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Original Article

Manifestations of Cervical Spine Involvement in Longstanding Ankylosing Spondylitis: Atlantoaxial Ankylosis and Atlantoaxial Subluxation

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Objective. To analyze radiologic findings of cervical involvement in ankylosing spondylitis (AS) patients, determine its association with structural severity and clinical variables, and to divide radiologic findings of atlantoaxial ankylosis (AAA) in AS patients into three anatomical components. **Methods.** The study includes 150 AS patients with either AAA (62 patients) or atlantoaxial subluxation (AAS, 88 patients) who underwent plain radiography of the cervical spine on flexion at our tertiary center for rheumatic diseases. The study subjects' medical records were reviewed. Lateral plain radiographs of the cervical spine were analyzed by a musculoskeletal radiologist. We compared the results of the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) between AAS and AAA patients to determine if mSASSS was related to severity or duration of AS. **Results.** The mean duration of illness in AS patients with AAA was 19.3 years, and in AAS patients 13.7 years ($p < 0.01$). The mean total mSASSS of AS patients with AAA was 40.1, and of AAS patients 16.5 ($p < 0.001$), and was positively associated with the development of AAA and AAS. The odds ratio (OR) of AAA development by cervical spine mSASSS change was higher (OR, 1.079) than the OR (1.049) of lumbar spine mSASSS even after adjusting for age, sex, and disease duration. **Conclusion.** Although AAA is described infrequently, we found from our data that it is another manifestation of cervical spine involvement in longstanding AS and is related to severity of AS reflected by higher cervical mSASSS. **(J Rheum Dis 2017;24:21-26)**

Key Words. Ankylosing spondylitis, Atlanto-axial joint, Anklyosis

INTRODUCTION

Ankylosing spondylitis (AS) is a chronic, progressive inflammatory disease that primarily affects the sacroiliac joints and the axial skeleton (spine) and, less frequently, peripheral joints and other extra-articular organs such as the eyes, skin, and cardiovascular system [1].

Structural damage, which leads to characteristic radiologic changes, is considered essential for establishing a diagnosis and outcome prediction in AS. The primary histopathologic change of this disease is an initial inflammatory and erosive process affecting the enthesis, which is followed by a healing process during which new bone is formed that eventually results in ankylosis [2].

The atlantoaxial region has a unique anatomy and function, containing synovial tissue and several ligaments closely arranged within a small, critical space [3]. Involvement of the atlantoaxial joint in rheumatoid arthritis is very well known, with anterior atlantoaxial subluxation (AAS) being the most common presentation. Atlantoaxial involvement in AS has also been reported and can lead to destruction of ligaments, cartilage, and bone, which in some cases results in atlantoaxial subluxation and neurological complications [4]. On the other hand, patients with AS accompanied by partial or complete ankylosis between the atlas and the dens of the axis (atlantoaxial ankylosis, AAA) have infrequently been described [5], and little is known about its prevalence and risk factors.

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The purpose of this study was to analyze radiologic and clinical findings of AAA and AAS in AS patients. We also investigated radiologic findings of the cervical spine to determine their correlations with clinical variables.

MATERIALS AND METHODS

Subjects

This was a retrospective study of 150 randomly selected AS patients (62 AS patients with AAA and 88 AS patients with AAS) who attended the rheumatology clinic at our tertiary center from January 2002 through February 2014. All patients fulfilled the modified New York criteria [6] and underwent a thorough physical examination including history taking by rheumatologists. All data for the study were recorded using standardized forms. Inflammatory back pain was defined according to the modified New York criteria [6]. Ocular involvement was the most frequent extra-articular manifestation and included anterior uveitis and terms such as iritis, iridocyclitis and cyclitis [1] confirmed by an ophthalmologist. Human leukocyte antigen (HLA)-B27 typing was done using the microcytotoxicity method. The study protocol was approved by the Hospital Ethics Committee and informed consent was waived because of the retrospective nature of the study (IRB permit number, 2014-04-010-007). A review of the medical records was conducted to investigate the associations between clinical factors, such as sex, age, symptom duration, uveitis/iritis, HLA-B27, and the presence of AAA in patients with AS.

