Case Report / Olgu Sunumu

Anti-CCP Antibody Positivity in a Patient with Ankylosing Spondylitis

Ankilozan Spondilitli Bir Hastada Anti-CCP Antikoru Pozitifliği

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ABSTRACT

Anti-cyclic citrullinated peptide (anti-CCP) antibodies are specific markers of rheumatoid arthritis. However, they can be detected in other rheumatic diseases. Herein, we aimed to present a rare case of positive anti-CCP antibody in a 40-year-old female patient with ankylosing spondylitis and review the literature.

Keywords: Sacroiliitis, ankylosing spondylitis, rehabilitation

ÖZET

Antisiklik sitrülin peptid (anti-CCP) antikorları romatoid artritin özgün belirteçleridir. Fakat diğer romatolojik hastalıklarda da saptanabilirler. Burada 40 yaşında ankilozan spondilitli bir kadın hastada, nadir görülen pozitif anti-ccp antikoru olgusunu sunmayı ve literatürü gözden geçirmeyi amaçladık.

Anahtar sözcükler: Sakroileit, ankilozan spondilit, rehabilitasyon

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Introduction

Anti-cyclic citrullinated peptide (anti-CCP) antibodies bind antigenic determinants that contain unusual amino acid citrulline, which is a posttranslational modification of the amino acid arginine by the enzyme peptidylarginine deiminase (1). They are characteristic and specific markers of rheumatoid arthritis (RA), and their presence especially at high titers indicates more aggressive disease (2). They can be used as prognostic markers of an erosive disease in early RA (3).

Ankylosing spondylitis (AS) is a chronic inflammatory disease mainly affecting axial spine and sacroiliac joints (4). It is a member of SpA group. Its pathogenesis is not clearly known, but immune mediated mechanisms including human leucocyte antigen (HLA)-B27, inflammatory cellular infiltrates, cytokines such as tumor necrosis factor-alpha and interleukin 10, and genetic and environmental factors are thought to be associated (5). No sufficient serological markers have been defined in AS for describing disease activity or predicting prognosis in AS, like rheumatoid factor and anti-CCP in RA and anti-double stranded DNA antibodies in systemic lupus erythematosus (6).

Despite anti-CCP is a specific marker of RA in predicting disease activity and as well as prognosis, in some studies they have been found to be linked with other types of inflammatory diseases including psoriatic arthritis (PsA) (7), spondyloarthritis (SpA)(6), Sjogren syndrome (8), and systemic sclerosis (9). In this case, we report an anti-CCP antibody positive female patient who presented with ankylosing spondylitis.

Case Report

A 40-year-old woman was admitted to our outpatient clinic with complaints of severe pain in low back and hips. The patient presented with a history of ten years of mild back pain which exacerbated progressively. Her low back pain was not improving with resting and not radiating to her legs. She was complaining of morning stiffness lasting thirty minutes in the mornings. Her past medical history did not include any rheumatologic symptom including arthralgia or joint swelling; or skin lesion such as psoriasis. She did not report a family history for any rheumatic disease.

Physical examination revealed limitation in the lumbar spine. Modified Schober: 4 cm, fingertip-to-floor distance: 15 cm. Sacroiliac compression tests and Gaenslen tests were bilaterally positive. Straight leg raising and femoral stretch tests were negative. She had no swelling, erythema or warmth in her peripheral joints. Bath Ankylosing Spondylitis Disease Activity Index (BASDAI): 4.8, Bath Ankylosing Spondylitis Functional Index (BASFI):6, Bath Ankylosing Spondylitis Metrology Index (BASMI): 2. Neurological examination was normal. In eye examination, uveitis was not detected.

Laboratory parameters showed the following: erythrocyte sedimentation rate (ESR) 10 mm/hr (normal range: 0-12 mm/hr), C-reactive protein (CRP) 4 mg/L (normal range: 0.00-5.00 mg/L). Complete blood count and routine biochemistry test results were within normal ranges. HLA-B27, antinuclear antibody (ANA) and rheumatoid factor (RF) were negative. Anti-CCP was 122.5 IU/ml (normal range: 0.00-20.00 IU/mL).

Lumbosacral spine X-ray and sacroiliac magnetic resonance imaging (MRI) showed grade 4 sacroiliitis on the left side (Figure 1, 2).

The patient was diagnosed as AS, and prescribed sulphasalazine 2g/day. At her first follow-up control, her symptoms such as pain and morning stiffness were reduced.

