Magnetic resonance imaging findings of the cervical spine in patients with rheumatoid arthritis. A cross-sectional study

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Abstract

Objectives

To investigate by magnetic resonance (MR) imaging the occurrence of cervical spine (CS) involvement in rheumatoid arthritis (RA) patients.

Methods

Fifty-one consecutive unselected patients, who fulfilled the revised American College of Rheumatology criteria for RA, were investigated. All patients had a complete physical and laboratory evaluation. Radiological evaluation included hand and wrist x-rays, as well as CS radiographs in anteroposterior, lateral and lateral in full flexion views. In addition, MR (Spin Echo T2-weighted sagittal scans [neutral and flexion position], plain and contrast enhanced T1-weighted sagittal and axial scans) was performed in all patients. Hand x-rays were evaluated according to the Larsen's criteria, while CS radiographs were evaluated according to Winfield classification. Disease activity was assessed by disease activity score for 28 joint indices (DAS-28).

Results

There were 42 females and 9 males with a mean age of 56.5 ± 10.4 years and mean disease duration 12.4 ± 8.5 years. Thirty-three patients (64.7%) had positive IgM rheumatoid factor (RF). Thirty patients presented clinical findings, mainly cervical pain and stiffness of CS (25 with positive and 5 with negative MR), while, radiological findings of CS involvement were found in 40 patients. Forty-four patients (86.2%) presented MR findings of CS involvement (peri-dental pannus 88%; dens erosion 23.5%; atlantoaxial subluxation 13.7%; subaxial subluxations 10%; brainstem compression 5.9%). Peridental pannus correlated with high DAS-28, positive IgM RF, and advanced erosive changes of the wrist and hand ($p < 0.05$) in the univariate analysis. However, multivariate logistic regression analysis did not confirm such correlation.

Conclusions

We conclude that the frequency of CS involvement in Greek RA patients is high but the destructive changes are mild. However, in patients with active erosive peripheral disease it is very probable to also have some changes in CS. These may be clinically important and in such cases, MR may offer valuable information.

Key words

Rheumatoid arthritis, cervical spine, magnetic resonance imaging, cervical spine radiographs, Larsen score, DAS-28.

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Introduction

The cervical spine (CS) is an important target organ in patients with rheumatoid arthritis (RA) and is affected in about two-thirds of cases (1-4). The atlantoaxial articulation is typically involved leading to non-traumatic dislocations with sometimes severe neurologic deficits or even death due to brainstem compression (5, 6). Therefore, early diagnosis and treatment is necessary to avoid irreversible neurologic sequelae. Since the clinical evaluation for potential neurologic complications of RA is frequently hampered by the presence of arthritis and deformations, objective diagnostic techniques are needed (7).

Previous studies have demonstrated that RA in Greece is milder, with less radiological joint destruction and fewer extraarticular manifestations (EAM), compared to northern European countries (8, 9).

Our purpose was to evaluate by magnetic resonance (MR) imaging the frequency of CS involvement in Greek patients with RA and the relationship between MR findings, x-rays and clinical findings.

Materials and methods

This cross-sectional study included 51 consecutive RA patients attending the outpatient clinic of our rheumatology department. Patients with neck trauma, neck infection or congenital abnormalities were excluded from the study. All patients fulfilled the revised American College of Rheumatology criteria (10).

The patients had a physical examination which included: (i) symptoms and signs of peripheral joints involvement such as (a) morning stiffness (minutes), (b) grip strength (mmHg), (c) total number of swollen and tender joints and disease activity score for 28 joint indices (DAS–28) (11); (ii) symptoms and signs of CS involvement, such as neck and occipital pain, stiffness and neurological symptoms and signs; (iii) symptoms and signs of EAM like rheumatoid nodules, pleurisy, sicca syndrome, scleritis, episcleritis, etc. In addition, the following laboratory parameters were investigated in all patients: (i) C-reactive protein (CRP), (ii) erythrocyte sedimentation rate (ESR), and (iii) IgM rheumatoid factor (RF).

The radiological evaluation consisted of CS x-rays (anteroposterior, lateral in neutral and flexion position) and wrist and hand x-rays in postero–anterior position. CS x-rays were evaluated according to the Winfield classification (atlantoaxial subluxation [AAS] of 2.5 mm or more, atlantoaxial impaction, disc space narrowing affecting upper cervical discs without osteophytosis, multiple subluxation of 1 mm or more, vertebral plate erosions and sclerosis, apophyseal joint erosions and sclerosis, osteoporosis) (12). Pairs of hand and wrist x-rays were evaluated using Larsen's criteria (13).

