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Subaxial cervical spine involvement in symptomatic rheumatoid arthritis patients: Comparison with cervical spondylosis

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ABSTRACT

Objective: To investigate the frequency, location, characteristics, and clinical significance of subaxial involvement (below C1–C2) in a series of patients with rheumatoid arthritis (RA) and symptomatic involvement of the cervical spine.
Methods: A total of 41 patients with RA were examined via cervical spine magnetic resonance imaging (MRI). A comparative analysis of the incidence of the different types of subaxial lesions was performed between these patients and 41 age- and sex-matched patients with symptomatic cervical spondylosis.
Results: Stenosis of the spinal canal was found at the subaxial level in 85% of RA patients, and at the atlantoaxial level in 44%. Comparative analysis between these patients and the cervical spondylosis patients revealed significant differences in the types and frequencies of subaxial lesions. For both conditions, signs of discopathy and end-plate osteophytosis were the most common abnormalities observed on magnetic resonance imaging (MRI). However, in the RA patients these abnormalities coincided with subchondral bone and ligamentous acute inflammatory changes and with secondary destruction (vertebral instability) or repair (vertebral ankyloses).

Only evidence of subaxial myelopathy was significantly associated with an increased risk of neurological dysfunction among the RA patients [Ranawat class II or III; $P = 0.01$; odds ratio (OR) = 11.43], although subaxial cord compression tended toward a significant association with the risk of neurological dysfunction ($P = 0.06$; OR = 3.95).
Conclusion: Subaxial stenosis seems to be the consequence of both the inflammatory process and mechanical-degenerative changes. Despite its frequency, it was not usually related to the occurrence of myelopathy symptoms, not even in cases with MRI evidence of spinal cord compression.

Cervical spine involvement is a relatively common characteristic of rheumatoid arthritis (RA). According to the literature, the prevalence of cervical spine lesions of any type among RA patients ranges from 25% to 88%, although only a small percentage (between 7% and 34%) develop severe neurological symptoms requiring surgery [1–14]. The inflammatory process typically leads to progressive joint destruction and ligamentous laxity, resulting in instability and subluxation of the cervical spine. Both the upper cervical spine (C1 and C2, including the atlantoaxial, atlanto-odontoid and atlanto-occipital joints) and the subaxial cervical spine (below C1–C2) may be involved.

Several studies have emphasized the clinical relevance of spinal cord compromise at the atlantoaxial level to RA patients based on magnetic resonance imaging (MRI) of the cervical spine [8,15] and the importance of MRI for assessing disease activity in the cervical spine [16–19].

Subaxial cervical spine involvement has been reported in 7–88% of patients and frequently occurs at multiple levels, causing stenosis of the spinal canal [1–14]. Its precise pathogenesis and

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Ethics approval: This study was approved by our institutional ethics committee. All patients provided informed consent before participating in the MRI study. The patients' clinical records and information were anonymized and de-identified prior to analysis. This study was conducted in accordance with the principles of the Declaration of Helsinki and the International Conference for Harmonization.

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clinical significance to RA are poorly understood. Few reports have explored subaxial involvement, in contrast to many publications on atlantoaxial involvement. As a result, it is unknown whether subaxial stenosis in the rheumatoid cervical spine is related to the inflammatory process, to degenerative changes, or to both. Another important issue is the clinical relevance of subaxial spinal canal stenosis, because only a small percentage of patients eventually develop neurological symptoms due to compressive myelopathy. Once a neurological deficit occurs, disease progression appears to be inevitable [20,21]. Thus, it would be particularly useful to establish which subsets of patients develop a neurological deficit and to develop methods for the early identification of these patients.

The objective of the present study was to investigate the frequency, location, characteristics, and clinical significance of subaxial spinal canal stenosis in a series of patients with RA and symptomatic involvement of the cervical spine.

Methods

Patients and controls

We studied 41 consecutive RA patients with cervical spine magnetic resonance imaging (MRI). All patients fulfilled the 1987 ACR classification criteria for RA [22]. None of these patients had a history of previous trauma or surgery of the craniocervical region.

All MRI studies were authorized by a consulting rheumatologist based on one or more of the following criteria: (a) severe neck pain not controlled with conservative management; (b) neurological symptoms or signs suggestive of cervical myelopathy; and (c) cervical pain with evidence of atlantoaxial subluxation on radiography. Clinical and laboratory data for each patient were collected according to a specifically designed protocol. The data obtained included patient age, gender, disease duration, serum rheumatoid factor levels, Steinbrocker stage [23], presence of rheumatoid nodules, evidence of erosions on radiography of the hands, wrists, and feet, erythrocyte sedimentation rate at the time of the study, and neurological impairment. The severity of the neurologic deficit was categorized according to the Ranawat classification of rheumatoid myelopathy as follows [24]: class I, neck pain without neurological deficit; class II, subjective weakness with hyperreflexia and dysesthesia; class IIIA, moderate objective weakness and signs of long tract involvement permitting some degree of self-sufficiency (ambulatory); and class IIIB, severe objective weakness, signs of long tract involvement, and a complete loss of self-sufficiency (bed- or chair-bound).