Radiologic assessment

All of the patients in this study underwent cervical spine radiography with anteroposterior (AP) open-mouth and full flexion lateral views and pelvis AP radiography. Multidetector computed tomography (MDCT) (Somatom Sensation 16 or Brilliance CT 64 Slice; Siemens, Forchheim, Germany) was performed in five patients due to neck discomfort in one patients, periauricular mass in one patient and non-specific neck pain in three patients.

Lateral and AP radiographs of the cervical spine were reviewed by an experienced musculoskeletal radiologist who was blinded to patients' clinical information. Radiologic AAS was defined as present when the distance between the posterior margin of the anterior arch of the atlas and the anterior aspect of the dens exceeded 3 mm in the lateral full flexion view [7]. Radiologic AAA was defined as present when loss of the atlantodental interval, or ankylosis of the facet joint, anterior longitudinal ligament, or anterior atlantooccipital membrane were noted on plain radiographs.

We arbitrarily subdivided radiologic findings of AAA in AS patients into three anatomical components: (1) component I - atlantodental ankylosis, in which there was loss of the atlantodental interval; (2) component II - atlantoaxial facet joint ankyloses, in which there was ankylosis of the facet joint; and (3) component III - ligamentous or membranous ankylosis, in which there was ankylosis of the anterior longitudinal ligament or anterior atlantooccipital membrane with the cervical spine. Most AS patients with AAA exhibited a mixture of these three components. Components of AAA and its involvement with the cervical spine were analyzed by the same radiologist after AAA was diagnosed. We compared the results of modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) between AAS and AAA to determine if mSASSS was related to the severity or duration of AS.

Statistical analyses

Data were analyzed using IBM SPSS Statistics software, version 21.0 for Windows (IBM Co., Armonk, NY, USA). Spearman correlation coefficients were calculated to estimate the relationship between mSASSS and clinical variables. Non-parametric variables were compared using the chi-square test, and the results obtained were reevaluated by multiple logistic regression analysis. In addition, the mean values between two continuous variables were compared using Student's t-test. The p-values less than 0.05 were considered statistically significant.

RESULTS

Patients characteristics

A total of 150 patients were investigated in this study. Out of the 150 patients, 94.0% were men and 98.0% were HLA-B27 positive. The frequency of eye involvement was 42.0%. These AS patients were divided into two groups as follows: group A, AS patients with AAA; and group B; AS patients with AAS. The mean age of group A was 40.1±8.2 years, compared with 34.6±10.9 years in group B. The mean disease duration in group A was 19.3 years, which was significantly longer than the 13.7 year duration of group B ($p<0.01$). Basic demographics, clinical findings, and mSASSS of both groups are summarized in Table 1. Clinical variables such as sex, ocular symptoms, and HLA-B27 positivity were not significantly different

Table 1. Basic demographic, clinical findings, and mSASSS of 150 patients

Characteristic	Group A* (n=62)	Group B† (n=88)	p-value
Age (yr)	40.1±8.2	34.6±10.9	0.001
Sex, male	61 (98.4)	80 (90.9)	0.081
Disease duration (yr)	19.3±7.7	13.7±9.0	<0.001
Ocular symptom	19 (30.6)	44 (50.0)	0.206
HLA-B27 positivity	61 (98.4)	86 (97.7)	1.000
mSASSS			
C-spine score	22.6±12.4	10.1±9.6	<0.001
L-spine score	17.5±18.9	6.4±11.2	<0.001
Total score	40.1±25.3	16.5±18.1	<0.001

Values are presented as mean±standard deviation and number (%). mSASSS: modified Stoke Ankylosing Spondylitis Spinal Score, HLA: human leukocyte antigen, AS: ankylosing spondylitis, AAA: atlantoaxial ankylosis, AAS: atlantoaxial subluxation. *AS patients with AAA, †AS patients with AAS.

Table 2. Odds ratio of AAA development according to disease duration and the change of mSASSS (compared with development of AAS)

Variable	Odds ratio	95% confidence interval
Disease duration		
Unadjusted	1.081	1.037~1.128
Adjusted for age, sex	1.065	1.010~1.123
Adjusted for age, sex and total mSASSS	1.055	0.998~1.116
Change of mSASSS		
C-spine*	1.079	1.042~1.118
L-spine*	1.049	1.018~1.081

AAA: atlantoaxial ankylosis, mSASSS: modified Stoke Ankylosing Spondylitis Spinal Score, AAS: atlantoaxial subluxation. *Adjusted for age, sex, disease duration.

between the two groups.

