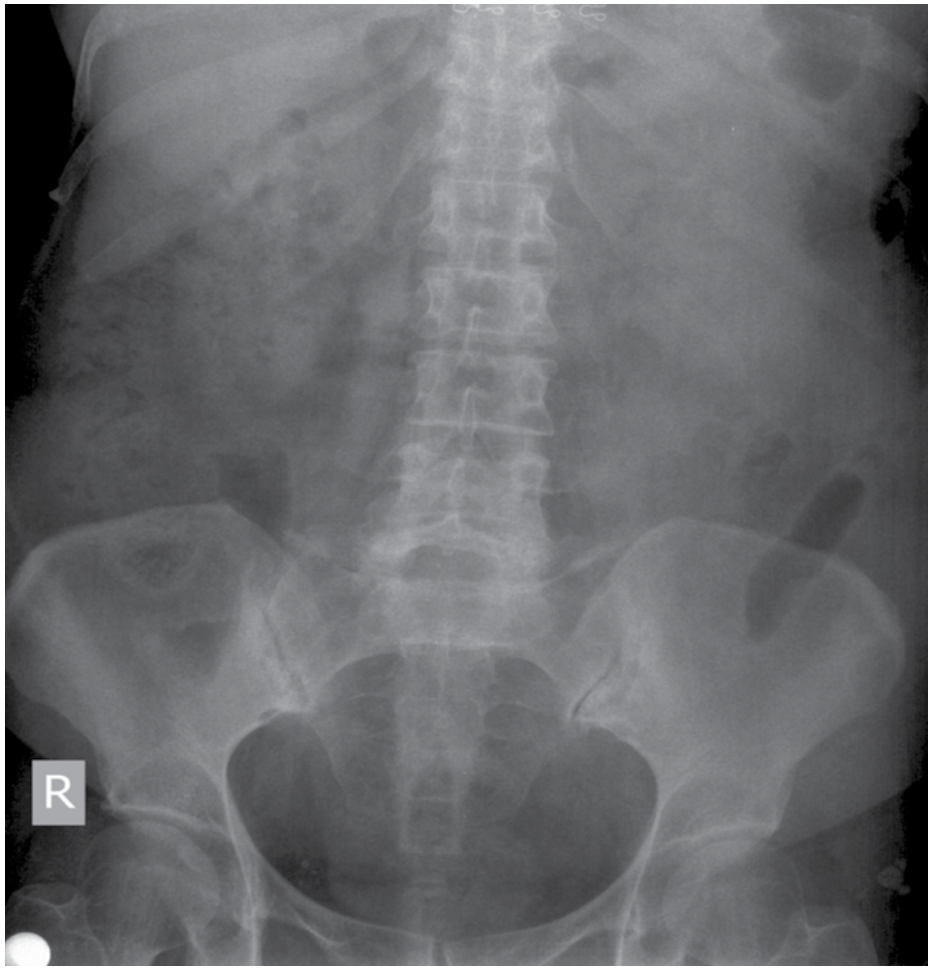

Figure 1. Bilateral grade 2 sacroiliitis with conventional x-ray

Table 2. Overview of the reported cases with the coexistence of systemic lupus erythematosus and ankylosing spondylitis, along with the present case

