CERVICAL SPINE LESIONS IN RHEUMATOID ARTHRITIS PATIENTS

Luana-Andreea Macovei*, Elena Rezuş
“Gr. T. Popa” University of Medicine Iasi
Faculty of Medicine
Department of Rheumatology and Medical Rehabilitation
Ist Clinical Rehabilitation Hospital, Rheumatology Department, Iasi, Romania
*Corresponding author. E-mail: luanam77@yahoo.com

CERVICAL SPINE LESIONS IN RHEUMATOID ARTHRITIS PATIENTS (Abstract): **Aim of the study:** to gather clinical and laboratory data on rheumatoid arthritis patients with cervical spine damage (incidence and prevalence, correlation between duration of disease and the time of lesion onset, to assess signs and symptoms and the role of laboratory investigations). The spine is an axial organ with an important role in support and resistance. It is a pillar with a very complex morphological and functional structure. The vertebral column is crossed by many kinematic chains. The main problem of the cervical spine caused by rheumatoid arthritis is cervical instability which describes all cervical lesions that can lead to neurovascular damage or major disturbance of pain generating statics at movement. The evolving disease shows chronic inflammation of the synovium, which is a self-maintained process and an immunologically induced phenomenon. The chronic inflammation of the synovium forms granulation tissue that invades peripheral joints towards the center and causes ligament cartilage and bone damage.

**Material and methods:** The present paper investigated cervical spine lesions in 107 rheumatoid arthritis patients who were admitted to the 1st Rheumatology Clinic of Iasi Rehabilitation Hospital between January 2013 and December 2014. Our study focused on assessing signs and symptoms seen in spine affected by rheumatic disease. **Results and Discussions:** the disease causes destructive lesions due to granulomatous infiltration of rachidian structures and medullary sheaths. These lesions lead to damaged discs and instability that produces subluxations and dislocations. The suboccipital region is most affected; in other regions of the spine, high lesions of C4-C5 prevail, where osteolysis damage of spinal apophyses are found. In atlas and axis joints, rheumatoid arthritis causes the inflammation of bursa, synovium and joint capsule and leads to synovial pannus formation. This causes the destruction of cartilage and subchondral bone. Atlantoaxial dislocation is caused by erosive synovitis of atlanto-epistrophic joint, atlanto-odontoid joint and serous bursitis separating the odontoid process from the transverse ligament. **Conclusions:** The dominant symptom of cervical spine damage was pain associated with stiffness and limited joint mobility, muscle stiffness, poor posture. **Keywords:** CERVICAL INSTABILITY, DISLOCATION, DESTRUCTIVE EROSIONS, RADIOLOGICAL CRITERIA.

Cervical spine lesions in rheumatoid arthritis (RA) patients lead to increased physical pain, with local radicular bone marrow involvement that aggravates the functional deficit, worsening the vital prognosis. The impairment of the cervical spine can be explained only partly by its morphological and dynamic characteristics (1).
During the evolutive process, the chronic inflammation of the synovial membrane is a self-maintained, immunologically induced process that leads to the formation of granulation tissue invading peripheral joints towards the center and causing cartilage and bone ligament lesions (2).

Atlanto-axial dislocation occurs at the C1-C2 segment (anterior more than 3 mm between the arch of C1 and the C2 odontoid, with synovial proliferation in the C2 odontoid joint and the anterior arch of C1 that can lead to rupture of the transverse ligament and alar ligaments) (3).

Other lesions of the cervical segment caused by rheumatoid arthritis include: vertical axial subluxation = collapse of the lateral joints between C1 and C2; lateral atlantoaxial subluxation with pain in the frontal and suboccipital region and anterior inclination of the head posture; posterior atlanto-axial subluxation; C2 and C3 are the most commonly affected, while 10 to 20 percent of C3 and C4 are affected. The therapeutic intervention depends on the moment of survey or on the presence or absence of neurological signs (4).

Destructive lesions found in the rest of the cervical spine affect mainly the C3-C4 and C4-C5 segments, the lower cervical spine being less affected (5).

The present study focused on monitoring clinical and laboratory data of cervical spine lesions in rheumatoid arthritis patients.

**Aims of the study:** The evaluation of the incidence and prevalence of cervical spine damage in rheumatoid arthritis cases hospitalized in the 1st Rheumatology Clinic, Iasi Rehabilitation Hospital, the correlation between the duration of the disease and the onset of cervical spine lesions in rheumatoid arthritis patients, the evaluation of signs and symptoms that occur in the rheumatoid damage of the cervical spine and the role of laboratory investigations in the diagnosis of vertebral instability (standard radiography, CT examination, MRI examination).