Comparison of AAA and AAS

AAA was found to be positively correlated with patient age, disease duration, and mSASSS. The odds ratio (OR) of AAA development according to disease duration compared with development of AAS was significantly higher even after adjusting for age (OR, 1.065; 95% confidence interval [CI], 1.010~1.123). However, after adjusting for mSASSS, the OR of developing AAA according to disease duration did not show a significant difference (OR, 1.055; 95% CI, 0.998~1.116) (Table 2). mSASSS (cervical, lumbar, and total) was found to positively correlate with the development of AAA and AAS. AS patients with AAA had higher mSASSS (cervical, lumbar, and total) than those with AAS (Table 1). The OR of AAA development according to the change in cervical spine mSASSS was especially higher (OR, 1.079; 95% CI, 1.042~1.118) compared with the OR (1.049; 95% CI, 1.018~1.081) of lumbar spine mSASSS even after adjusting for age, sex, and disease duration (Table 2).

Anatomical components of AAA in AS patients

We arbitrarily subdivided radiologic findings of AAA in AS patients into three anatomical components. Among the 62 AS patients with AAA, 55 patients (88.7%) showed anterior atlantodental ankylosis (component I), making it the most frequently involved lesion, while 33 patients (53.2%) had atlantoaxial facet joint ankylosis (component II) and 38 patients (61.3%) exhibited ligamentous or membranous ankylosis (component III, anterior longitudinal ligament [ALL], anterior atlantooccipital membrane).

There were 21 patients (33.9%) that exhibited all three components of AAA (Figure 1), two patients that exhibited only atlantoaxial facet joint ankylosis (component II, Figure 2) with sparing of anterior atlantoaxial joint or ALL, and one patient who showed only ligamentous or membranous ankylosis (component III, Figure 3) without involvement of anterior atlantoaxial joint or facet joint. The components of AAA in the 62 AS patients, in the order of frequency, were as follows: component I, atlantodental ankylosis (88.7%, 55/62); component III, ligamentous or membranous ankylosis (61.3%, 38/62); and component II, atlantoaxial facet joint ankylosis (53.2%, 33/62). The most frequent mixture of AAA components, in the order of frequency, were as follows: component I, II, and III (33.9%, 21/62), component I and III (25.8%, 16/62), component I and II (9.7%, 6/62), and component II and III (6.5%, 4/62).

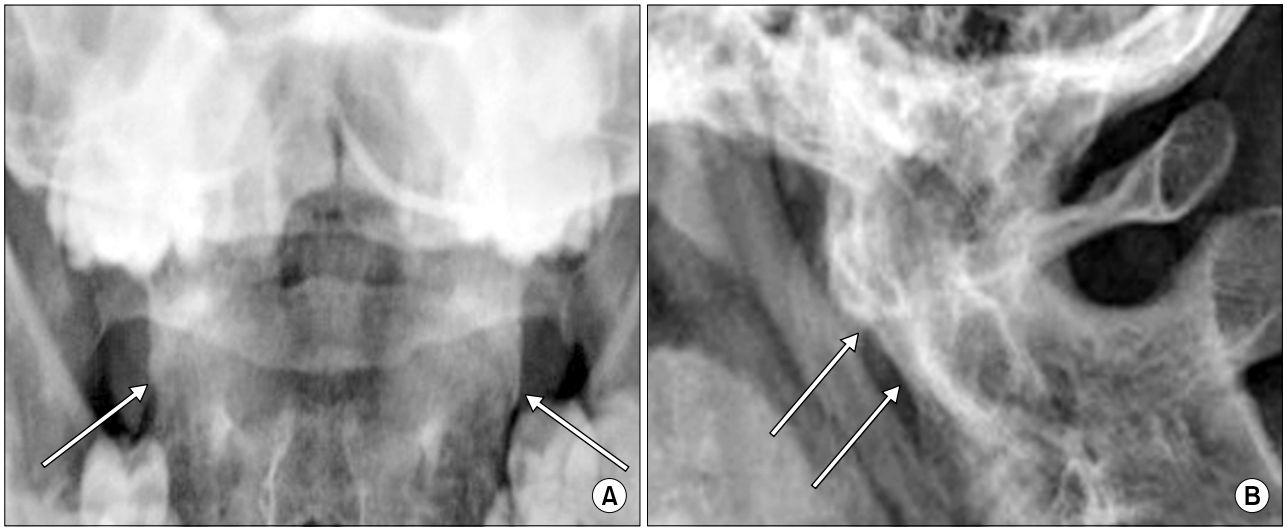

Figure 1. (A) A 31-year-old ankylosing spondylitis patient with duration of 9 years. An anteroposterior open-mouth view of the cervical spine shows obliteration of atlantoaxial facet joints (arrows, component II). (B) A lateral radiograph of the cervical spine with full flexion of the same patient shows bony ankylosis of the atlantoaxial joint space and ankylosis of anterior longitudinal ligament (arrows, component I and III).

