The Cervical Spine Involvement in Rheumatoid Arthritis
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Citation

Abstract
Background and Objectives: There is not any information about the cervical spine involvement and risk factors of that in the patients with rheumatoid arthritis in Azerbaijan of Iran. We conducted this study to consider the frequency of cervical spine involvement in the patients with rheumatoid arthritis in Azerbaijan of Iran and to correlate the different factors reflecting the disease severity with the involvement of cervical spine.
Settings and design: From April 2009 to September 2010, 100 consecutive unselected patients with RA being followed at the outpatient rheumatology clinic of the University Hospital of Sina were investigated.
Patients and methods: We investigated 100 consecutive unselected patients with rheumatoid arthritis who fulfilled the revised American College of Rheumatology criteria for rheumatoid arthritis. All patients had a complete physical and laboratory evaluation. Patients had a radiological evaluation of cervical spine in anteroposterior, lateral, and lateral in full flexion views. Radiographs were evaluated according to Winfield classification.
Results: There were 79 women (79%) and 21 men (21%) with a mean age of disease 45.6 ± 11.9 years and mean disease duration 5.86 ± 5.43 years. Forty (40%) patients presented radiological findings suggesting cervical spine involvement. Common radiological findings were disc space narrowing (27%), anterior atlantoaxial subluxation (17%), subaxial subluxation (14%) and apophyseal joint erosion (11%). There is significant correlation between disease duration with SAS and disc space narrowing and DAS28 with disc space narrowing.
Conclusions: Plain radiographs of the cervical spine should be obtained regularly to seek cervical spine manifestations even in patients without cervical symptoms.

INTRODUCTION
Rheumatoid arthritis (RA) is a chronic, systemic inflammatory disorder of unknown etiology characterized by erosive synovitis. It affects 0.33 of the Iranian people.1 Cervical spine involvement is one of the causes of morbidity and mortality in the patients with rheumatoid arthritis. The frequency of cervical spine involvement varies largely depending on the series reviewed. It has been reported to be in 17-86% of patients with RA.2 The most important cervical spine involvement in RA is atlantoaxial subluxation (AAS), which may be horizontal or vertical in direction. However, significant subaxial disease is common and usually coexists with the AAS.3 4 Although radiological abnormalities may remain asymptomatic for years, these patients are at continued risk of neurological complications and even sudden death from medullary compression. The association between various clinical factors and cervical spine involvement in RA spine has been investigated.5 6 However, there has been little investigation about the relationship between the various clinical and laboratory factors and type of radiographic cervical spine involvement in RA. There is not any information about the cervical spine involvement and risk factors of that in the patients with rheumatoid arthritis in Azerbaijan of Iran. We conducted this study to consider the frequency of cervical spine involvement in the patients with rheumatoid arthritis in Azerbaijan of Iran and to correlate the different factors reflecting the disease severity with the involvement of cervical spine.

MATERIALS AND METHODS
From April 2009 to September 2010, 100 consecutive unselected patients with RA being followed at the outpatient rheumatology clinic of the University Hospital of Sina were investigated. The study has been approved by the ethical committee of Tabriz University of Medical Sciences. Informed consent was obtained from the participants. All patients fulfilled the revised American College of Rheumatology criteria (ACR).10 Patients with pregnancy, neck trauma, neck infections, or congenital abnormalities were excluded from the study.
The following parameters were entered on a questionnaire:

Radiography of anteroposterior, lateral in neutral and flexion position of cervical spine was performed in all patients. Radiographies were evaluated according to the modified Winfield classification\textsuperscript{13, 14}. AAS was measured by recording the shortest distance between the posterior surface of the anterior arch of the atlas to the anterior surface of the odontoid peg. A distance ≥ 2.5 mm was taken as significant. Vertical subluxation was recorded as present if the tip of the odontoid peg lay > 4.5 mm above the line described by McGregor (a line drawn between the hard palate and the most caudal point of the occipital curve). Radiological evaluation of the cervical spine did not include open-mouth anterior-posterior view of C1–C2, thus we did not assess C1–C2 lateral joint destruction and lateral AAS. Multiple subaxial subluxation (SAS) was recorded as present if displacement between adjacent vertebral bodies was > 1 mm. A shift > 1 mm is considered abnormal according to the Smith criteria.\textsuperscript{5} Disk space narrowing at C2–C3, C3–C4, and C4–C5 was recorded only if there was a relative lack of osteophytosis. Disk space narrowing at lower levels in the cervical spine was not documented, since degenerative changes are frequently superimposed. Apophyseal joint erosion was also investigated.

**STATISTICAL ANALYSIS**

Data were analyzed using the SPSS 13.0 statistical software. The chi-square and student’s t tests were used to compare differences between groups. The level of statistical significance was established at $P \leq 0.05$.

**RESULTS**

There were 79 women and 21 men (Female : male=3.8:1). Mean age of patients was $45.6 \pm 11.9$ years and mean disease duration $5.86 \pm 5.43$ years. The RF was positive in 75 cases (75%). Twenty percent of patients had DAS 28 < 3.2, 50% DAS28 3.2-5.1 and 30% DAS28>5.1.

Forty (40%) patients presented radiological findings suggesting cervical spine involvement. Thirty one of them were women and nine men (Female : male=3.4:1). Difference between sex of patients with and without radiological cervical spine involvement was not significant. Table 1 shows radiological findings of our patients. Common radiological findings were disc space narrowing, AAS, SAS and apophyseal joint erosion.

**Figure 1**

Table 1: Radiological findings of 100 patients with RA

<table>
<thead>
<tr>
<th>Radiological Findings</th>
<th>Number of RA</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disc space narrowing</td>
<td>27</td>
<td>27</td>
</tr>
<tr>
<td>Anterior AAS</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>SAS &gt; 1 mm</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Apophyseal joint erosion</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Vertebrale plate erosion and sclerosis</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Odontoid erosions</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Vertical subluxation</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Seventy RA patients presented clinical findings related to cervical spine involvement (Table 2). The most common clinical symptom was neck pain and stiffness. Neck pain was most common in patients with SAS and disc space narrowing (Table 3). Limitation of motion was commonly seen in patients with disc space narrowing and AAS (Table 3).

**Figure 2**

Table 2: Clinical features of cervical spine involvement in RA patients

<table>
<thead>
<tr>
<th>Symptoms and Signs</th>
<th>Number of Patients</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neck pain</td>
<td>70</td>
<td>70</td>
</tr>
<tr>
<td>Neck stiffness</td>
<td>53</td>
<td>53</td>
</tr>
<tr>
<td>Decreased ROM</td>
<td>36</td>
<td>36</td>
</tr>
<tr>
<td>Flexion</td>
<td>10</td>
<td>27.7</td>
</tr>
<tr>
<td>Extension</td>
<td>8</td>
<td>22.2</td>
</tr>
<tr>
<td>Lateral flexion</td>
<td>15</td>
<td>41.6</td>
</tr>
<tr>
<td>Rotation</td>
<td>3</td>
<td>8.3</td>
</tr>
<tr>
<td>Tingling or numbness</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Babinski sign</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Figure 3**

Table 3. Some clinical findings according to the type of radiological cervical spine involvement in RA patients

<table>
<thead>
<tr>
<th>Radiological involvement</th>
<th>Neck pain %</th>
<th>Cervical stiffness %</th>
<th>Decreased ROM</th>
<th>Numbrness %</th>
<th>Babinski %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior AAS</td>
<td>17.9</td>
<td>5.7</td>
<td>14.3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Vertical subluxation</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SAS &gt; 1 mm</td>
<td>33.3</td>
<td>5.8</td>
<td>8.6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Disc space narrowing</td>
<td>18.6</td>
<td>22.6</td>
<td>19.4</td>
<td>33.3</td>
<td>8.3</td>
</tr>
<tr>
<td>Apophyseal joint erosion</td>
<td>4.3</td>
<td>5.7</td>
<td>8.3</td>
<td>4.3</td>
<td>0</td>
</tr>
</tbody>
</table>

