A case of ankylosing spondylitis in female siblings

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ABSTRACT

Historically, ankylosing spondylitis (AS) was thought to be more common in males than in females. However, recent research into AS epidemiology has revealed an increasing incidence of female patients. First, 24-year-old patient A sought medical attention for severe pain in her lower back and buttocks. Then, 4 years later, patient B, 22 years old, the younger sibling of patient A, sought medical attention for the same symptoms. Both patients were diagnosed with AS. We note that the older sister's diagnosis was delayed by 5 years for a number of reasons, including the gender-specific nature of the disease. At the same time, the younger sister was diagnosed with AS immediately because the older sister had already been diagnosed. This case highlights the gender differences in the AS diagnosis. Despite the traditional understanding of the disease as predominantly affecting males, clinicians should consider and highlight the increasing prevalence of AS in females to avoid misdiagnosis.

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Introduction

Ankylosing spondylitis (AS) belongs to a group of rare autoimmune diseases, affecting 9 to 30 people out of every 10,000 in the general population.[1] With a male-to-female prevalence rate of 3:1, AS has historically been considered to be more prevalent in males than in females.[2] However, recent research on the epidemiology of AS has revealed that female patients have an increasing incidence of the illness.[3] Concurrently, scientists have observed that the disease course exhibits gender-specific characteristics that make it more challenging to diagnose AS.[4-7]

Case Report

Two female sibling patients diagnosed with ankylosing spondyloarthritis came under our observation.

Patient A, a 24-year-old, sought medical attention for the first time in 2019. During her examination, she complained of significant movement limitation in her spine, particularly in her lumbar spine, severe pain in her lower back and buttocks that decreased with movement and increased with prolonged hypodynamia, and stiffness in her spine that persisted for more than an hour in the morning. According to the history of the disease, pain in the area of the ileosacral joints first appeared at the age of 19, and she did not associate the debut of the pain syndrome with anything. She sought medical help and underwent general clinical laboratory examination and radiography of the lumbar spine, but no pathologic abnormalities were found. After seeing a neurologist, she was given a

diagnosis of back pain and received courses of non-steroidal anti-inflammatory drug (NSAID) therapy (diclofenac) with short-term positive effects. The patient noted the persistence of permanent moderate pain syndrome until 2018. In 2018, following strong emotional stress (loss of a child in a car accident), the patient noted a strong deterioration of her condition, characterized by severe pain in her ileosacral joints and significant limitation of mobility, and therefore sought medical help. Past medical history revealed that she only experienced acute respiratory virus illnesses and childhood infections; otherwise, she grew up and developed in line with her age. There is no joint disease observed in the family, and the family history is calm.

During the examination, there was strong lumbar discomfort, positive results for the Schober and Thomayer tests, and the maximum distance between the ankles had decreased to 80 cm. The results of laboratory testing showed positive HLA-B27, a rise in C-reactive protein (CRP) to 15.9 mg/L (normally up to 5.0 mg/L), and an increase in erythrocyte sedimentation rate (ESR) to up to 50 mm/hour (normal from 2 to 15 mm/hour). A summary of the important laboratory results and the disease activity index are presented in Table 1. Instrumental studies based on magnetic resonance imaging (MRI) of the spine and sacroiliac joint revealed inflammatory changes in the thoracic and lumbar spine and bilateral stage 3 sacroiliitis. Figure 1 displays the MRI images. Ankylosing Spondylitis Disease Activity Score (ASDAS) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) indicated a high level of disease activity. The patient was diagnosed with AS based on the modified New York criteria and was prescribed therapy according to the AS clinical protocol of the Ministry of Health of the Republic of Kazakhstan (sulfasalazine 2 g). Against the background of sulfasalazine administration, she noted positive dynamics in the form of regression of pain syndrome and morning stiffness. The patient was transferred under observation to a rheumatologist at the place of residence.

4 years later, patient B, 22 years old, the younger sibling of patient A, went to the doctor. She reported stiffness in the mornings lasting up to 15 minutes, overall weakness, and lower back and buttocks discomfort that worsened with prolonged hypodynamia and lessened with activity. The patient states that her complaints first appeared 1.5 years ago when she fell from her height on her coccyx while skiing. After the fall, she began to notice pain in the lower back and buttocks. Throughout a period of a year and a half, the patient used NSAIDs with occasional short-term positive effects. The patient also started to have worsening pain syndrome and a decline in her quality of life, which pushed her to seek medical attention. Past medical history showed that she grew and developed as was expected with her age, with the only illnesses she had experienced being severe respiratory viruses and childhood infections. It was discovered that there was a family history of AS while studying hereditary anamnesis. Upon examination, the hip and ileosacral joints were painful. Upon examining the spine using the BASMI scale, no abnormalities from the norm were found. Laboratory tests revealed that the ESR grew to 26 mm/hour (normal is 2 to 15 mm/hour), the CRP to 6.6 mg/L (normally up is 5.0 mg/L), and the HLA-B27 test resulted in a positive result. The thoracic and lumbar spines showed degenerative-dystrophic alterations on MRI, which is indicative of bilateral stage 2 sacroiliitis, according to the instrumental examinations. Based on the ASDAS and

Table 1. Summary of important laboratory findings and disease activity index.