The following joints were assessed: four proximal interphalangeal, five metacarpophalangeals and the wrist bilaterally. The scoring of each joint had six stages from 0 (normal) to 5. The wrist was considered as a unit and the score was multiplied by five. Thus, the score ranges from 0-140. The erosive changes were considered as mild or moderate when the score ranged between 0-80, and severe erosive changes when the radiological score was > 80. The x-rays were interpreted by one experienced radiologist (AKZ) who was unaware of the patients' name, clinical status and MR findings.

MR imaging was performed on a 1.5-tesla unit (Gyroscan ACS NT; Philips Medical Systems, Best, The Netherlands™) using a phased array neck coil. The study protocol consisted of: (i) sagittal turbo spin echo T2-weighted scans (TR/TE, 3000/120 msec); (ii) axial and sagittal gradient echo T2-weighted scans (TR/TE, 500/12 msec; flip angle 25°), in neutral position and flexion; and (iii) sagittal and fat suppressed axial plain and contrast enhanced (immediately after bolus intravenous injection of 0.1 mmol/kg gadopentetate dimeglumine Gd-DTPA - Magnevist, Schering, Germany™) spin echo T1-weighted scans (TR/TE, 525/13 msec). Flexion scans were performed with the neck kept flexed by sponge supports. The flexion angle varied from 20° to 40°. For all sequences the slice thickness was 3 mm, the intersection gap 0.3 mm, the acquisition matrix 250 x 256

matrix and the field of view 270 mm. The scan duration for T1-weighted sequences was 2.5 min and therefore fibrotic pannus was not as intensively enhanced as active pannus (14). The MR images were interpreted in consensus by two experienced radiologists (AKZ and MIA) who were blinded to the patients name, the clinical status and the plain film findings. The parameters used were (7):

(1) Dens erosion classified as normal, less than 50% erosion, or 50% or more erosion (three-point scale).
(2) Presence or absence of AAS was evaluated in neutral and flexion position (atlantoaxial distance ≥ 2.5 mm) (two-point scale).
(3) Presence or absence of compression of the brainstem (two-point scale).
(4) Subarachnoid space (level C_2), classified as normal space, and decreased space (two-point scale) in neutral and in flexion position.
(5) Fat body caudal to the clivus classified, as present or absent (two-point scale).
(6) Amount of hypervascular-active pannus (enhanced soft tissue mass around the dens) classified as absent, small (≤ 5 mm), large (≥ 5 mm) (three-point scale).
(7) Cervicomedullary angle, which is the line between the two lines on respectively, the ventral side at the medulla oblongata or brainstem and the cervical cord in degrees (normal ≤ 135°).
(8) Atlantoaxial impaction (normal: dens under the line of McRae) (two point scale).
(9) Presence or absence of vertebral plate erosions.
(10) Presence or absence of subaxial subluxation (SAS) in neutral and inflexion position.

Radiological and MR studies were performed the same day.

All subjects included in the study signed a written informed consent form. The study was performed with the approval of the Institutional Review Board.

Statistical analysis

The relationship of MR with clinical, laboratory and radiological parameters was evaluated using the x^2 test. These parameters were considered as categorical, according to the following classification: age (≤ 45 / > 45 years), gender (women/men), disease duration (≤ 5 / > 5 years), EAM (yes / no), ESR (≤ 30 / > 30), IgM RF (yes / no), Larsen's score (≤ 80 / > 80), DAS–28 (≤ 3.2 / > 3.2), CRP (6 ≤ / > 6), CS x-rays (yes / no), clinical signs (yes / no).

Amultivariate logistic regression analysis was conducted, using radiographic damage and MR imaging damage as dependent parameters. These parameters were dichotomized (presence vs absence of damage). Only parameters presenting a statistically significant association with pannus in the univariate analysis were included in the model.

Results

The clinical and radiological findings are shown in Table I. There were 42 females and 9 males with a mean age of 56.5 ± 10.4 years and disease duration of 12.4± 8.5 years. Thirty-three patients had positive IgM RF. Thirty patients presented clinical findings of CS involvement, mainly cervical pain and stiffness (25 with positive and 5 with negative MR), while radiological findings of CS involvement were found in 40 patients.

Forty-four out of 51 patients (86.2%) presented with MR findings of CS involvement (Table I). More specifically: peridental pannus formation was found in 88.0% of patients (≥ 5 mm in 9 out of 44 patients) (Table II, Fig. 1), dens erosion in 23.5% (≥ 50% in 3 out of 12 patients), AAS in 13.7%, (7 patients in flexion position and 5 in neutral position), and SAS 10.0% (5 patients in flexion position and 4 in neutral position) (Fig. 2). More specifically: 9 out of 12 patients with dens erosions had Larsen score > 80. Thirty out

Table I. Demographic, clinical and imaging findings of patients with established rheumatoid arthritis.