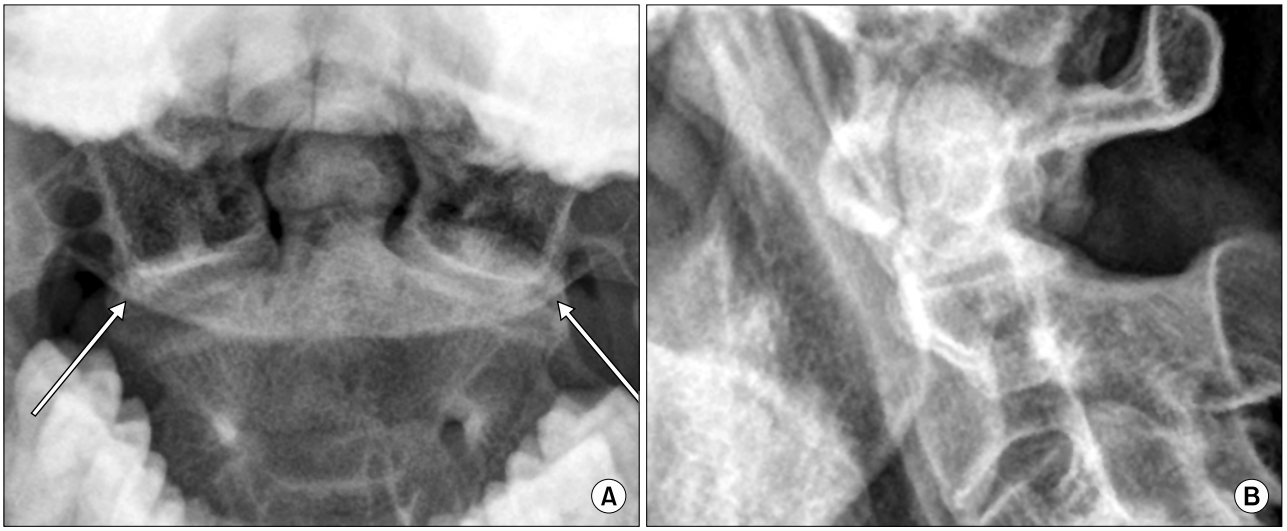

Figure 2. (A) A 34-year-old ankylosing spondylitis patient with a disease duration of 10 years. An anteroposterior open-mouth view of the cervical spine reveals obliteration of atlantoaxial facet joint (arrows, component II). (B) A lateral radiograph of the cervical spine with full flexion of the same patient shows sparing of the atlantoaxial joint space.

DISCUSSION

Data at our tertiary center for rheumatic disease are in line with the previous investigations showing that the cervical spine is frequently affected and that the risk of cervical spine involvement is associated with older age and longer disease duration [8-10]. Moreover, we found that a higher mSASSS, especially cervical spine mSASSS, was closely associated with the development of AAA in AS patients.

Lee et al. [11] reported in their study of 61 AS patients with disease duration over 7 years that that 37 patients (60.6%) revealed a certain extent of the atlantodental ossification. The presence of partial or complete atlantodental ankylosis was seen over 30% of the patients. The Bath Ankylosing Spondylitis Radiology Index (BASRI) cervical spine score and the atlantodental ossification levels correlated with disease duration. Zygapophyseal (ZA) involvement was observed in 49 patients (80.3%), including 23 with ZA fusion (37.7%).

