Case report

Coexisting ankylosing spondylitis and rheumatoid arthritis: A case report with literature review

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A 30-year-old female patient with coexisting ankylosing spondylitis and rheumatoid arthritis was diagnosed and treated. The human leukocyte antigen (HLA)-B27 is a predisposing factor of ankylosing spondylitis and HLA-DR4 is a predisposing factor of rheumatoid arthritis. This patient was HLA-B27 and HLA-DR4 positive, and ankylosing spondylitis manifested before rheumatoid arthritis. After disease modifying anti-rheumatic drugs successfully arrested ankylosing spondylitis activity the patient conceived and delivered a healthy baby. One year later, she developed peripheral polyarthritis and was diagnosed with rheumatoid arthritis. We hypothesized that pregnancy may be one of the environmental factors that can activate rheumatoid arthritis, and that disease modifying anti-rheumatic drugs play an important role in keeping the disease under control.


Ankylosing spondylitis (AS) and rheumatoid arthritis (RA) are two common types of rheumatic disease. Each disease can be characterized by specific symptoms, serological tests and radiologic changes. However, the clinical manifestations of the two diseases are similar, including morning stiffness, peripheral arthritis, and erosion changes on radiography. Hence, sometimes the diagnosis can be difficult.

Recent studies suggest that various factors, including major histocompatibility complex type II (MHC-II) antigen, various mediators of inflammation, cytokines, chemotactic factors, genetic susceptibility, immunologic disorders, and environmental factors, may cause these diseases, but the pathogenesis is still unknown. We hypothesized that pregnancy may be one of the environmental factors that can cause AS and RA associated together in patients who are positive for human leukocyte antigen subtypes (HLA)-B27 and HLA-DR4.

The typical symptoms of AS and RA are totally different. However, we suggest that if an RA patient has an extra-articular symptom of AS or an AS patient has a peripheral joint symptom of RA, more tests are needed to determine whether coexisting AS and RA are present. Regular treatment with systemic disease-modifying anti-rheumatic drugs (DMARDs) may delay the disease process.

CASE REPORT

A 30-year-old female had a 7-year history of pain in the lumbosacral area and a 1-year history of pain in the joints of both hands, which had been exacerbated for the previous 2 months. Seven years prior (May 2003) to admission to our institution, the patient felt pain in the lumbosacral area, and found it was hard to turn her body over at night, although the pain would lessen after activation in the morning. The woman underwent a physical examination on hospital admission. Her general health status was good and auscultation of the heart and lungs was normal. No swelling and tenderness in the joints of the four limbs was observed. The Patrick’s test in the left leg and the Schober test were positive. Laboratory examinations are shown in Table. CT of the lumbosacral area showed destruction of the bilateral articular surfaces of the left sacroiliac joint, but the joint space remained normal. No obvious X-ray changes were noted in the joints of both hands.

According to evaluation of symptoms and signs as well as radiologic examination, our diagnosis was AS. She was given meloxicam 15 mg per day as symptomatic treatment, and oral DMARDs (sulfasalazine 1.5 g per day, hydroxychloroquine 0.4 g per day) to control the disease. After the disease stabilized, the patient was discharged from hospital. In the following years, the patient continued regular use of DMARDs to control the disease.

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Thanks to the systemic treatment, the symptoms and signs both improved.

Six months after drug withdrawal, the patient conceived and delivered a healthy baby. Because of the pregnancy, the patient had stopped taking anti-rheumatic drugs for two years. However, one year prior to seeking medical help, she developed pain in the joints of both hands and elbows, predominantly in the metacarpophalangeal (MCP) joints. This was accompanied with morning stiffness. Two months prior to presenting at our hospital, the joint pain became worse and involved the wrists and knees. She did not have a dry mouth, dry eyes or Raynaud’s phenomenon. She came to our hospital as an AS patient. Her vital signs and her consciousness level were normal. No tumefaction was found in the shallow lymph nodes, and her lungs, heart, and abdomen were also normal. Activation of the spinal column and both lower extremities were normal. However, the Patrick’s test was positive. The symptom of tenderness of the MCP joint, wrist and proximal end of the finger joints was positive, but activity in these joints was not limited. Laboratory examinations are shown in Table. CT examination showed bilateral bony sclerosis of the sacroiliac joints, and the bone of the left sacroiliac joint had been destroyed, that were in accordance with changes seen in AS (Figure 1). DR of the hands showed that parts of the joint space of the carpal bones of both hands were fuzzy, and the local sclerotin had been destroyed (Figure 2). These findings were in accordance with radiological changes seen in RA.

Our diagnosis was coexisting AS and RA. We gave the patient DMARDs, leflunomide, hydroxychloroquine sulfate, and total glucosides of paeony capsules. The patient was finally discharged from the hospital when the disease became under control.

