Original Article

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Clinical and MR Predictors of Retro-Odontoid Pseudotumor Regression Following Posterior Fixation in Patients with Atlantoaxial Instability 환축 불안정 환자에서 후방 고정술 후 치상돌기 후방 가성종양 퇴행의 임상 및 자기공명영상 예측 인자

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Purpose To identify clinical and MR predictors of retro-odontoid pseudotumor (ROP) regression after posterior fixation in patients with atlantoaxial instability.

Materials and Methods We included patients who had undergone posterior fixation for atlantoaxial instability and preoperative and postoperative MR imaging. Patients were classified into two groups according to the degree of ROP regression after posterior fixation: regression (≥ 10% reduction) and no regression (< 10% reduction). Mann–Whitney and Fisher's exact tests were performed to identify the clinical (age and sex) and MR predictors (preoperative ROP thickness, ROP type, MR signal homogeneity of the ROP, spinal cord signal change, spinal cord atrophy, ossified posterior longitudinal ligament, os odontoideum, and atlantodental interval) associated with ROP regression.

Results We retrospectively assessed 11 consecutive patients (7 female; median age, 66 years [range, 31–84 years]). Posterior fixation induced ROP regression in eight (72.7%) patients. Older age and greater preoperative ROP thickness significantly correlated with ROP regression ($p = 0.024$ and 0.012, respectively). All patients with preoperative ROP thickness > 5 mm exhibited ROP regression. The other variables were not significantly associated with ROP regression.

Conclusion Older age and thicker preoperative ROP are associated with ROP regression after posterior fixation in patients with atlantoaxial instability.

Index terms Retro-Odontoid Pseudotumor; Atlantoaxial Instability; Magnetic Resonance Imaging

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INTRODUCTION

Retro-odontoid pseudotumor (ROP) is a non-neoplastic soft tissue proliferation of the craniovertebral junction, which can cause cord compression and cervical myelopathy (1). Although the exact causes of ROP formation and growth remain unclear, ROP has been associated with various pathologies such as idiopathic atlantoaxial instability, os odontoideum, atlas hypoplasia, subaxial ankylosis (including ossification of the posterior longitudinal ligament), and diffuse idiopathic skeletal hyperostosis (2-4). Moreover, it is associated with rheumatoid arthritis, calcium pyrophosphate dihydrate crystal deposition disease, and long-term hemodialysis (5, 6). Histopathologically, ROP is characterized by a noninflammatory mass predominantly composed of fibrocartilaginous tissue that develops due to chronic mechanical stress or pseudarthrosis of the odontoid process (7). Conversely, in patients with rheumatoid arthritis, the retroodontoid lesion is commonly considered an inflammatory pannus secondary to an inflammatory process that causes the erosion of the bone and cartilage in the synovial joints, leading to periarticular tissue overgrowth (8).

Chronic atlantoaxial instability can compress the upper cervical cord, and concurrent ROP formation can worsen cord compression and accelerate neurological deterioration if not promptly treated (9). Historically, the transoral anterior approach to the craniovertebral junction has been considered the gold standard of anterior decompression. It can achieve rapid decompression of the spinal cord via the direct resection of the ROP (10-12). However, this procedure entails a high risk of pulmonary complications, infections, cerebrospinal fluid leakage, and spinal cord damage (13, 14). Thus, no consensus exists regarding the optimal surgical treatment (15).

Posterior fixation has recently emerged as a promising surgical strategy for treating atlantoaxial instability. Through occipitocervical or atlantoaxial fusion, chronic atlantoaxial instability and mechanical stress are surgically reduced, preventing further stress on the atlantoaxial joint (16). This approach results in notable neurological and symptomatic improvements (17). Additionally, several studies have reported spontaneous regression of ROP without direct removal, after C1–2 or O–C2 fixation (18-22).

Few studies have analyzed the relationship between preoperative MR findings of ROP and ROP regression after posterior fixation (23, 24). In this study, we hypothesized that preoperative clinical and MR findings could be useful for predicting surgical outcomes, particularly ROP regression, after posterior fixation. This study aimed to identify the clinical and MR predictors of ROP regression after posterior fixation in patients with atlantoaxial instability.

MATERIALS AND METHODS

This study was approved by our Institutional Review Board and the requirement for informed consent was waived because of its retrospective nature (IRB No. B-2308-848-103).

STUDY POPULATION

We searched for patients who had been diagnosed with retrodental pseudotumors, ROPs, or retrodental cysts between March 2016 and December 2021 based on cervical spine MRI

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findings from our institution's picture archiving and communication system and electronic medical records. We excluded patients who had not undergone posterior fixation, those without preoperative or postoperative MRI, or those without atlantoaxial instability. Atlantoaxial instability was defined as atlantodental intervals \geq 3 mm in preoperative cervical spine lateral radiographs.