Number of patients	51
Women/men	42/9
Mean age (years) (± SD)	56.5±10.4
Mean disease duration (years) (± SD)	12.4± 8.5
Extraarticular manifestations, no. (%)	19 (37.2)
Clinical findings of cervical spine involvement, no. (%)	30 (58.8)
Radiological findings of cervical spine involvement, no. (%)	40 (78.4)
Magnetic resonance findings of cervical spine, no. (%)	44 (86.2)
IgM rheumatoid factor, no. (%)	33 (64.7)
Disease modifying anti-rheumatic drug therapy	
Methotrexate and prednisone, no. (%)	22 (43.3)
Methotrexate and cyclosporine Aand prednisone, no. (%)	21 (41.1)
Cyclosporine Aand prednisone, no. (%)	8 (15.6)

Table II. Magnetic resonance findings of the cervical spine in patients with rheumatoid arthritis.

Magnetic resonance findings	Patients (n = 51)	%
Peridental pannus formation	44	88.0
Dens erosions	12	23.5
Atlantoaxial subluxation	7	13.7
Subaxial subluxations	5	10.0
Fat body caudal to the clivus	5	10.0
Narrowing of the anterior subarachnoid space (level C_2)	4	8.0
Vertebral plate erosions	4	8.0
Cervicomedullary angle < 135°	3	6.0
Brainstem compression	3	5.9
Atlanto-axial impaction	0	0