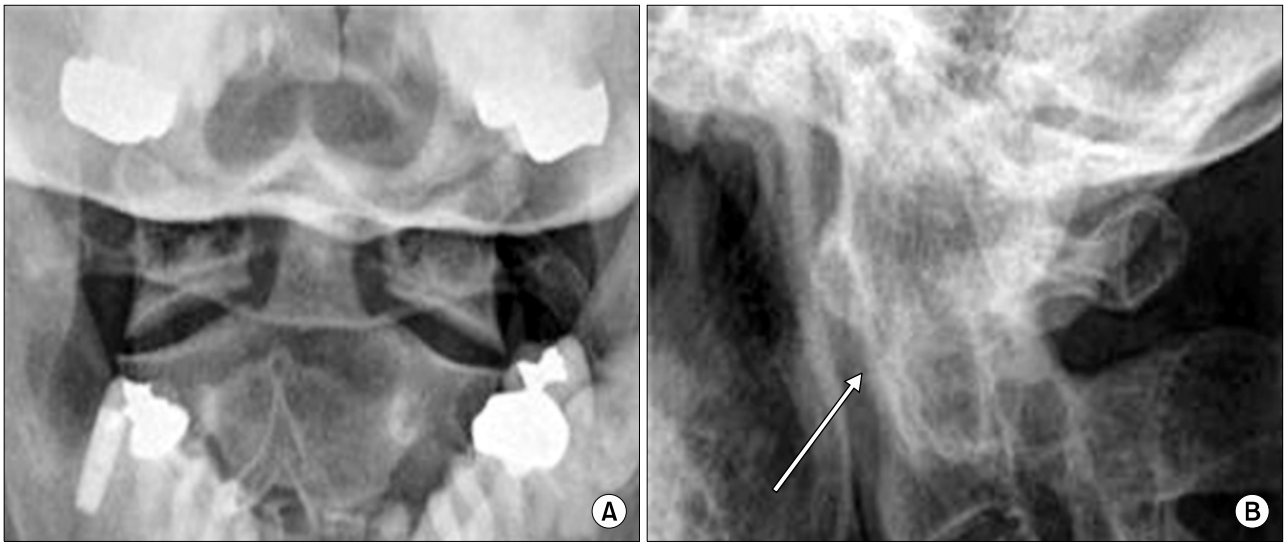

Figure 3. (A) A 33-year-old ankylosing spondylitis patient with duration of 8 years. An anteroposterior open-mouth view of the cervical spine reveals sparing of the atlantoaxial facet joint. (B) A lateral radiograph of the cervical spine with full flexion of the same patient shows ankylosis of anterior longitudinal ligament (arrow, component III).

Our study supports previous reports [11] because among the components we described earlier, component I and III were noted more frequently than component II in AAA patients in our study, and component I and III are known to be associated with joint stability. This observation means that AS patients with AAA have a more stable atlantoaxial joint than AS patients with AAS. The mSASSS is a four-point scoring system for lateral radiographs of the lumbar and cervical spine. The anterior vertebral columns (VC) of the cervical (lower border of C2 to upper border of T1) and lumbar (lower border of T12 to upper border of S1) segments (a total of 24 VCs) are scored using a lateral view for the presence of erosion and/or sclerosis and/or squaring (1 point), syndesmophytes (2 points), and bridging syndesmophytes (3 points). Thus, the total score ranges from 0 to 72, and mSASSS has been shown to reliably track disease progression over time [6]. AS patients with AAA are known to have a lower prevalence of clinically significant neurological complications. This might be due to atlantodental ankylosis (component I in our study) or facet joint ankylosis (component III in our study) that develops in a considerable proportion of patients with AS, as these could provide joint stability for the cervical spine and prevent further neurological compromise [11].

The radiographic abnormalities affecting atlantoaxial joint include erosion, sclerosis, and bony ankylosis [11]. Some investigators have suggested that facet joint inflammation is the essential element that leads to impaired spinal motion in patients with AS [12-14]. Facet joint ankylosis is known to occur exclusively in patients with spondyloarthropathies, and is especially remarkable in the cervical spine [12-15]. The key lesions of AS consist of a combination of synovitis at the apophyseal and sacroiliac joints and enthesitis. The inflammatory process of the synovial and adjacent ligamentous structures initially leads to erosive changes on these elements, followed by healing during which there is ossification or formation of new bone, the final outcome of which is bony ankylosis [2,12,16]. Similar inflammatory and healing processes are assumed to take place in the atlantoaxial region, which contains several ligaments and synovial tissues. In the present study, some degree of ossification was observed between the atlas and the dens in a considerable number of patients with longstanding AS.