Discussion

Anti-CCP antibodies are accepted as specific markers of rheumatoid arthritis (RA) and have been included in the revised classification criteria for diagnosis of RA (10). They have been used as markers to differentiate early rheumatoid arthritis from undifferentiated polyarthritis (11). Furthermore, it is suggested to be sited in serological markers also including HLA-B27, HLA-DR4, HLA-DR2, rheumatoid factor which are used in differential diagnosis from AS (12). In 2005, Vander Cruyssen et al. (13) analyzed serum samples of 192 patients with PsA and detected anti-CCP in 7.8% of the patients. They emphasized two hypotheses about anti-CCP positivity in the patients with PsA. First, anti-CCP patients might be present in the patients with PsA. Second, after several years, concomitant RA might occur in these patients. Bogliolo et al. (14) found anti-CCP positivity in small

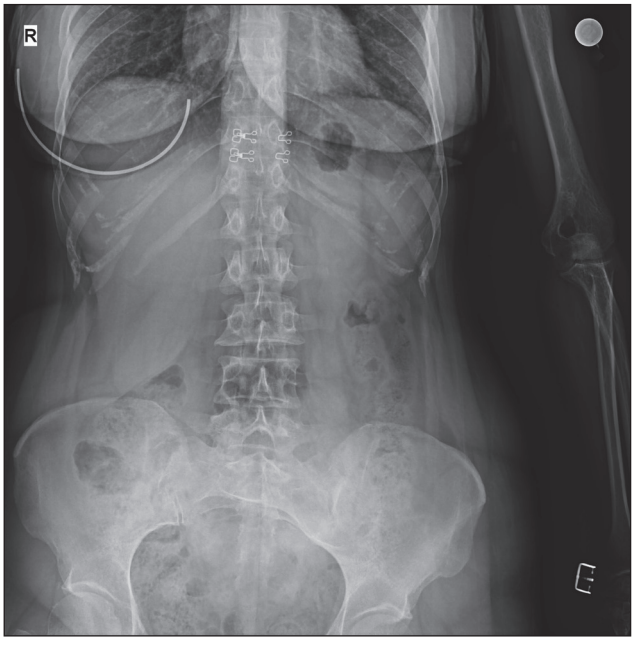

Figure 1. Anteroposterior lumbosacral x-ray showing complete fusion of left sacroiliac joint space.

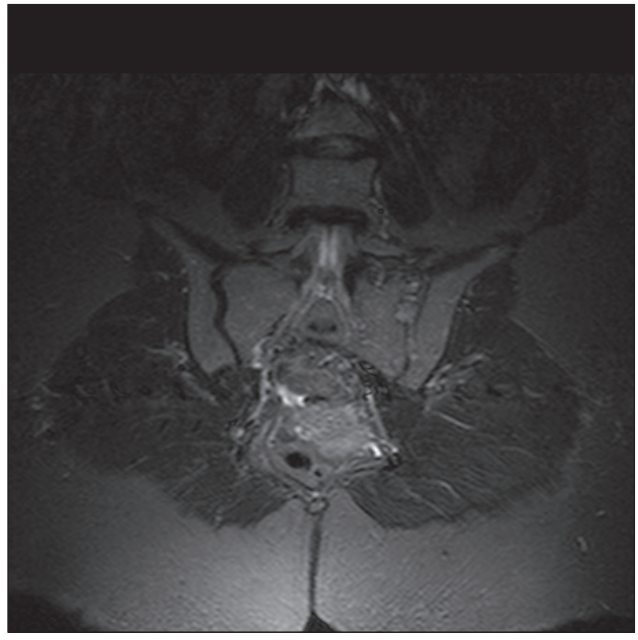

Figure 2. STIR MRI confirming ankylosis of left sacroiliac joint.

but significant proportion of patients with PsA and suggested that it was associated with erosive arthritis and multiple joint involvements. On the other hand, Abdel Fattah et al. reported anti-CCP positivity as 17.5% in Egyptian PsA patients and they concluded that it was associated with joint erosions and physical disability (15). They advocated another hypothesis that anti-CCP positive PsA patients might suffer from an overlap with a preclinical form of RA. Korendowych et al. (16) found that 5.6% of PsA patients were positive for anti-CCP antibodies and similarly confirmed that anti-CCP was a marker of disease severity in PsA. Alenius et al. (17) reported that the presence of anti-CCP antibodies was linked with polyarthritic disease, however did not relate to radiological changes or functional impairment.

Anti-CCP positivity in SpA has been previously mentioned in the literature. Recently, Payet et al. (10) conducted a study in 1162 patients with various rheumatic diseases and found anti-CCP positivity as 70% in RA, 10.7% in PsA and 2.6% in other types of SpA. Kim et al. (6) detected anti-CCP antibodies in 4% of 625 patients with ankylosing spondylitis. They reported that the presence of titers of anti-CCP antibodies over three times the normal upper limit was significantly associated with peripheral arthritis in the patients with AS. Although our patient had a titer of anti-CCP greater than six times the upper limit of normal, she did not have peripheral arthritis.

Our patient fulfilled the modified New York Criteria for AS (18). HLA typing was negative for B27. Her clinical picture was compatible with AS, and did not resemble other rheumatic diseases including RA and PsA. Her BASDAI score was 4.8, indicating high disease activity. However she did not have any painful or swollen joints as an evidence for peripheral joint involvement. We have three theories about anti-CCP positivity in our patient. First, presence of anti-CCP may be associated with high disease activity. Second one is occurrence of anti-CCP antibodies years before the clinical manifestation of RA. And the third one is a possible overlap with a preclinical form of RA.

Since anti-CCP antibodies are thought to be high sensitive and specific for RA, the presence of anti-CCP antibodies may lead into mistake in the differential diagnosis. Therefore, other diseases including PsA and SpA should be kept in mind in case of anti-CCP positivity. Further studies are warranted to recognize other diseases that may lead to anti-CCP positivity.

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