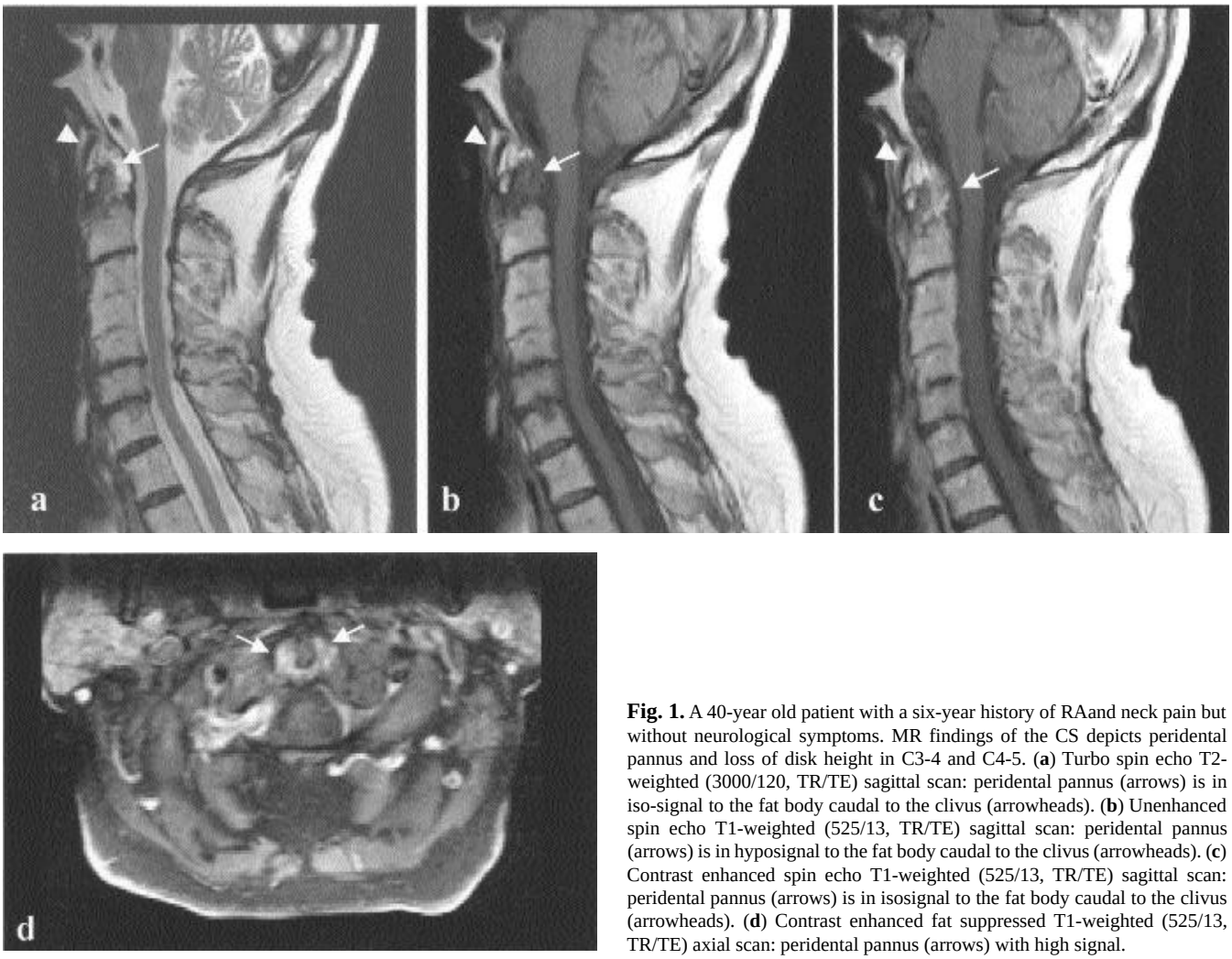

Fig. 1. A 40-year old patient with a six-year history of RAand neck pain but without neurological symptoms. MR findings of the CS depicts peridental pannus and loss of disk height in C3-4 and C4-5. (**a**) Turbo spin echo T2-weighted (3000/120, TR/TE) sagittal scan: peridental pannus (arrows) is in iso-signal to the fat body caudal to the clivus (arrowheads). (**b**) Unenhanced spin echo T1-weighted (525/13, TR/TE) sagittal scan: peridental pannus (arrows) is in hyposignal to the fat body caudal to the clivus (arrowheads). (**c**) Contrast enhanced spin echo T1-weighted (525/13, TR/TE) sagittal scan: peridental pannus (arrows) is in isosignal to the fat body caudal to the clivus (arrowheads). (**d**) Contrast enhanced fat suppressed T1-weighted (525/13, TR/TE) axial scan: peridental pannus (arrows) with high signal.

of 44 with peridental pannus had DAS-28 > 3.2. In addition, 15 out of 44 patients with peridental pannus had Larsen score > 80. Flexion MR depicted brainstem in 3 patients, while neutral MR showed brainstem compression in only one of them. Moreover, a decrease of anterior subarachnoid space (< 2 mm) at C_2 level was observed in 2 patients and only in flexion MR. A large AAS was observed in x-rays in all patients with brainstem compression. Occipital pain was the only clinical complain in these patients. None of the patients had atlantoaxial impaction (Table II).

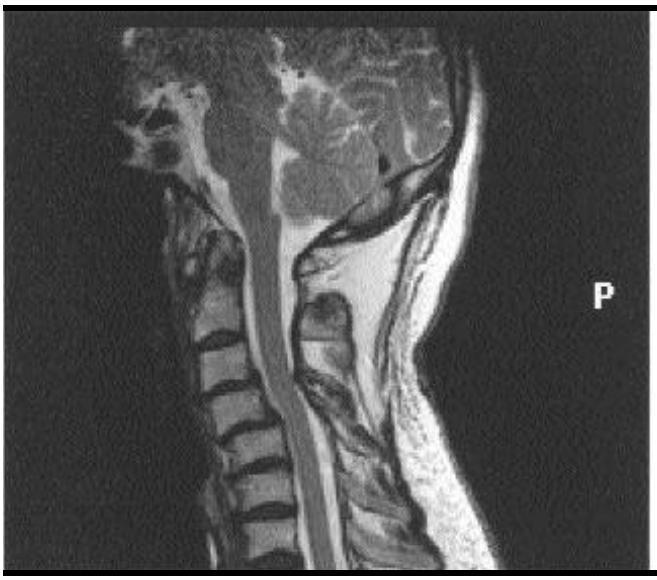

Fig. 2. A 40-year old patient with a six-year history of RA: a turbo spin echo T2-weighted (3000/120, TR/TE) sagittal scan shows SAS at the C4-5 level.

Using the MR as a gold standard for the assessment of peridental synovitis, the sensitivity and specificity of clinical-neurological evaluation was 56.8% and 28.6% respectively.

Seventeen patients had AAS according to the atlantoaxial distance measurements made on functional x-rays (flexion) (Table III). In contrast only 7 patients had AAS according to the measurements made on functional MR imaging (flexion) (Table III). Using functional x-rays as gold standard for AAS evaluation, the sensitivity and specificity of functional MR imaging

Table III. Atlantoaxial distance at flexion x-ray and magnetic resonance finding. Presence of atlantoaxial subluxation when atlantoaxial distance ≥ 2.5 mm.