**MATERIAL AND METHODS**

The study included a group of 107 RA patients who were admitted to the 1st Rheumatology Clinic, Iasi Rehabilitation Hospital between January 2013 and December 2014.

The inclusion criteria were the 1987 ACR classification criteria for RA and the results of the radiological examination (2).

Exclusion criteria included RA patients who did not show clinical or radiological damage to the cervical spine and RA patients with only degenerative changes. The demographic characteristics in the group of patients were initially evaluated through descriptive statistical methods; statistical correlations between clinical and laboratory parameters (e.g. Pearson correlation) were subsequently performed.

T-student and chi-square tests were used for the statistical evaluation of data. They were clinically significant when p is less than or equal to 0.05. The database was systemized with Excel (Microsoft Office), and the statistical analysis used the statistical programs MedCalc and Epi Info 2000.

**RESULTS**

RA incidence and prevalence are reported differently according to the diagnostic criteria used in population studies (table I).

Out of the total number of 20 (18.69%) RA patients with cervical spine involvement admitted during the study period, 13...
(12.14%) were women and 7 (6.54%) were men. A predominant involvement of female patients was noted, showing a regular sex distribution of RA patients and cases with cervical lesions in the sense that female cases are about three times more frequent than male cases. Female gender is a factor of poor prognosis of the disease.

**TABLE I**

Incidenc and prevalence in the study group

<table>
<thead>
<tr>
<th>Year</th>
<th>2013</th>
<th>2014</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of RA patients</td>
<td>46</td>
<td>61</td>
<td>107</td>
</tr>
<tr>
<td>RA with cervical damage - new cases</td>
<td>6</td>
<td>9</td>
<td>15</td>
</tr>
<tr>
<td>RA with cervical damage - reappraisal</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Incidence of cervical damage in RA patients</td>
<td>13.33%</td>
<td>20.00%</td>
<td>33.33%</td>
</tr>
<tr>
<td>Prevalence of cervical damage in RA patients</td>
<td>17.39%</td>
<td>14.75%</td>
<td>32.14%</td>
</tr>
</tbody>
</table>

54.4% of the study group patients were from urban areas, possibly explained by the higher medical visit rate of the urban group. The values related to the duration (in years) of RA were dispersed, ranging from 0 to 35 years of disease, most patients (64.5%) being in the group with a duration of less than 5 years (table II).

**TABLE II**

Distribution of the study group according to the duration of the disease

<table>
<thead>
<tr>
<th>Years</th>
<th>&lt; 5</th>
<th>5-10</th>
<th>10-15</th>
<th>15-20</th>
<th>&gt;20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients in the study group (%)</td>
<td>61.31</td>
<td>14.50</td>
<td>5.60</td>
<td>3.40</td>
<td>4.40</td>
</tr>
</tbody>
</table>

The study group patients were aged over 45 years and cervical lesions were present in patients with a duration of the disease of at least 10 years in cases with onset before the age of 65 and occurred early in patients with senile RA. Damage to the cervical spine was higher in elderly patients with a longer duration of the disease and especially in the more severe types of disease.

Specific symptoms occurred gradually in most patients from a period of several months to several years. The dominant symptom was joint pain exacerbated at night associated with prolonged morning stiffness and swelling of various joint areas that have led to functional impairment, the higher, the more regions were affected by arthritis. Several clinical onset forms were observed, i.e. monoarticular, oligoarticular, polyarticular. Other onset forms were extraarticular manifestations such as muscle pain, tendonitis or ductal syndromes (especially carpal tunnel syndrome). The polyarticular type of disease onset with rapid development of deformities and joint ankyloses was mostly seen in patients with cervical damage.

**TABLE III**

Distribution of general signs in RA patients

<table>
<thead>
<tr>
<th>General signs</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthenia, fatigue</td>
<td>97</td>
</tr>
<tr>
<td>Loss of appetite</td>
<td>45</td>
</tr>
<tr>
<td>Transient arthralgia</td>
<td>91</td>
</tr>
<tr>
<td>Raynaud’s syndrome, acrocyanosis</td>
<td>49</td>
</tr>
<tr>
<td>Weight loss</td>
<td>12</td>
</tr>
<tr>
<td>Irritability</td>
<td>83</td>
</tr>
<tr>
<td>Depression, insomnia</td>
<td>85</td>
</tr>
</tbody>
</table>
Cervical spine lesions in rheumatoid arthritis patients

The main clinical manifestations were pain, swelling, morning stiffness and functional discomfort (table III).

Inflammatory cervicalgia and cervical stiffness was present in all study group patients studied, but the elderly with senile RA, aged 65 years, cervicalgia showed also degenerative changes. Signs suggesting the localization of the rheumatoid process at the cervical level in the study group were found in varying proportions (tab. IV).