A comparative study of the incidence of the different types of subaxial lesions was performed with a randomly selected cohort of 41 patients with symptomatic cervical spondylosis matched for age, sex, and calendar year, who also underwent cervical spine MRI due to severe neck pain that was not controlled by conservative management and/or cervicobrachial neuralgia.

The study was approved by our institutional ethics committee. All patients provided informed consent before participating in the MRI study. The patients' clinical records and information were anonymized and de-identified prior to analysis.

MR imaging protocol

MRI examinations were performed using 1.5 T imaging units (Gyroscan ACS NT or Gyroscan Intera; Philips Medical System, Best, the Netherlands). Each imaging series was obtained using a quadrature transmit/receive neck coil in a supine position in which the neck was in a neutral position. The following sequences were used: (1) a sagittal T1-weighted spin-echo series with 423–450/17 (repetition time in ms/echo time in ms), a section thickness of 4 mm, a section gap of 0.4 mm, a field of view of 250 × 250 mm^2, a rectangular field of view of 100% or 80%, 2 signals acquired, and an acquisition matrix of 256 × 256; (2) a sagittal T2-weighted fast spin-echo series with 3216–3230/120, an echo train length of 17 mm, a section thickness of 4 mm, a section gap of 0.4 mm, a field of view of 260 × 260 mm^2, a rectangular field of view of 100% or 80%, 6 signals acquired, and an acquisition matrix of 256 × 256 or 251 × 512; and (3) 2 transverse 3-dimensional T2 fast field-echo series, one located at the atlantoaxial joint and the other located at the subaxial cervical spine depending on the observation of stenosis on the sagittal images, with 31–34/14, a section thickness of 4 mm, 32–36 sections, a field of view of 230 × 230 mm^2, a rectangular field of view of 60–65%, 4 signals acquired, a flip angle of 5°, and an acquisition matrix of 256 × 256.

In 19 patients, MRI was completed using a sagittal STIR series with 1736–1754/14, an inversion time of 160 ms, an echo train length of 5 or 13 mm, a section thickness of 4 mm, a section gap of 0.8 mm, a field of view of 250 × 250 or 275 × 275 mm, a rectangular field of view of 100% or 80%, 3 signals acquired, and an acquisition matrix of 256 × 256 or 251 × 512 mm.

Analysis of the MR images

The images were independently reviewed by two of the authors (J.A.N. and M.S.; 11 and 9 years' experience in musculoskeletal radiology, respectively) who were blinded to the clinical information and all other patient data. In cases of interobserver differences, a consensus was achieved for each score.

For each study, the spinal canal was evaluated at the atlantoaxial and subaxial (below C1–C2) levels and was classified as follows: (1) normal, (2) stenosed without spinal cord compression, or (3) stenosed with spinal cord compression (with or without cord signal intensity changes).

The MR images of the atlantoaxial joint (C1–C2) were reviewed, paying particular attention to the presence of periodontoid synovitis, odontoid erosions, bone marrow edema (BME), stenosis of the spinal canal, anterior, posterior or superior vertebral subluxation, upper cervical cord or brainstem compression, alterations in the signal intensity of the spinal cord, and alterations in the cervicomedullary angle.

At the subaxial spine level, the MR images were evaluated for the presence of stenosis of the subaxial canal, spinal cord compression, alterations in the signal intensity of the spinal cord, BME, spinous process damage (sharpening, erosions, sclerosis, and fusion), inflammatory involvement of the cervical spine ligaments, synovitis of the uncovertebral joints and the interapophyseal joints, pannus formation, vertebral ankylosis (VA), vertebral subluxations, discopathy (disk, bulging, disruption, and/or herniation), ligamentum flavum hypertrophy, degenerative spinal osteophytosis, sclerosis, and/or hypertrophy of the uncovertebral joints and the interapophyseal joints, and congenital spinal stenosis.

The MR images from a given patient were presented in a randomized manner to the reviewers and were interpreted twice, with an interval of 4–24 months (mean of 12 months) between the 2 interpretations to ensure intraobserver reliability.

Clinical definitions

We defined stenosis of the atlantoaxial spinal canal as a posterior atlanto-dental interval, measured from the posterior aspect of the dens to the anterior aspect of the C1 lamina, of less than 14 mm. At the subaxial level, stenosis was defined as a sagittal diameter of the subaxial spinal canal of than 14 mm. Spinal cord compression was defined as obstruction of the subarachnoid space (disappearance of the cerebrospinal fluid in both