	Patient A	Patient B
ESR	50 m/hour Increased	26 m/hour Increased
CRP	15.9 mg/L Increased	6.6 mg/L Increased
HLA B27	Positive High genetic risk	Positive High genetic risk
Cytokines sCD40OL MDS PGGF-AA PDGF-AB/BB VEGF-A	Increased	Increased
BASDAI score	5.3 High	2 Moderate
ASDAS CRP score	3.1 High	2 Moderate

ESR, erythrocyte sedimentation rate; CRP, c-reactive protein; sCD40l, soluble CD40-ligand; MDC, macrophage-derived chemokine; PGGF-AA, platelet-derived growth gactor AA; PGGF-AB, platelet-derived growth gactor AB; VEGF-A, vascular endothelial growth factor A; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; ASDAS, Ankylosing Spondylitis Disease Activity Score.

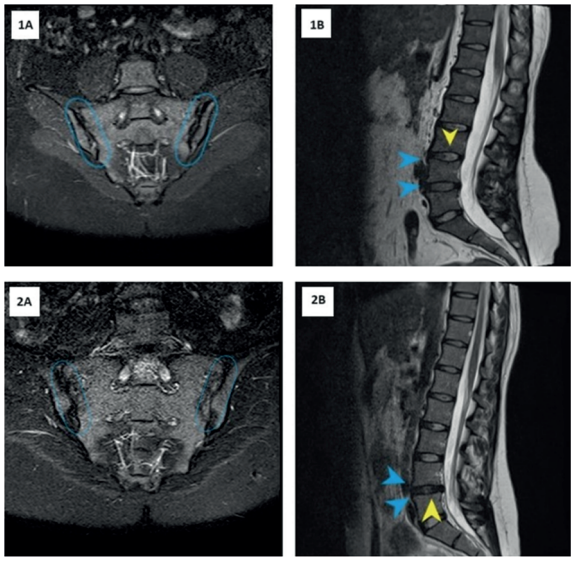

Figure 1. 1A) Magnetic resonance imaging (MRI) findings in patient A. Grade 3 sacroiliitis: the contours of the articular surfaces are uneven, and jagged due to subchondral sclerosis and erosions in STIR sequence; 1B) MRI findings in patient A. Degenerative changes of the spine: sharpening of the thoracic and lumbar vertebrae by small osteophytes (blue arrows), sclerosis of the end plates of the vertebral bodies (yellow arrow) in T1 sequence; 2A) MRI findings in patient B. Grade 2 sacroiliitis: subchondral sclerosis of the ileosacral joints on both sides in STIR sequence; 2B) MRI findings in patient B. Lower thoracic and lumbar vertebrae marginal sharpening by small osteophytes (blue arrows), sclerosis of the end plates of the vertebral bodies (yellow arrow) in T1 sequence.

BASDAI scales, a considerable degree of disease activity was noted. A diagnosis of AS was made using modified New York criteria, considering the patient's hereditary anamnesis, the patient's scant clinical manifestations during the objective examination, and the presence of sacroiliitis based on MRI data. Therapy was prescribed following the AS clinical protocol of the Ministry of Health of the Republic of Kazakhstan (sulfasalazine 2 g), in dynamics with improvement in the form of reduced pain syndrome.

Discussion

In contrast to other autoimmune disorders, AS has long been thought to affect primarily men. Male patients have a three times greater frequency of AS than female patients, as shown by epidemiologic research.[2] However, the proportion of female patients is rising in the present day. According to a study by Feldtkeller *et al.*, which examined 3000 patients from the German AS Society, the number of women diagnosed with AS increased from 10% in 1960 to 46% in 1990.[8]

In this clinical case, we can observe that the elder sister's diagnosis was delayed for 5 years, possibly as a result of the traditional understanding of the disease as mostly affecting males, as well as phenotypic aspects, such as a prolonged lack of radiologic abnormalities typical of the disease in women.

Recent research on the impact of gender characteristics on AS has shown that there is not only a rise in prevalence but also certain variations in the disease's course depending on gender. Thus, based on data from a study of 1514 patients from the Spanish registry of AS patients, it was discovered that, for patients with the same duration of the disease, men had greater structural lesions and radiologic alterations than women.[7]

Along with morning stiffness and an obvious joint pain syndrome, patient A also had a BASDAI score of 5.3, which is similar to the outcomes of other researchers who indicate that women have a more severe pain syndrome than males. A study of gender variations in AS, including 130 patients in Morocco, discovered the same data; moreover, women exhibited greater disease activity, as measured by a higher BASDAI score and more acute morning stiffness.[6] We did not observe any extraarticular manifestations in our patients, despite other publications reporting a greater prevalence of such manifestations, particularly enthesitis.[4]

Our ability to adequately compare the sisters' illness onset is limited by the 5 years that passed between the elder sister's diagnosis and the absence of an MRI diagnostic throughout this time. We cannot, however, rule out the possibility that the older sister's debut was devoid of MRI results. This is consistent with research showing that it is harder to identify AS in women than in males. Thus, Hwang *et al*., in their study of 7744 patients living in the USA with AS, emphasized that the historical view of AS as a predominantly male disease may lead to a delay in the diagnosis of AS in women.[5]

It is essential to note that the younger sister's heritage of AS was a crucial factor in the diagnostic search for the condition. Siblings had an 82% greater incidence of AS than the overall population, according to research data.[9] When the younger sister immediately sought medical assistance, she was instantly diagnosed with AS because the elder sister already had the diagnosis.

Conclusions

This case highlights gender differences in diagnosing AS. Despite the traditional understanding of the disease as predominantly affecting males, doctors should emphasize the increasing prevalence of AS among females to prevent misdiagnosis.

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