	Nashel et al. (3) 1982	Olivieri et al. (4) 1989	Korkmaz et al. (5) 2006	Chandrasekhara et al. (6) 2008	Singh et al. (7) 2010	Jiang et al. (8) 2010	Mrabet et al. (9) 2011	Kook et al. (10) 2011	Tarhan et al. (current study)
Gender	Male	Female	Female	Female	Male	Male	Female	Female	Female
Age (years)	43	42	26	21	35	29	34	21	55
Treatment	Phenylbutazone, Indomethacin, Corticosteroid	Corticosteroid, Hydroxychloroquine	Methotrexate, Indomethacin, Cyclophosphamide, Azathioprine, Corticosteroid	Methotrexate, Hydroxychloroquine, Corticosteroid	Not reported	Diclofenac, Sulfasalazine, Methotrexate, Cyclophosphamide, Azathioprine, Corticosteroid	Indomethacin, Corticosteroid, Hydroxychloroquine, Methotrexate	Corticosteroid, Hydroxychloroquine, Sulfasalazine	Corticosteroid, Hydroxychloroquine, Azathioprine
Accompanying diseases	——	——	Hereditary coproporphyria	Dermatomyositis, Hypothyroidism	——	Hypoparathyroidism	——	——	——
Mucocutaneous involvement	Malar rash, alopecia, discoid skin lesions	Malar rash, mouth ulcers, alopecia, Raynaud's phenomenon, digital vasculitis	——	Malar rash, alopecia, Raynaud's phenomenon, photosensitivity	Malar rash, discoid rash	Malar rash	Malar rash, discoid rash, mouth ulcers	Malar rash	Malar rash
Arthritis	Ankle, knee, proximal interphalangeal, metacarpophalangeal	Knee, ankle, wrist	Knee, ankle	Knee, wrist, elbow	——	——	——	Knee	Wrist, proximal interphalangeal, metacarpophalangeal
Renal involvement	Positive	Positive	Positive	Negative	Positive	Positive	Negative	Negative	Positive
Haematological involvement	——	——	Leukopenia, thrombocytopenia	Anaemia	Anaemia	Anaemia	Anaemia	Leukopenia,	Anaemia, leukopenia
Antinuclear Antibody	Homogenous; titre not available	1/640 diffuse	Positive; pattern and titre not available	Peripheral; titre not available	Positive; pattern and titre not available	Positive; pattern and titre not available	1/800 diffuse; titre not available	1/640 speckled; titre not available	1/320 peripheral and speckled
Other immunologic tests and HLA typing	HLA A1, A2, B8, C3, DR2, DR3 HLA B27	Anti-ds DNA, hypocomplementemia HLA-A2, A24, B18, Cw2, DR3, DR7, DQw2, DQw3	Lupus band test, Anti-ds DNA HLA A2, A31, B40, DR1,DR3,B27, hypocomplementemia	Anti-dsDNA, hypocomplementemia	Anti-dsDNA, HLA-B27	Anti-dsDNA, anti SSA, HLA-B27	Anti-dsDNA, lupus band test, HLA-B27	Anti-dsDNA	Anti-dsDNA, hypocomplementemia, HLA-B27
Sacroiliac Joint X-Ray	Grade 4 bilateral sacroiliitis	Grade 3 bilateral sacroiliitis	Sacroiliitis	Grade 2 bilateral sacroiliitis	Grade 1 bilateral sacroiliitis	Bilateral sacroiliitis	Grade 2 bilateral sacroiliitis	Bilateral sacroiliitis	Grade 2 bilateral sacroiliitis
Sacroiliac Joint CT	Not available	Not available	Not available	Bilateral sacroiliitis	Not available	Bilateral grade 3 sacroiliitis	Bilateral sacroiliitis	Not available	Not available
Sacroiliac Joint MRI	———	———	———	———	———	———	———	———	Bilateral active sacroiliitis
Lumbar/dorsal spine X-Ray	Syndesmophytes	Subchondral osteitis	Not available	Not available	Not available	Not available	Syndesmophytes	Not available	Normal
Lateral calcaneal X-Ray	Not available	Spurs	Not available	Not available	Not available	Not available	Spurs	Not available	Spurs

Anti-dsDNA: anti-double stranded DNA; CT: computed tomography; MRI: magnetic resonance imaging

after the initial diagnosis of SLE. Hepatitis B and C viruses, human immunodeficiency virus and Brucella serology were negative. The chest x-ray was normal. Her family history was not positive for SLE or AS.

The symptoms of inflammatory low-back pain remitted with non-steroidal anti-inflammatory drug (NSAID) treatment. Also, she continued to receive low dose methylprednisolone (4 mg/d), AZA (2 mg/kg/d) and trandolapril (2 mg/d). Clinical symptoms and findings, as well as laboratory test results and treatment over time are shown in Table 1.

Discussion

The coexistence of SLE and AS is very rare, and, to the best of our knowledge, the present case is only the ninth reported case in the English literature. In this 55 year-old female patient, the diagnosis of SLE preceded the diagnosis of AS by 8 years. From the point of view of SLE, arthritis, malar rash, leucopenia, anaemia, type V membranous lupus nephritis, positive lupus serology and hypocomplementemia were present. On the other hand, typical inflammatory low-back pain, HLA-B27 positivity, the presence of bilateral active sacroiliitis with MRI and bilateral calcaneal spurs with plain radiography supported the additional diagnosis of AS. This patient met both the American College of Rheumatology (ACR) criteria for SLE, and the Assessment in Ankylosing Spondylitis (ASAS) criteria for AS (1, 2).

