

Prevalence of Ossification of Posterior Longitudinal Ligament in Patients with Ankylosing Spondylitis

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ABSTRACT. *Objective.* To determine the prevalence of ossification of the posterior longitudinal ligament (OPLL) in patients with ankylosing spondylitis (AS).

Methods. A cross-sectional radiological examination was performed in patients diagnosed with AS. A bone and joint radiologist screened and confirmed the cervical radiographs of these patients. A review of the medical records was also conducted to investigate the relationship between the clinical manifestations and the actual expression of OPLL in patients with AS.

Results. Among 544 patients with AS, 470 (86.4%) were men and 96.1% were HLA-B27-positive. The mean age was 34.3 ± 9.3 years and mean disease duration was 12.4 ± 7.2 years. After reviewing the cervical radiographs, OPLL was found in 19 patients (3.5%; 95% CI 1.9, 5.0). The mean age of these 19 patients was 39.9 ± 10.7 years, and the male to female ratio was 18:1. Interestingly, a statistically significant number of patients who expressed OPLL were older ($p = 0.007$). However, we were unable to determine whether OPLL was significantly associated with AS disease duration, peripheral arthritis, anterior uveitis/iritis, HLA-B27, anterior atlantoaxial subluxation, diffuse idiopathic skeletal hyperostosis, or other paraspinal ligament disorders.

Conclusion. Our study showed that the frequency of OPLL in Korean patients with AS was 3.5%, which was considerably lower than previously reported values (15.5% in 103 Mexican AS). We were able to determine that OPLL in AS was associated with older age. (First Release Nov 15 2007; J Rheumatol 2007;34:2460–2)

Key Indexing Terms:

OSSIFICATION OF POSTERIOR LONGITUDINAL LIGAMENT
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Ossification of the posterior longitudinal ligament (OPLL) is a hyperostotic condition of the spine that causes severe neurologic symptoms induced by spinal cord compression¹, found predominantly in the cervical spine and frequently between the C2 and C4 vertebral levels².

OPLL has been associated with other paraspinal ligament disorders³ such as cervical spondylosis, diffuse idiopathic skeletal hyperostosis (DISH), and ankylosing spondylitis (AS). Without a decisive prevalence of OPLL in the AS population, Ramos-Remus, *et al*^{4,5} reported that 15.5% of their patients with AS expressed OPLL. However, these results are limited by the small sample size for the prevalence study.

In light of this, our goal was not only to determine more

precisely the prevalence of OPLL in patients with AS, but also to investigate the associations between the clinical manifestations and the presence of OPLL in AS.

MATERIALS AND METHODS

Subjects. A total of 544 consecutive patients with AS who met the modified New York criteria⁶ with cervical radiograph(s) in The Hospital for Rheumatic Diseases were recruited.

Review of cervical spine. Cervical spine radiographs with neutral and full-flexion lateral views of the patients with AS were reviewed by an experienced bone and joint radiologist (KBJ) blinded to patients' clinical information. OPLL was indicated by the presence of heterotopic ossification in the posterior longitudinal ligament on the lateral cervical radiograph². We investigated the presence of OPLL, anterior atlantoaxial subluxation (AAS), and other related hyperostotic conditions, such as DISH and nuchal ligament calcification. The criterion for definite diagnosis of DISH was the presence of 4 or more vertebral bodies with contiguous ligamentous ossification and calcification, known as Resnick's criteria⁷. Morphologically, the ossification can be categorized into 4 types: (1) a localized type, such as circumscribed ossification of the ligament corresponding to the level of the intervertebral disc; (2) a segmental ossification behind each vertebral body; (3) a continuous ossified mass extending over several vertebrae; and (4) a mixture of these 2 types². The type of OPLL and its involvement with the cervical spines were also analyzed by the same radiologist, after OPLL was diagnosed.

Review of clinical measures. A review of the medical records was conducted to investigate the associations between clinical measures, such as sex, age, symptom duration, uveitis/iritis, peripheral arthritis, and HLA-B27, and the presence of OPLL in patients with AS.

Statistical analysis. Clinical data of AS and the radiographic characteristics of OPLL were descriptively analyzed. The differences in disease frequencies

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were analyzed using chi-square or Fisher's exact tests. Differences between 2 variables were compared using 2-tailed t tests. Multiple logistic regression analysis was performed to evaluate the association of various independent variables on OPLL. A p value less than 0.05 was regarded as statistically significant.

RESULTS

Among 544 patients with AS, the mean age was 34.3 ± 9.3 and the mean disease duration was 12.4 ± 7.2 years. Of the patients, 86.4% were men and 528 (97.1%) were HLA-B27-positive. The frequency of eye involvement and peripheral arthritis was 26.5% and 46%, respectively (Table 1).

Upon review of the cervical radiographs, 19 patients (3.5%; 95% CI 1.9, 5.0) were diagnosed with OPLL. OPLL was shown to have a correlation only with age ($p = 0.007$ for linear association; Table 2).