**DISCUSSION**

At the beginning, this patient mainly had pain in the sacroiliac joints and destruction of bone without obvious symptoms in the peripheral facet joints. Symmetric pan-artritic changes in both hands and elbows were seen subsequently. Recent reports have presented cases in which AS and RA were associated. However, it is rare for two types of disease to occur over a long period of time (6 years) as we reported in this work. In AS-RA-associated cases, some patients have AS at a young age and, after the disease has been quiescent for several years or decades, RA emerges, which is what was seen in our patient.

In general, AS and RA are considered to be two independent diseases. AS and RA have different genetic factors, pathogeneses, and clinical features, and the probability that a single patient will develop both AS and RA is low. AS primarily involves the central axis joints and is always accompanied by lumbodorsal pain as a result of inflammation. Enthesopathy is seen as pathological changes such as those in the knees, ankles, metatarsus, hip joints and other weight-bearing joints. These changes are asymmetric and rarely involve pain in the joints of the upper extremity. RA mostly involves the facets of limbs and is more commonly seen in the upper extremities. Most patients experience pain on the facets of the four limbs, which is accompanied by early-morning stiffness in both hands and synovitis. However, involvement of the sacroiliac joint is rare. If the differential diagnosis is difficult, we can examine the levels of HLA-B27, HLA-DR4, HLA-DR2, rheumatoid factor (RF) and anti-CCP antibody.

Some authors have suggested that AS and RA had identical or similar causes because of the particular genetic backgrounds that may lead a patient to develop AS or RA. So, if a patient simultaneously has the predisposing gene HLA-B27 of AS and predisposing gene HLA-DR4 of RA, and is affected by an environmental agent, AS and RA can coexist. Some authors have suggested that awareness of the possible coexistence of AS and RA may be of therapeutic importance because patients might otherwise be denied such therapeutic agents as chloroquine, which are not known to be beneficial in AS but are often helpful in RA. The influence of HLA-B27 antigen on the course of RA and the influence of HLA-DR4 on the course of AS is not clear. However, previous studies have suggested that there is no erosive polyarthritis in RF positive AS patients, and sacroiliac joint involvement is not commonly seen in RA patients who are HLA-B27 positive.
Our patient was a young female in whom AS and RA coexisted. She was HLA-B27 and HLA-DR4 positive, demonstrating that genetic factors do play a decisive role in the disease process. RA symptoms emerged after pregnancy, which means that pregnancy may be the environmental agent that caused AS and RA to coexist in this case. In addition, the association between AS and RA may be a symptom of an unknown disease but, at present, it can be understood as two diseases that can overlap occasionally.

Since Fallet et al⁸ reported 9 cases of coexisting RA and AS, reports in the English literature have been sporadic. Until 1998, there were fewer than 60 case reports. In the previous decades, 20 similar cases had been reported in China. The incidence of AS-RA-associated cases is 1 per 50,000 to 1 per 238,000⁹,¹⁰ and given this probability, more cases should have been reported; the under-reporting may be the result of lack of clinical observation or examination. Some patients with AS do not have the typical symptoms and signs of an involvement in the central axis joints, and peripheral arthritis can also be covered by the manifestations of RA. However, if the symptoms of RA are highlighted, then the HLA-B27 test and radiologic examination of the sacroiliac joint are rarely done in routine practice. However, a patient with negative results for RF and HLA-B27 can also have coexistent AS and RA.¹⁰ All of the reasons described above can result in a missed diagnosis of coexistent AS and RA. Consequently, if one sees a young patient with RA with extra-articular symptoms of AS and evident pathological changes in the hip joints (e.g., myotenositis, iridocyclitis, sinus bradycardia), we should ask if there is low-back pain to discover if AS and RA coexist, and a HLA-B27 test and radiologic examination of the sacroiliac joint should be performed. Meanwhile, if one sees an AS patient with symptoms in the peripheral joints, testing for the HLA-DR2 gene, HLA-DR4 gene, and anti-CCP antibody should be performed. Some authors have suggested that radionuclide scanning and CT may be important for detecting sacroiliac disease, not only in AS patients but also in RA patients who may have lumbar pain and sacroiliac lesions.¹¹ Both methods are particularly useful in detecting early AS abnormalities, but are not commonly performed in China.

When our patient was first discharged from hospital, her condition improved after systemic treatment of AS. After years of follow-up, her condition was stable without obvious disease progress. This may be the result of the reinforcement of systemic and regular treatment with DMARDs. However, she discontinued therapy because of pregnancy, which may be one of the reasons behind the development of RA. Along with the rapid development of genetic diagnostics and widespread use of biologic agents, the AS-RA-associated patients will hopefully get a definitive diagnosis and be treated appropriately in a timely fashion.

REFERENCES


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