The present case is the first case of AS-SLE coexistence in which the diagnosis of AS has

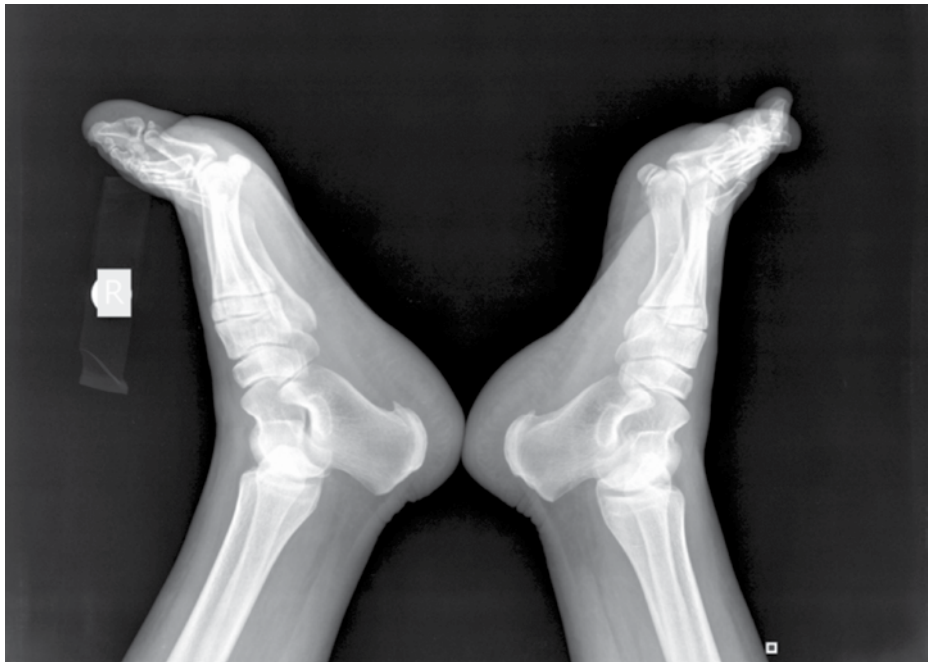

Figure 2. Lateral view of the calcaneus with spur formation

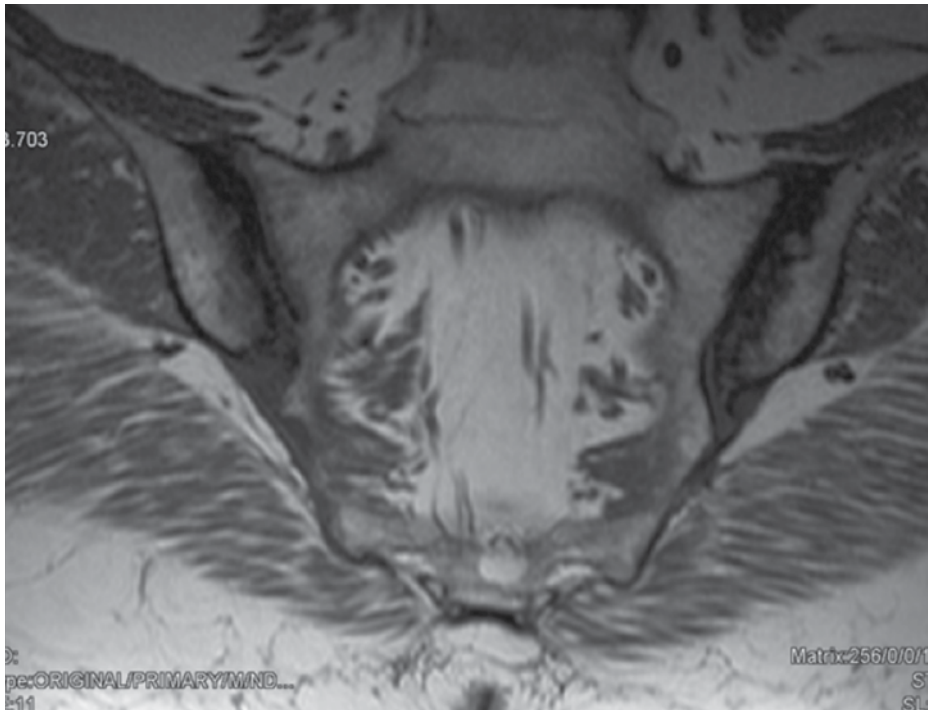

Figure 3. T1 weighted coronal MR image; there is subchondral sclerosis at the iliac sides of sacroiliac joints which represents chronic sacroiliitis

been further confirmed with MRI findings. The presence of bilateral active sacroiliitis was confirmed by bone marrow oedema in T2-weighted STIR sequences and contrast enhancement in T1-weighted sequences. MRI is clearly more sensitive than conventional radiography for the detection of sacroiliitis (11). In the previous case reports, the presence of sacroiliitis was mostly shown by conventional radiography (3, 4, 5, 7, 10), while Chandrasekhara et al. (6), Jiang et al. (8) and Mrabet et al. (9) additionally used computerised tomography (CT). Although CT of the SIJs cannot detect acute inflammatory changes in the bone marrow, it is superior to MRI and conventional radiography in visualising erosions and bony sclerosis. The routine use of CT is not recommended because of the relatively high dose of gonadal radiation and a lack of consensus on how to interpret the SIJ findings of CT (11).