The types of ossification were as follows in the order of frequency: segmental (31.6%), continuous (26.3%), localized (21.1%), and mixed (21.1%). The highest involvement of ossification was found at the level of C4 (63.2%), C5 (57.9%), and C3 (52.6%) (Table 3).

DISCUSSION

OPLL has been occasionally reported to be associated with

Table 1. Demographic and clinical characteristics of patients with AS.

Variables	Patients with AS, n = 544
Age, mean \pm SD, yrs	34.3 \pm 9.3
AS disease duration, mean \pm SD, yrs	12.4 \pm 7.2
Male, n (%)	470 (86.4)
OPLL, n (%)	19 (3.5)
History of anterior uveitis/iritis, n (%)	144 (26.5)
History of peripheral arthritis, n (%)	250 (46)
HLA-B27, n (%)	528 (97.1)
Anterior atlantoaxial subluxation, n (%)	75 (13.8)
Cervical DISH, n (%)	6 (1.1)
Nuchal ligament calcification, n (%)	52 (9.6)

AS: ankylosing spondylitis; DISH: diffuse idiopathic skeletal hyperostosis; OPLL: ossification of posterior longitudinal ligament.

AS^{2,8,9}. Recently, OPLL was found with a frequency between 15.5% and 29% in AS and related spondyloarthropathies^{4,5}. However, we found that the prevalence of OPLL in Korean patients with AS was 3.5%. What is causing this difference?

The reason for the discrepancy has not been determined, but several possibilities are plausible. Many clinical studies have suggested that OPLL is a multifactorial disease and that complex genetic and environmental factors contribute to its expression¹⁰⁻¹³. Therefore, the discrepancy could be attributable to differences between genetic backgrounds and demographic characteristics such as age or the sex ratio. Unfortunately, not enough information from a study on a Mexican population⁵ was available for comparison with our study. Various metabolic disorders, including hypoparathyroidism, hypophosphatemic rickets, and non-insulin-dependent diabetes mellitus could also account for the different results¹⁴.

It has been suggested that the frequency of OPLL expression is higher in older age groups². We were able to confirm that older patients with AS were more likely to express OPLL than younger patients.

Tsuyama² reported that the segmental type was the most common (39%), followed by mixed type (29.2%). The types of ossification in AS characterized in our study were as follows: segmental (31.6%), continuous (26.3%), localized (21.1%), and mixed (21.1%).

There are some limitations to our study. Although computed tomography clearly reveals the ossification, this study was performed with simple radiography. Therefore, a small lesion within the spinal canal could not be detected even by experienced radiologists. In spite of being analyzed by an expert, intra- and interobserver reliability assessments were not performed to validate the results. Due to the small OPLL sample size, we were unable to determine whether the OPLL observed in AS was statistically associated with clinical measures such as disease duration, peripheral arthritis, anterior uveitis/iritis, HLA-B27, anterior AAS, DISH, or other paraspinal ligament disorders.

Nevertheless, this is the largest prevalence study of OPLL

Table 2. Clinical data of the AS patients comparing those with and without OPLL.

Variables	OPLL		p
	Present, n = 19	Absent, n = 525	
Age, mean (SD), yrs	39.9 (10.7)	34.1 (9.2)	0.007
AS disease duration, mean (SD), yrs	13.3 (7.8)	12.4 (7.2)	NS
Male, n (%)	18 (94.7)	452 (96.2)	NS
History of anterior uveitis/iritis, n (%)	7 (36.8)	137 (26.1)	NS
History of peripheral arthritis, n (%)	6 (31.6)	244 (46.5)	NS
HLA-B27, n (%)	17 (89.5)	511 (97.3)	NS
Anterior atlantoaxial subluxation, n (%)	1 (5.3)	74 (14.1)	NS
Cervical DISH, n (%)	1 (5.3)	5 (1.0)	NS
Nuchal ligament calcification, n (%)	3 (15.8)	49 (9.3)	NS

AS: ankylosing spondylitis; DISH: diffuse idiopathic skeletal hyperostosis; OPLL: ossification of posterior longitudinal ligament.

Table 3. Radiographic characteristics in cervical spines of 19 patients with OPLL.

Type of OPLL, n (%)	
Segmental	6 (31.6)
Continuous	5 (26.3)
Localized	4 (21.1)
Mixed	4 (21.1)
Involved cervical spine, n (%)	
C4	12 (63.2)
C5	11 (57.9)
C3	10 (52.6)
C6	8 (42.1)
C2	5 (26.3)
C7	4 (21.1)
C1	1 (5.3)

OPLL: ossification of posterior longitudinal ligament.

in AS to date. Although we did not directly compare OPLL patients with AS with a control group, the percentage of OPLL in AS was much higher than that of OPLL in the same ethnic population^{2,15}. Given this result, we might assume that OPLL is highly associated with AS.

We confirmed that the prevalence of OPLL patients with AS was 3.5% in Korea. However, the prevalence of OPLL in AS is still far from certain, and the frequencies of OPLL in AS are often different and dependent on the study design. Further well designed, comprehensive epidemiologic surveys are needed to ascertain an accurate frequency of OPLL in AS.

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