The dominant element was cervical and cervical-cephalic pain associated with stiffness of the extensor, trapezius or sternocleidomastoid muscle. Almost half of the patients showed a poor posture of the cephalic extremity with slight anteflexion.

16% of patients had severe neurological damage caused by cervical changes, while the altered sensitivity seen in the dermatomes of the cervical plexus roots was frequent.

**TABLE IV**

<table>
<thead>
<tr>
<th>Clinical signs of cervical damage in rheumatoid arthritis</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scalp tenderness</td>
<td>66%</td>
</tr>
<tr>
<td>Tenderness of the spinous apophyses, cervical chain</td>
<td>95%</td>
</tr>
<tr>
<td>Altered sensitivity of the cervical region and upper limbs</td>
<td>45%</td>
</tr>
<tr>
<td>Muscle tenderness</td>
<td>74%</td>
</tr>
<tr>
<td>Muscle weakness in regional muscles and upper limb end</td>
<td>54%</td>
</tr>
<tr>
<td>Fasciculations</td>
<td>1%</td>
</tr>
<tr>
<td>Transient hearing loss</td>
<td>3%</td>
</tr>
<tr>
<td>Sensory ataxia</td>
<td>1%</td>
</tr>
<tr>
<td>Sensitivity of the carotid sinus</td>
<td>9%</td>
</tr>
</tbody>
</table>

The study of global and segmental mobility of the cervical spine showed a severe limitation of movements in the upper region in 37% of the cases and an overall mobility limitation in 41% of the patients.

**TABLE V**

<table>
<thead>
<tr>
<th>Extraarticular manifestation</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subcutaneous nodules</td>
<td>39.7</td>
</tr>
<tr>
<td>Tenosynovitis</td>
<td>31.0</td>
</tr>
<tr>
<td>Myopathy</td>
<td>36.3</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>6.1</td>
</tr>
<tr>
<td>Rheumatoid lung</td>
<td>24.3</td>
</tr>
<tr>
<td>Pleurisy</td>
<td>0.93</td>
</tr>
<tr>
<td>Pulmonary fibrosis</td>
<td>7.5</td>
</tr>
</tbody>
</table>

In patients with severe cervical damage, extraarticular manifestations included changes in the skin, subcutaneous tissue and juxtaarticular tissues, respiratory and cardiovascular systems (table V).

Skin manifestations – 39.7% subcutaneous nodules were seen in patients with cervical lesions. This was correlated with a relatively long duration of the disease and with severe forms of the disease. They were associated with seropositive forms of the disease and with other systemic manifestations such as rheumatoid lung.

Nonspecific cutaneous manifestations (pale skin, hypopilosity, dull brittle nails, hyperpigmentation) were also seen. Some of them express the inflammatory anemia caused by the long evolution of the disease in the selected patients.

Skeletal muscles and tendons - the study group patients often showed myalgia (in the shoulder girdle) and muscle weakness,
clinically expressed as muscle atrophy caused by inactivity, secondary to the joint pain of the disease. The anatomo-pathological basis was represented by degenerative lesions of muscle fibers.

**Respiratory manifestations** - multinodular rheumatoid lung, radiographically shown, clinically manifested as dry cough, moderate dyspnea and intermittent hemoptysis were present in 14 (58.3%) patients. Pleurisy was observed in 1 (0.93%) patient; as the pleurisy was quantitatively reduced, it was reabsorbed following appropriate antibiotic and anti-inflammatory therapy.

**Cardiovascular manifestations** - difficult to assess, given that patients in the study group were over 45 years old and physiological changes of involution are closely intricated with pathological changes that cannot be properly classified. Chest pain, dyspnoea on exertion or tachycardia are difficult to interpret. Arterial hypertension was present in 63% of patients.

**Digestive manifestations** - clinically, 14 (35%) patients had hepatomegaly at baseline. Following administration of NSAIDs, 31% of patients had epigastralgia and heartburn. Gastric or gastroduodenal ulcer, radiographically shown, was present in 3 (15.00%) patients.

**Neurologic manifestations** - compressive neuropathies, such as carpal tunnel syndrome, were found in 9 (45%) patients and resulted from existing periarticular changes. The manifestations were more pronounced in the dominant limb. Damaged brachial plexus roots gave rise to radicular syndromes characterized by pain, paresthesia, hypoesthesia in the corresponding dermatome and the decrease of osteotendon reflexes. A significant percentage of patients showed this manifestation. These clinical changes were present mainly in patients with specific cervical radiological changes, such as subaxial dislocation. Cervical-brachial neuralgia was seen in 7 (6.54%) patients.