Although AAA in AS has been described infrequently, we found, on the basis of data from our tertiary center for rheumatic disease that AAA and AAS are similar in that they represent late presentations of AS and occur in patients after a long disease course. We also found that AAA is another manifestation of cervical spine involvement in longstanding AS and is related to severity of AS reflected by higher cervical mSASSS. We concluded from our data that higher cervical mSASSS is more related with the development of AAA than the development of AAS. We also found that AS patients with AAA have a more stable atlantoaxial joint than AS patients with AAS.

Although this study was carefully planned, there were

some limitations. First, since all the radiographs were evaluated once by one radiologist, information regarding intra- and inter-observer variation could not be obtained. Second, this was a retrospective analysis and thus there was a risk of associated issues including potential selection bias and incomplete data collection. Since our study was performed on patients who were referred to tertiary medical centers, these subjects might represent a relatively severe group with a more progressive disease course. To overcome these problems, longitudinal studies and continuous observation of radiographic changes will be required in a greater number of patients. Third, because only five patients underwent CT scans, we did not have access to detailed descriptions of radiologic findings. Lastly, this study lacked some information regarding clinical and laboratory findings.

CONCLUSION

According to data at our tertiary center for rheumatic disease, AAA is more frequent than AAS in AS patients with a longer disease duration and higher cervical spine mSASSS. AAA in AS does not cause as much cervical instability as AAS in AS. Therefore, if AAA can be identified using plain radiography, it may be possible to prevent unnecessary exams or procedures such as atlantoaxial fusion, which are usually required in AAS as the disease progresses.

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Gouveia EB, Elmann D, Morales MS. Ankylosing spondylitis and uveitis: overview. Rev Bras Reumatol 2012;52:742-56.
2. Archer JR, Keat AC. Ankylosing spondylitis: time to focus on ankylosis. J Rheumatol 1999;26:761-4.
3. Martel W. The occipito-atlanto-axial joints in rheumatoid arthritis and ankylosing spondylitis. Am J Roentgenol Radium Ther Nucl Med 1961;86:223-40.
4. Hunter T. The spinal complications of ankylosing spondylitis. Semin Arthritis Rheum 1989;19:172-82.
5. Liang CL, Lu K, Lee TC, Lin YC, Chen HJ. Dissociation of atlantoaxial junction in ankylosing spondylitis: case report. J Trauma 2002;53:1173-5.
6. van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. Arthritis Rheum 1984;27:361-8.
7. Kauppi M, Neva MH. Sensitivity of lateral view cervical spine radiographs taken in the neutral position in atlantoaxial subluxation in rheumatic diseases. Clin Rheumatol 1998;17:511-4.
8. Meijers KA, van Voss SF, François RJ. Radiological changes in the cervical spine in ankylosing spondylitis. Ann Rheum Dis 1968;27:333-8.
9. Lee HS, Kim TH, Yun HR, Park YW, Jung SS, Bae SC, et al. Radiologic changes of cervical spine in ankylosing spondylitis. Clin Rheumatol 2001;20:262-6.
10. El Maghraoui A, Bensabbah R, Bahiri R, Bezza A, Guedira N, Hajjaj-Hassouni N. Cervical spine involvement in ankylosing spondylitis. Clin Rheumatol 2003;22:94-8.
11. Lee JY, Kim JI, Park JY, Choe JY, Kim CG, Chung SH, et al. Cervical spine involvement in longstanding ankylosing spondylitis. Clin Exp Rheumatol 2005;23:331-8.
12. Sanzhang C, Rothschild BM. Zygapophyseal and costovertebral/costotransverse joints: an anatomic assessment of arthritis impact. Br J Rheumatol 1993;32:1066-71.
13. Simkin PA, Downey DJ, Kilcoyne RF. Apophyseal arthritis limits lumbar motion in patients with ankylosing spondylitis. Arthritis Rheum 1988;31:798-802.
14. Russell AS, Jackson F. Computer assisted tomography of the apophyseal changes in patients with ankylosing spondylitis. J Rheumatol 1986;13:581-5.
15. Laiho K, Kauppi M. The cervical spine in patients with ankylosing spondylitis. Clin Exp Rheumatol 2002;20:738.
16. Ball J. Enthesopathy of rheumatoid and ankylosing spondylitis. Ann Rheum Dis 1971;30:213-23.