MRI PROTOCOL

Preoperative cervical spine MRIs were performed using 3T MRI systems (Achieva and Ingenia, Philips Healthcare, Best, The Netherlands). Postoperative cervical spine MRIs were performed using 3 and 1.5T MR systems (Amira, Siemens Healthineers, Erlangen, Germany; Ingenia and Intera, Philips Healthcare, Best, The Netherlands). At our institution, postoperative MRIs are routinely performed approximately one month after surgery, regardless of the patient' s symptoms and signs. MR images were obtained in the supine and neutral position without intentional flexion or extension of the neck.

The preoperative MRI protocol included T1-weighted turbo spin-echo axial and sagittal imaging (axial images: repetition time [TR], 500–676 ms; echo time [TE], 8–15 ms; sagittal images: TR, 400–554 ms; and TE, 8–15 ms) and T2-weighted turbo spin-echo axial and sagittal imaging (axial images: TR, 4286–5000 ms; TE, 100–120 ms; sagittal images: TR, 2004–3573 ms; and TE, 100–150 ms). The remaining MRI parameters included the following: slice thickness, 3 mm; field of view, $130-140 \times 130-140$ mm (axial images) and $240-250 \times 240-250$ mm (sagittal images); matrix, 216–256 \times 210–254 (axial images) and 448–512 \times 248–263 (sagittal images); flip angle, 90°; echo train length, 6–33; and number of excitations, 2–4.

For postoperative MRIs, T2-weighted turbo spin-echo sagittal and axial images were obtained with TRs of 2070–5577 and 2451–3573 ms and TEs of 80–120 ms and 2451–3573 ms for axial and sagittal images, respectively. The remaining MRI parameters were as follows: slice thickness, 3 mm; field of view, $140-150 \times 140-150$ mm (axial images) and 240-250 \times 240-250 mm (sagittal images); matrix, 200–256 \times 170–251 (axial images) and 304–512 \times 255–304 (sagittal images); flip angle, 90°–180°; echo train length, 11–24; and number of excitations, 2–4.

MRI ANALYSIS

Two readers (an attending radiologist with 20 years of experience in spine radiology [J.W.L.] and a third-year radiology resident [J.K.]) analyzed all the MR images and reached a consensus on detailed measurements.

The ROP thickness was measured as follows: first, we identified the thickest portion of the ROP in the sagittal plane by using axial T2-weighted images. After identifying the posterior cortical margin of the odontoid process on the sagittal T1-weighted images, we measured the transverse diameter of the ROP on the sagittal T2 images. Specifically, we measured the anteroposterior distance from the most posterior cortical margin of the odontoid process to the posterior margin of the ROP (Fig. 1).

Additionally, the following parameters were evaluated on the preoperative MR images: type of ROP, MR signal homogeneity of the solid portion, ROP enhancement, spinal cord atrophy, spinal cord signal change, lesions associated with ROP (ossified posterior longitudinal ligament and os odontoideum), and atlantodental intervals. Based on the presence of a cystic Fig. 1. Measurement method of retro-odontoid pseudotumor thickness.

A. First, using T2-weighted images, the thickest portion of the ROP in the axial plane is identified.

B. The posterior cortical margin of the odontoid process is identified on sagittal T1-weighted images.

C. The transverse diameter of the ROP is measured on sagittal T2-weighted images. Specifically, the anteroposterior distance from the most posterior cortical margin of the odontoid process to the posterior margin of the ROP is measured (double-headed arrow). ROP = retro-odontoid pseudotumor

component, ROP was classified as "purely solid" and "solid and cystic" types (Fig. 2). For solid and cystic types, the size of the cystic component was measured in the craniocaudal dimension on sagittal T2-weighted images. The MR signal homogeneity of the solid portion was classified as homogeneous or heterogeneous based on the signal intensity on T2-weighted images. When the solid portion of an ROP exhibited uniformly low intensity on T2-weighted imaging, it was classified as homogeneous, whereas ROPs with regions exhibiting high signal intensity on T2-weighted images were classified as heterogeneous. For patients who underwent contrast-enhanced cervical spine MRI, the presence of enhancement in the solid portion of the ROP was also evaluated. Furthermore, spinal cord signal changes and atrophy were evaluated as they are potentially associated with ROP thickness. The atlantodental interval was assessed in patients with os odontoideum by measuring the shortest distance between the posterior cortical margin of the anterior arch of the atlas and anterior cortical margin of the axis body.