Pt. no	X-ray atlantoaxial distance flexion (mm)	Magnetic resonance finding atlantoaxial distance flexion (mm)
1	3.5	2.3
2	8	6.0
3	3	2.0
4	8	7.0
5	9	5.5
6	3	2.8
7	3	2.5
8	4	2.4
9	3	2.4
10	4	3.0
11	5	2.8
12	3	2.2
13	3	2.2
14	5	2.4
15	3	1.7
16	3	2.2
17	4	2.4

Table IV. Multivariate logistic regression analysis. Dependent variables: radiographic damage and magnetic resonance imaging (adjusted for age and gender).

	Cervical spine damage					
	Radiographic damage (yes/no)			Magnetic resonance imaging damage (yes/no)		
	Odds ratio	95% CI	p	Odds ratio	95% CI	p
Larsen score	1.01	0.97-1.04	0.98	0.98	(0.96-10.1)	0.98
DAS-28*	0.92	0.55-1.56	0.78	0.67	(0.33-1.49)	0.67
Rheumatoid factor	1.56	0.32-7.42	0.58	5.30	(0.39-73.13)	0.21

* Disease activity score for 28 joint indices.

was 41.2% and 100% respectively.

Peridental pannus was associated with (i) high DAS-28, (ii) positive IgM RF, and (iii) advanced erosive changes of the hands and wrist ($p < 0.05$).

Table IVshows the results of multivariate logistic regression analysis. None of the parameters included in the model presents any significant association with radiographic or MR imaging damage.

Discussion

Early detection of CS involvement in RA patients is of great value to adapt treatment appropriately and thus to limit pain or neurologic sequelae (6). Imaging techniques such as x-ray have been used for the evaluation of CS involvement. However, osseous lesions detected by conventional x-ray appear latter in the course of the disease since they are secondary to mechanical instability, rather than to the acute inflammatory process (15-17). MR imaging has the unique potential of direct and detailed synovial visualization especially in contrast enhanced axial images, resulting in the early diagnosis of cranio-cervical RA (18).

In this study, MR imaging revealed increased frequency of CS involvement and especially peridental pannus formation, which is in accordance with previous studies (5,7). Nevertheless, severe CS changes namely dens erosions, subarachnoid space encroachment at the atlantoaxial level and brainstem compression were less frequent than in previous studies (7). In line with these findings, previous studies have demonstrated that RAin Greece is milder, compared to northern European countries, with less radiological joint destruction and fewer EAM (8). Genetic and enviromental factors have been considered to be responsible for these striking differences in disease expression (8, 9).

The CS in this study was evaluated in neutral and in flexion position. Narrowing of the subarachnoid space at the atlantoaxial level was observed only in flexion images. However, this finding was not associated with cord compression. This is in agreement with previous studies where flexion images depicted cord compression only if the subarachoid space was already decreased in neutral images (6). The degree of AAS evaluated in x-rays in flexion was significantly larger than those measured in MR flexion images. This is probably explained by the different position of the patient during these two examinations. X-rays are taken with the patient in upright position reaching a maximal flexion as the gravity pulls the head downwards. MR images are taken with the patient in supine position and flexion obtained using sponge supports, is never maximal. Other reasons for this discordance between the x-rays and the MR finding is that the degree of AAS is overestimated in x-rays due to magnification and underestimated in gradient echo T2 weighted sequences (19, 20).

In agreement with other studies we did not find any correlation between the presence of pannus and neurologic signs. This is probably because the progress of CS lesions in RApatients is slow and therefore allows the central nervous system to adapt to the new situation (5).

A lack of correlation between the presence of pannus in CS and laboratory indicators of inflammation was found in this study. A possible explanation is that RA is a polyarticular disease and inflammatory synovium of CS depicted by MR represents only a part of the total disease burden (21).

CS involvement has been previously associated with the extent of erosions in peripheral joints, the presence of RF and continuous high disease activity (21-25). In the present study pannus formation was positively correlated with peripheral joint erosive changes, positive IgM RF and DAS-28. However, in multivariated regression analysis

did not confirm these correlations.

A lack of correlation between radiographic and MR findings of CS involvement and clinical findings has been found in this study and this is in agreement with other reports (25). This is probably because conventional x-rays detect CS involvement only at the late stages of the disease while MR imaging by depicting inflammatory synovium reveals CS lesions earlier (24).

In conclusion, in Greek patients with RA the frequency of CS involvement and peridental pannus formation is high but the destructive changes are mild. However, in patients with active erosive peripheral disease it is very probable to also have some changes in CS. These may be clinically important and in such cases, MR may offer valuable information.

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