The main clinical and laboratory findings of the eight previously reported patients with SLE and AS coexistence, together with the present case, are summarised in Table 2. While SLE generally occurs in females, AS is more frequently seen in males. Interestingly, most of the reported patients with the coexistence of SLE and AS, including the present case, are female (F/M: 6/3). In most cases, including the present case, SLE symptoms preceded those of AS (F/M: 5/4) (4, 5, 6, 9). On the other hand, the association between HLA-B27 and AS is well known, and the HLA-B27 molecule plays a role in the pathogenesis of AS. HLA-B27 was positive in four of the previously reported cases (3, 7, 8, 9), as seen in the present case.

Although rare, isolated sacroiliitis without fulfilling the diagnosis of AS can also be seen in connective tissue diseases such as SLE. De Smet et al. (12) described elevated radionuclide count uptake ratios in the sacroiliac joints of 9 patients with active SLE, who also had radiologic signs of sacroiliitis. These authors reported that the uptake ratios returned to normal in patients achieving remission. Nassonova et al. (13) detected the presence of sacroiliitis using conventional radiography in 22 out of 43 male patients with SLE and reported that NSAIDs were not effective as a treatment. However, low-back pain and symptoms of morning stiffness regressed with NSAID treatment in the current case. Vivas et al. (14) also investigated the presence of sacroiliitis in 16 male patients with SLE, and detected unilateral sacroiliitis in four, and bilateral sacroiliitis in four. HLA-B27 was reported to be negative in all of these patients. The presence of unilateral sacroiliitis confirmed with CT was reported in another case report, in a 28 year-old female patient with SLE (15).

The coexistence of these two diseases with different genetic backgrounds in the same patient is much lower than expected based upon their prevalence in the general population. It has been suggested that the combination of HLA-B27 with HLA-A1 and HLA-DR2, or with HLA-A1 and HLA-DR3, is very rare (3). The rare combinations of the susceptibility genes of AS and SLE were speculated to explain the rarity of the coexistence of these two diseases. However, epidemiological data concerning the exact genetic risks for the coexistence of SLE and AS are not yet available (10).

In conclusion, the coexistence of SLE and AS is very rare. Including the present case, there are only nine reported cases. Most of the cases are female and SLE generally precedes the occurrence of AS. The present case is also notable as both MRI confirmation of bilateral active sacroiliitis with bone marrow oedema and HLA-B27 positivity are reported.

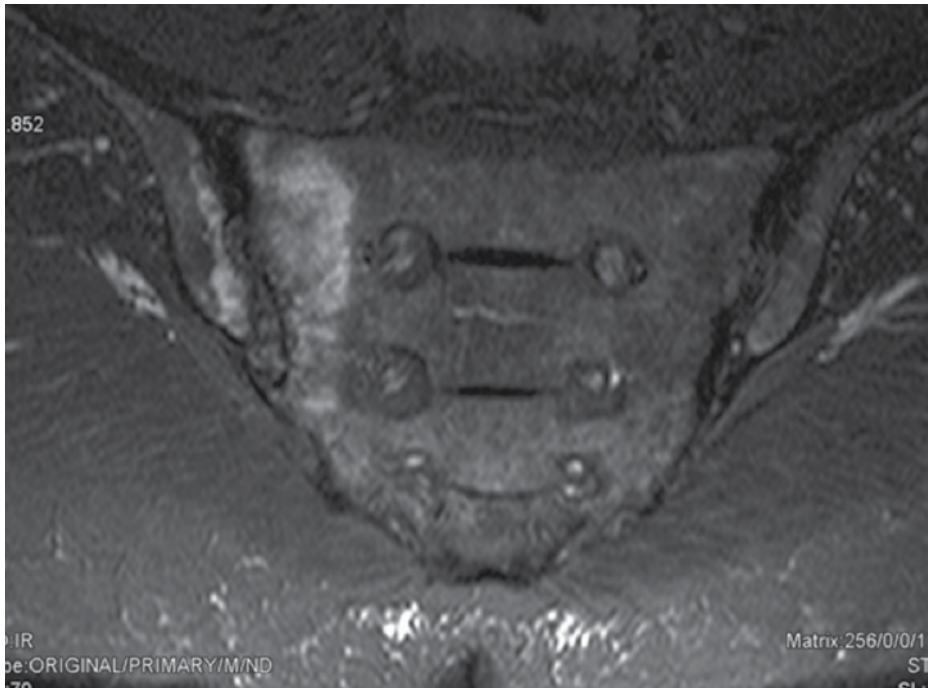

Figure 4. Coronal STIR MR image shows bilateral active sacroiliitis, more prominent on the right side (there is extensive bone marrow edema both sides of the right sacroiliac joint)

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