The ROP thickness on postoperative MRI was also assessed using the aforementioned method. Additionally, the cyst size and spinal cord characteristics were compared with those on preoperative MR images. The ROP regression rate was calculated using the following formula: ([preoperative thickness] – [postoperative thickness]) / (preoperative thickness) \times 100. We defined a regression rate > 30% as definite regression, 10%–30% as intermediate regression, and < 10% as no regression, based on a recent study that reported an approximately 10% median ROP regression on one-month follow-up MR images, upper limit of its 95% confidence interval being approximately 30% (22).

CLINICAL CHARACTERISTICS

The following data were retrieved from electronic medical records: clinical symptoms,

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Fig. 2. An 83-year-old male with a solid and cystic retro-odontoid pseudotumor (Case 1). A-D. Sagittal T1-weighted (A), sagittal T2-weighted (B), axial T2-weighted (C), and sagittal contrast-enhanced T1-weighted MR images (D) show mass-like hypertrophied retro-odontoid soft tissue (arrow).

medical history related to ROP, operative procedure, date of operation, and date of preoperative and postoperative MRI examinations. We calculated the time intervals between the preoperative MRI and the surgery and between the surgery and the postoperative MRI.

STATISTICAL ANALYSIS

Univariate linear regression was performed to identify factors associated with preoperative ROP thickness. The tested variables were age, sex, ROP type, and MR signal homogeneity of the ROP. The Kruskal–Wallis test was used to compare age, preoperative ROP thickness, and atlantodental interval between patients exhibiting no regression, those exhibiting intermediate regression, and those exhibiting definite regression after posterior fixation. Fisher's exact test was performed for analyses based on sex, ROP type, MR signal homogeneity of ROP, spinal cord signal change, spinal cord atrophy, ossified posterior longitudinal ligament, and os odontoideum. To identify MR predictors for ROP regression after posterior fixation, patients were dichotomized into a no regression group (regression rate < 10%) and a regression group

(regression rate \geq 10%). Age, ROP thickness, and atlantodental interval were compared between the groups using Mann–Whitney tests, and Fisher's exact test was performed for assessments based on sex, ROP type, MR signal homogeneity of the ROP, spinal cord signal change, spinal cord atrophy, ossified posterior longitudinal ligament, and os odontoideum. All statistical analyses were performed using STATA version 16.1 (StataCorp LLC, College Station, TX, USA). Statistical significance was set at $p < 0.05$.

RESULTS

We identified 23 patients diagnosed with retrodental pseudotumor, ROP, or retrodental cyst based on cervical spine MRI findings. Among them, we excluded six who had not undergone surgery, four who had undergone laminectomy or laminoplasty below the C2 level, and one who had undergone C1 posterior arch resection without posterior fixation, as well as one who had not undergone postoperative MRI. Finally, 11 patients (7 female and 4 male; age: median, 66 years; interquartile range, 55.5–74 years; range, 31–84 years) were included in this study; their baseline characteristics are presented in Table 1. None of the patients was diagnosed with rheumatoid arthritis. All patients exhibited atlantoaxial instability on preoperative lateral

Table 1. Clinical Characteristics of the Included Patients

*We deemed myelopathy is present if a patient had decreased fine motor skills (e.g., hand clumsiness) and gait disturbance. $F =$ female, $M =$ male

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NA = not applicable, ROP = retro-odontoid pseudotumor

cervical spine radiographs. The median interval between the preoperative MRI and the surgery was 2 days (interquartile range, 2–42.5 days), and that between the surgery and the postoperative MRI was 34 days (interquartile range, 31.5–41.5 days). Among the 11 included patients, postoperative MRIs were obtained approximately one month postoperatively in 10 patients. One patient missed the one-month follow-up MRI for unknown reason and underwent a cervical MRI 3 years postoperatively due to dysphagia.

The MRI findings and ROP regression rates are summarized in Table 2. Of the 11 included patients, 8 (72.7%) had regression rates \geq 10%, including five and three with definite and intermediate regression, respectively. All patients with preoperative ROP thicknesses > 5 mm exhibited ROP regression. At the one-month follow-up, the median ROP regression rate was

Fig. 3. A 75-year-old female with retro-odontoid pseudotumor (Case 5).