Facial paralysis was observed in 2 (10%) patients, probably caused by the damage of the spinal nucleus of the trigeminal nerve, as patients had atlantoaxial dislocation. Several patients showed symptoms of dysphagia and dysphonia, which can be attributed to altered hypoglossal nerve (XII), vagus nerve (X) and glossopharyngeal nerve (IX). By using the Red-lung-Johnell method, radiological changes such as vertical atlanto-axial dislocation were seen in these patients.

**Renal manifestations.** The research showed that 2 (10%) patients had a proteinuria of 1.5 g / 24 hours, one patient having a proteinuria of 1g / 24 hours. A high frequency of urinary tract infections was seen in women (38.6%) due to associated risk factors found in RA patients with decreased immune defense, hormonal changes, frequent hospitalizations and consumption of NSAIDs.

**Hematologic changes** - anemia was present in 17 (8.00%) patients (out of the total number of 20 patients). The most common cases showed normocytic and hypochromic anemia, as well as and hyposideremia; serum Fe values were low in some patients. The anemia seen in these patients can be attributed to the long evolution of the inflammatory disease and it is associated with iron absorption disorders, moderate decrease of erythropoiesis, hemolysis and blood loss.

3% of the study group patients had clinical manifestations of diplopia that might be caused by the damage of the abducens nerve (VI).

The following laboratory parameters and their correlations were followed in patients with cervical lesions caused by RA: biological inflammatory syndrome,
immunological changes - rheumatoid factors, standard radiological examination - flexion / extension; CT and MRI were used in patients with neurological symptoms.

Inflammatory syndrome - the assessment of ESR and CRP values, the blood count were useful for both diagnosis and the survey of the progression of the disease by determining their dynamics.

Anterior atlanto-axial dislocation was the most common form of cervical instability (65% of study group patients). Combined dislocations such as anterior atlanto-axial dislocation associated with the subaxial dislocation were far less numerous, 7 (35%) patients, as compared with 13 (65%) patients with anterior atlanto-axial dislocation. Other forms of dislocations were much less common.

The radiological examination has shown fractures of the odontoid in 1 patient; erosions of the interapophyseal joint in 4.2%; odontoid secondary osteosclerosis in 2.5%; the appearance of diffuse osteoporosis was associated with about 47% of the total number of patients. CT was performed in 4 patients and MRI in 3 patients.

**DISCUSSIONS**

*Anterior atlanto-axial subluxation* is the most frequent classical involvement of cervical spine in RA. The profile radiography of the cervical spine, C1-C2 - centered, shows a distance of more than 3 mm between the posterior edge of the anterior arch of the atlas and the anterior edge of the odontoid apophysis. The anterior subluxation of the atlas to the axis is possible due to the rupture or distension of the transverse and cruciform ligaments, following the chronic inflammation of the atlanto-axial joint (6, 2).

Subluxation causes the narrowing of the retro-odontoid part of the spinal canal and the compromise of the neuraxis at the bulbo-medullary junction.

Clinically, the alteration of this joint can be completely asymptomatic, with a latent evolution, or may lead to severe cervical pain, high and posterior with inflammatory rhythm. Neurological complications are quite rare and include Lhermitte’s sign or neurological signs of the upper limb: sensory disorders, movement disorders (3,4).

The literature reports also cases of sudden death (5), mostly following road accidents or during intubation for general anesthesia. Therefore, the arthritic condition must be systematically investigated before any surgical intervention (4,8).

Our findings showed also that the positive diagnosis is based on radiological examination (profile radiography of the cervical spine, C1-C2-centered, dynamic, flexion and extension) and on CT examination (a posterior detachment of the odontoid apophysis related to the anterior arch of the atlas is observed on the cross sections of the spine) similar to the reports of other authors (11,12).

The cervical spine damage in RA might involve also the middle and lower spine under the form of posterior interapophyseal arthritis. This could cause joint slipping or subluxations between vertebral bodies. These lesions are easily noticed on dynamic flexion / extension radiographs. These areas of the cervical spine are affected in 15% of the cases. The results concur with literature data already mentioned (13,14).

**CONCLUSIONS**

Our study showed that cervical spine lesions lead to increased physical pain, with local radicular bone marrow involvement that aggravates the functional deficit, worsening the vital prognosis.

The main disorder of the cervical spine
damaged by rheumatoid arthritis is cervical instability. The damage of the cervical segment caused by RA occurs late in the evolution of the disease, when destructive cartilage and bone lesions, axial deformities, extensive muscular atrophy and, in some cases, even fibrous or bony ankylosis are present.

The dominant symptom of cervical spine damage was pain associated with limited joint mobility, muscle stiffness and poor posture.

REFERENCES