Radiological findings of cervical spine involvement were not related to sex, neck pain,
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Figure 4

Table 4: Correlation between Radiological cervical spine involvement with DAS, CRP, ESR and disease duration in RA patients

<table>
<thead>
<tr>
<th>Radiological involvement variant</th>
<th>DAS&lt;3.2</th>
<th>DAS&gt;3.2</th>
<th>Disc space narrowing</th>
<th>Apophyseal joint erosion</th>
<th>Vertical subluxation</th>
</tr>
</thead>
<tbody>
<tr>
<td>D-value</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>p-value</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

DISCUSSION

In the present study the cervical spine was involved in 40% of patients. In Chellapandiana study\(^1\) and Marko\(^\text{a}\) study radiological cervical spine involvement was detected on 42.7% and 44% respectively. But Anastasia et al reported cervical spine involvement in 88.5% of their patients.\(^1\) Disc space narrowing and AAS were the most common radiological findings in our patients. Vertical subluxation was not observed probably because we used the McGregor method for its evaluation. Although this method is sufficient, in some cases the tip of the odontoid process was not visible in all radiographs. This was to avoid the difficulty of defining the hard palate and the eroded odontoid. We tried to overcome this inconvenience by repeating the unacceptable radiographs. In contrast of our study Weissman\(^\text{a}\) reported vertical subluxation in 20% of their patients. But in Anastasia et al study like our study the incidence of vertical subluxation was very low.\(^1\)

The effect of disease duration on cervical spine involvement is controversial. Cervical spine involvement has been reported within 2 years of RA onset.\(^1\) In a 5 year study by Pellicci et al in 106 RA patients radiological evidence of cervical spine involvement was seen in 43% of patients at baseline and 76% at last follow-up.\(^1\) In our study there was significant correlation between disease duration with only disc space narrowing and SAS.

We did not find any study about relationship between various clinical and laboratory parameters and radiographic subtypes (for example AAS or SAS, etc) in literature. Some studies showed that CRP concentration at onset of RA may predict the subsequent development of cervical spine involvement.\(^20,21\) In our study there was not any relation between CRP and cervical spine involvement but ESR relate with apophyseal joint erosion. There is general agreement that seronegative disease is less severe.\(^22\) But in our study there was no correlation with IgM RF and cervical spine involvement. This result was like with Anastasia et al study\(^1\). There is general agreement that the symptoms and signs vary widely across patients and show no correlation with the severity of radiological damage. At least 15% of patients with radiological lesions are asymptomatic.\(^22,22\) This makes it difficult to determine the optimal timing and methods of radiological monitoring, particularly as subluxation can develop rapidly. Pain in the cervical spine and/or suboccipital region is the most common manifestation. Decreased ROM is common. In our study 40% of patients had radiological cervical spine involvement but 70% had pain and 53% stiffness in cervical spine. Therefore neck pain in rheumatoid arthritis is not necessarily related to radiological involvement and many of patients’ radiological involvement were asymptomatic. Cervical pain was common on SAS, and cervical stiffness and decreased ROM were common on disc space narrowing (Table 3).

CONCLUSION

The frequency of cervical spine involvement in RA varies from study to study. Lack of uniformity in the selection of various radiographic projections might be a cause. Patients with cervical spine involvement may remain asymptomatic until late stages. But they are always at risk for neurological compromise and sudden death. In this context, it becomes important to identify these patients. Therefore, plain radiography of the cervical spine should be obtained regularly to seek cervical spine manifestations, even in patients without cervical symptoms.

References
5. Smith PH, Benn RT, Sharp J. Natural history of
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