Gender Differences in Clinical Features and Anti-TNF Agent Use in Korean Ankylosing Spondylitis Patients

Chang Hoon Lee¹, Myeung Su Lee¹, Kwi Young Kang², Su Jin Mun³, Ji Min Kim⁴, Ho Seung Yun³, Seung Gi Kwak³, Ji Hyeon Ju³, Kyung Su Park³, Ho-Youn Kim³, Sung-Hwan Park³

Department of Internal Medicine, School of Medicine, Wonkwang University¹, Iksan, Chungbuk National University College of Medicine², Cheongju, The Catholic University of Korea School of Medicine³, Seoul, Division of Rheumatology, Department of Internal Medicine, Pusan National University Yangsan Hospital, Pusan National University School of Medicine⁴, Yangsan, Korea

Objective. The aim of this study was to assess the gender differences in the clinical presentation and treatment patterns between Korean women and men with ankylosing spondylitis (AS).

Methods. We retrospectively analyzed the data from extensive clinical assessments of 721 patients (162 women and 559 men) with AS, who were diagnosed at Seoul St. Mary’s Hospital, between January 2000 and September 2009. Clinical data, regarding the disease onset, disease duration, clinical presentations, status of human leukocyte antigen (HLA)-B27, and bone mineral density, were determined using a dual-energy X-ray absorptiometry (DEXA). Finally, we analyzed the medical treatments prescribed for these patients.

Results. The ratio of men to women was 3.45:1. Compared to men, women were older at the time of diagnosis, had shorter disease durations, and were diagnosed in earlier stages of the disease. More women had a history of uveitis at diagnosis than men. Back pain was the main presenting symptom, and its prevalence was the same in both genders. Fewer women showed cervical and thoracic axial involvement than men. Initially, more women had wrist and hand pain than men; however, at some point, peripheral arthritis development was equally likely in both genders. Women experienced shoulder pain, during the disease course, more often than men. On the other hand, men presented with knee and hip pain more often than women. Sulfasalazine and anti-TNF agents were more often prescribed to women.

Conclusion. The presentation and progression of AS showed a difference between women and men. Because of these differences, AS should be considered when a women presents with peripheral arthritis or uveitis in the early stage of the disease.

Key Words. Differences, Clinical presentation, Women, Ankylosing spondylitis, Men

Introduction

Ankylosing spondylitis (AS) is a chronic systemic inflammatory disorder. It is a seronegative spondyloarthropathy characterized by sacroiliitis and spondylitis. Although AS has historically been observed primarily in men, recent studies have shown that a significant proportion of patients with AS are women, with the ratio of men to women approaching 2-3 : 1 (1-3). The incorrect assumption that AS affects men almost exclusively has persisted throughout the first half of the twentieth century. Axial involvement with back pain are common features of AS, but a definitive diagnosis can be delayed because of the current lack of specific diagnostic indices. The differences in clinical presentation and disease course between men and women may also contribute to a delay in diagnosis.

The aim of this study was to compare the disease features of AS in women and men in order to better characterize any
gender differences in clinical features, medications, and bone mineral density, which would help elucidate the potential influence of gender on the severity of AS in patients.

**Materials and Methods**

We retrospectively analyzed the medical records of AS patients who visited the Rheumatology Department at Seoul St. Mary’s Hospital between January 2000 and August 2009 to identify patients who met the European Spondyloarthropathy Study Group Criteria (4) with radiographic sacroiliitis or Modified New York Criteria for AS (5). Patients who were thought to have degenerative arthritis and patients with a history of inflammatory bowel disease or psoriasis were excluded. A total of 162 women and 559 men met these criteria. The patient data that we analyzed addressed 2 aspects of the disease: (1) disease presentation at the time of diagnosis and (2) disease course.

**Disease onset, presentation, duration, and delay in diagnosis**

In order to determine the delay in diagnosis, we determined patient age at the time of disease onset and diagnosis; the delay was calculated by deducting the age at disease onset from the age at disease diagnosis. Disease duration was obtained by deducting the date of disease onset from the date of investigation.

**Clinical features**

We analyzed clinical features of AS, including first presenting symptom, initial site of pain, and history of uveitis at the time of disease onset. Data regarding history of peripheral arthritis, uveitis, and enthesitis and the site of axial involvement and peripheral arthritis were collected during the course of the disease. We also assessed human leukocyte antigen (HLA)-B27 status, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level, familial history of AS in first-degree relatives and X-ray pictures of the sacroiliac joints and spine. Bone mineral density of L-spine and femur were measured using dual-energy X-ray absorptiometry (DEXA). Osteoporosis was defined as a T-score less than or equal to -2.5 at the spine or hip. We also investigated the patients’ medication history, including the use of nonsteroidal anti-inflammatory drugs (NSAIDs), methotrexate, sulfasalazine, and anti-tumor necrosis factor (anti-TNF) agents.

**Statistical analysis**

Statistical analyses were performed using the Statistical Package for Social Sciences version 12.0. One-way analysis of variance and independent t tests were used to compare age at diagnosis, disease duration, and delay in diagnosis between men and women. Chi-square tests were used to compare the status of HLA-B27, the site of the first presenting symptom, a history of uveitis, site of peripheral arthritis and axial involvement, osteoporosis, and drug use. The comparison of T-scores in bone mineral density was adjusted for age (p<0.05).

**Results**

**Baseline characteristics**

In total, 721 patients (162 women, 559 men) were included in this study (Table 1). The ratio of male to female patients was 3.45 : 1. The mean age of women at the time of diagnosis was greater than that of men (39.6±11.1 years vs. 36.7±10.9, p=0.451). However, there tended to be a shorter delay in diagnosis (27.0±34.8 months [women] vs. 40.4±44.2 months [men], p<0.001) and a shorter disease duration in case of women (6.16±4.23 years [women] vs. 7.04±5.32 years [men], p=0.004). Furthermore, the number of first-degree relatives with AS in cases of women was greater than that in cases of men. Compared to men, women had lower CRP levels (1.1±1.73 mg/dL [women] vs. 1.86±3.80 mg/dL [men], p<0.019) at the first visit time and were less likely to be HLA-B27 positive (88.3% [women] vs. 96% [men], p<0.001). There were no significant differences in the rates of positive familial history between the genders.

**Table 1. Clinical features compared between women and men with ankylosing spondylitis**

<table>
<thead>
<tr>
<th></th>
<th>Women (N=162)</th>
<th>Men (N=559)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>41±11.3</td>
<td>37.9±11.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean age of onset, years</td>
<td>33.6±11.3</td>
<td>29.6±10.7</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean age of diagnosis, years</td>
<td>39.6±11.1</td>
<td>36.7±10.9</td>
<td>0.451</td>
</tr>
<tr>
<td>Mean duration of AS, years</td>
<td>6.16±4.23</td>
<td>7.04±5.32</td>
<td>0.004</td>
</tr>
<tr>
<td>Delay in diagnosis, months</td>
<td>27.0±34.8</td>
<td>40.4±44.2</td>
<td>0.001</td>
</tr>
<tr>
<td>ESR (mm/hr)</td>
<td>31.6±25.9</td>
<td>27.2±26.0</td>
<td>0.070</td>
</tr>
<tr>
<td>CRP (mg/dL)</td>
<td>1.1±1.73</td>
<td>1.86±3.80</td>
<td>0.019</td>
</tr>
<tr>
<td>HLA-B27-positive</td>
<td>144/162 (88.3%)</td>
<td>507/528 (96%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Data are shown in mean±SD or %. AS: ankylosing spondylitis, HLA: human leukocyte antigen