A. Preoperative sagittal T2-weighted MR image (arrow) reveals an ROP of thickness 6.5 mm. B-D. Cervical spine MR image (arrow in B) obtained 3 years after the posterior fixation due to dysphagia shows considerable ROP regression. Axial T2-weighted MR images also show a significant decrease in the ROP thickness after posterior fixation when comparing preoperative MR images (C) with postoperative MR images (D). ROP = retro-odontoid pseudotumor

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19.4%. Remarkably, one patient who underwent a follow-up MRI 3 years postoperatively showed significant ROP regression, with a regression rate of 58.5% (Fig. 3). The three patients with no ROP regression had comorbidities of os odontoideum, C1 posterior hypoplasia, and cervical kyphosis due to neurofibromatosis. Among the five patients with "solid and cystic" type ROP, four exhibited complete resolution or a considerable reduction in cyst size after posterior fixation (Fig. 4). However, in one patient with clustered microcysts, the cystic component did not regress after posterior fixation (Case 6). None of the eight patients who had undergone contrast-enhanced MRI exhibited ROP enhancement. Out of 8 patients with contrast enhanced MRI, 6 patients experienced > 10% ROP regression after posterior fixation, with a median regression rate of 27.6%. In the subgroup of 7 patients with spinal cord changes, four who had spinal cord atrophy in the preoperative MRI exhibited persistent spinal cord signal changes and spinal cord atrophy after posterior fixation. Of the remaining three patients with spinal cord sig-

Fig. 4. A 53-year-old female with a "solid and cystic" type retro-odontoid pseudotumor (Case 4). A. Sagittal T2-weighted MR image (arrow) show a cyst measuring 17 mm craniocaudally. B. Axial T2-weighted MR image show the cystic portion on the left side of the ROP. C, D. Postoperative MR image show the complete disappearance of the cyst after posterior fixation. ROP = retro-odontoid pseudotumor

Table 3. Univariate Linear Regression Analysis for the Identification of Factors associated with Preoperative ROP Thickness

 $*_{p\text{-value}}$ < 0.05.

ROP = retro-odontoid pseudotumor

Table 4. Clinical and MR Characteristics of the Definite Regression, Intermediate Regression, and No Regression Groups

Data are n or median (interquartile range) values.

ROP regression classification: definite, regression rate > 30%; intermediate, regression rate 10%–30%; no, regression rate < 10%.

 $*_{p$ -value < 0.05.

ROP = retro-odontoid pseudotumor

nal change but without spinal cord atrophy, two showed complete resolution of the spinal cord signal change, whereas one showed persistent spinal cord signal change after posterior fixation.

The results of the univariate linear regression analysis to identify factors associated with preoperative ROP thickness are summarized in Table 3. Patient age significantly correlated with the preoperative ROP thickness ($p = 0.034$). Other variables, including sex, ROP type, and MR signal homogeneity, were not significantly associated with preoperative ROP thickness.

Table 4 shows a comparison of the definite, intermediate, and no regression groups after posterior fixation. The preoperative ROP thickness significantly differed among the three groups ($p = 0.040$). The three groups did not differ significantly in terms of age ($p = 0.053$) or other variables (sex, ROP type, MR signal homogeneity, spinal cord signal change, spinal cord atrophy, ossified posterior longitudinal ligament, os odontoideum, and atlantodental interval).

The results of the Mann–Whitney and Fisher's exact tests to identify clinical and MR predictors of ROP regression after posterior fixation are summarized in Table 5. Patient age and pre-

Table 5. Clinical and MR Predictors for Retro-Odontoid Pseudotumor Regression after Posterior Fixation

Data are *n* or median (interquartile range) values.

Patients were dichotomized as regression group if the regression rate was \geq 10%; no regression group, < 10%. $*_{p-value}$ < 0.05.

ROP = retro-odontoid pseudotumor

operative ROP thickness significantly correlated with ROP regression ($p = 0.024$ and 0.012, respectively). Other variables, including sex, ROP type, MR signal homogeneity, spinal cord signal change, spinal cord atrophy, ossified posterior longitudinal ligament, os odontoideum, and atlantodental interval, were not significantly associated with ROP regression.

DISCUSSION

In this study, we examined the clinical and MR predictors of ROP regression after posterior fixation in patients with atlantoaxial instability, identifying a positive association between patient age and preoperative ROP thickness; that is, older age was associated with a thicker ROP thickness. A higher ROP regression rate was associated with an older age and thicker preoperative ROP thickness. Interestingly, all patients with preoperative ROP thicknesses > 5 mm exhibited ROP regression.

The patient's age and preoperative ROP thickness exhibited a positive linear association. This finding is consistent with that of a previous study that identified chronicity of atlantoaxial instability as the main cause of ROP development and thickening (7). Moreover, older age and greater preoperative ROP thickness were associated with ROP regression after posterior fixation in patients with atlantoaxial instability. Thus, older patients with thick preoperative ROPs should be considered candidates for posterior fixation because they are likely to experience favorable postoperative outcomes.

In our study, patients were classified as regression group if ROP regression was more than 10%. Conversely, a study that performed a follow-up MRI 3 years after posterior fixation defined > 50% ROP regression as sufficient (22). However, according to Niwa et al. (22), the median ROP regression on the one-month follow-up MRI was approximately 10%, and the upper limit of the 95% confidence interval was approximately 30%. Therefore, we defined the cutoffs for ROP regression as 10% and 30%, considering that most of our included patients underwent follow-up MRI just one month after posterior fixation.

Among the five patients with cystic components in the ROP, four experienced regression of the cystic components. Generally, the cystic component of ROP is purportedly caused by chronic mechanical stress due to atlantoaxial instability, which leads to reactive proliferation of the synovium or fibrocartilage as well as loculated fluid collection (8, 25, 26). We believe that the regression of the cystic component in our patients supports the hypothesis that it is caused by instability-induced degeneration.

ROP enhancement is known to be caused by neovascularization and active inflammation around the ROP (27). Although we did not perform a biopsy of the ROP, our patients likely had low proportions of vascular and inflammatory components around the ROP based on the absence of enhancement on contrast-enhanced imaging. Moreover, 75% of the patients with non-enhancing ROPs experienced ROP regression, although a direct comparison between the ROP regression rates according to contrast enhancement was not feasible in this study. Thus, regardless of the presence of ROP enhancement after contrast agent administration, posterior fixation may benefit patients with ROP.

This study had several limitations. First, a small number of patients were included. Although we identified several statistically significant factors associated with ROP regression,

appropriate statistical power might not have been achieved. Therefore, further studies with larger sample sizes are warranted. Second, the interval between the surgery and follow-up MRI was relatively short in most patients. This is because, at our institution, long-term followup MR imaging is usually performed only for patients with atypical symptoms, which were only observed in only one patient in this study postoperatively. Third, our inclusion of only patients who had undergone posterior fixation and none with inflammatory arthritis, such as rheumatoid arthritis, which is a known cause of ROP, might have resulted in a selection bias.

In conclusion, older age and thicker preoperative ROP thickness are associated with ROP regression after posterior fixation in patients with atlantoaxial instability.

Availability of Data and Material

All data generated or analyzed during the study are included in this published article.

Author Contributions

Conceptualization, L.J.W.; data curation, K.J., L.J.W.; formal analysis, K.J., K.Y., L.E.; investigation, K.J., L.E.; methodology, K.Y.; project administration, K.Y.; supervision, L.J.W.; writing—original draft, K.J., K.Y.; and writing—review & editing, K.Y., L.E., L.J.W.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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환축 불안정 환자에서 후방 고정술 후 치상돌기 후방 가성종양 퇴행의 임상 및 자기공명영상 예측 인자

김지수 $1 \cdot 2$ 영준 $1 \cdot 0$ 영준 $1 \cdot 0$ 준우 $1,2$

목적 치상돌기 후방부 가성 종양(retro-odontoid pseudotumor; 이하 ROP)이 있는 환자 중, 경추 후방 유합술 후 가성 종양의 퇴행에 대한 임상 및 MR 예측 인자를 조사한다. **대상과 방법** 2016년 3월부터 2021년 12월까지 경추 후방 유합술을 받은 만성 환축추 불안정 성 환자 중, 수술 전후의 MRI가 모두 있는 환자를 대상으로 하였다. 수술 후 ROP 두께가 감 소한 정도에 따라, 10% 이상 감소한 그룹과, 10% 미만으로 감소한 그룹으로 분류한 후 ROP 의 퇴행과 관련된 임상 특성(나이 및 성별) 및 MR 영상 소견을 분석하여 통계 분석하였다.

결과 조건을 만족하는 11명의 환자 중 수술 후 8명의 환자에서 ROP 두께가 감소하였으며 (72.7%), 가성 종양의 퇴행에 환자의 나이(p = 0.024)와 수술 전 ROP의 두께(p = 0.012)가 유 의하게 연관되었다. 성별, ROP의 유형, ROP의 MR signal 균일성, 척수 신호 변화, 척수 위 축, 후종인대골화증, 치상돌기골, 그리고 환추상돌기간격은 ROP의 퇴행과 유의한 연관이 없었다.

결론 만성 환축추 불안정성 환자 중, 연령이 높고, 수술 전 ROP의 두께가 더 두꺼울수록 경추 후방 유합술 후 ROP 퇴행이 더 많이 진행되었다.

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