

Neurophysiologic Study in Patients With Rheumatoid Arthritis With Atlantoaxial Subluxation

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Introduction: Radiological studies show that 80% of rheumatoid arthritis (RA) patients with more than 10 years present spinal afflictions and 40% of those patients will present neurological deterioration. The somesthetic evoked potential (SEP) and the transcortical magnetic stimulation (TMS) are neurophysiologic studies that may be useful in early diagnosis of neurological damage.

Objective: To compare the results of the neurophysiologic studies (SEP and TMS) carried out on patients affected with RA without neurological clinic, with or without atlantoaxial subluxation (AAS), and in this way evaluate the efficacy of early diagnosis of the affection of the spinal medulla by electrodiagnostic methods.

Material and methods: Cases and controls study that included 29 patients affected with RA of more than 3 years evolution. All of the patients had 2 electrophysiological techniques carried out on them: SEP and TMS in the neurophysiologic laboratory.

Results: Twenty-nine patients participated in the study, of which 21 were females and 8 males. In the group affected with AAS 2 patients presented anomaly in the SEP (11.7%) and 7 in the TMS (41.1%). In the group without AAS 2 presented an altered TMS (16.6%), but no alteration in the SEP. No patient affected or not with AAS, presented alteration of both electrophysiological tests. No significant differences were found between the positivity of the RF or the presence of erosions and the affection of the atlantoaxial joint. No differences between the age of outset or years of evolution and the AAS.

Conclusions: In our study patients with AAS showed a greater trend towards the presence of alterations in the electrophysiological studies than the patients without AAS.

Key words: Rheumatoid arthritis. Cervical spine. Neurophysiologic studies.

Estudio neurofisiológico en pacientes con artritis reumatoide y subluxación atloaxoidea

Introducción: Los estudios radiológicos demuestran que el 80% de los pacientes afectos de artritis reumatoide con más de 10 años de evolución presentan afectación cervical y que el 40% de ellos presentaba deterioro neurológico. Los potenciales evocados somestésicos (PES) y la estimulación magnética transcortical (PEM) son estudios neurofisiológicos que pueden ser útiles para un diagnóstico precoz de daño neurológico.

Objetivo: Comparar los resultados de los estudios neurofisiológicos (PES y PEM) practicados a pacientes afectos de artritis reumatoide sin clínica neurológica, con y sin subluxación atloaxoidea (SAA), y valorar la eficacia del diagnóstico precoz de la afección de la médula espinal por métodos de electrodiagnóstico.

Material y métodos: Se trata de un estudio de casos y controles que ha incluido a 29 pacientes afectos de artritis reumatoide de más de 3 años de evolución. A todos los pacientes se les han practicado 2 técnicas electrofisiológicas: PES y PEM en el laboratorio de neurofisiología y se han separado los dos grupos según presentaran o no SAA.

Resultados: Participaron en el estudio 29 pacientes, 21 mujeres y 8 varones. En el grupo con SAA, 2 pacientes presentaron una anomalía en el PES (11,7%) y 7 en la PEM (41,1%). En el grupo sin SAA 2 presentaron una PEM alterada (16,6%) y ninguno alteración en el PES. Ningún paciente, afecto o no de SAA, presentó alteración de ambas pruebas electrofisiológicas. No se encontraron diferencias significativas entre la positividad del factor reumatoide o la presencia de erosiones y la afectación de la articulación atloaxoidea. Tampoco se encontraron diferencias entre la edad de presentación o los años de evolución y la SAA.

Conclusiones: En nuestro estudio los pacientes con SAA mostraron una mayor tendencia a presentar alteraciones en los estudios neurofisiológicos que los pacientes sin SAA.

Palabras clave: Artritis reumatoide. Columna cervical. Estudios neurofisiológicos.

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Introduction

The cervical column is commonly affected in rheumatoid arthritis (RA).¹⁻³ The most common affection is atlantoaxial subluxation (AAS) that can present as 1 of several types: anterior subluxation, which is most frequent, vertical, lateral, and posterior.³ Prevalence of AAS varies from 19% to 70% of RA affected patients,¹⁻⁴ and can present itself from the onset. It is related to disease activity and erosions in the peripheral joints and with a reduction in bone mass.^{2,3,5-7} Radiological studies demonstrate that 80% of patients with RA have cervical affection at 10 years and 40% of them will have a neurological deficit.⁸

Clinical manifestations of AAS are cervical pain, rigidity, reduction in mobility as well as motor, and sensitive deficits that can be caused both by mechanical compression of the spinal cord and by vascular alterations.^{1,9} Mortality increases in patients with RA and cervical column affection, though this is rarely the cause of death.^{8,10,11}

A simple x-ray of the cervical column, mainly in maximal flexion and extension on the lateral projection, is the most frequently employed diagnostic method to see a reduction in space.¹² Radiographs can show no pathologic signs when there are neurological alterations or, on the contrary, a radiograph that shows an important AAS can appear in a patient without spinal cord affection.^{13,14}

Magnetic resonance (MR) can measure with a higher degree of certainty the diameter, and can indicate the etiology of the compression (ie, if there is pannus).^{13,14} The affection of the spinal column detected through MR is a predictive factor for the deterioration of myelopathy in patients with RA, even in the absence of clinical signs.¹³ Somatesthetic evoked potentials (SEP) and transcortical magnetic stimulation (TMS) are neurophysiological studies that can be useful for an early diagnosis of neurological damage. SEP study sensitive conduction that occurs mainly through the posterior columns and TMS studies motor conduction on the anterolateral columns. Normality of both tests signals to an integrity of the spinal cord, and have been shown to prove neuronal damage in patients with normal imaging testing.^{12,15}

In the present study we compare the results of neurophysiological testing practiced on patients with RA, with or without AAS, with no neurological clinical symptoms or signs, thus evaluating the efficacy of early diagnosis of spinal cord affection by electrodiagnostic methods.

Material and Methods

Design: it is a descriptive study of a series of patient cases with RA of more than 3 years since onset; in this study we compared the characteristics of patients with AAS and those without it.

Patients were selected from the rheumatology outpatient clinic who complied with the American College of Rheumatology 1987 criteria for the classification of RA. Patients were included as cases if they came to their visits in a regular manner and had a known diagnosis of AAS; for controls, patients who had RA but not AAS were included. All patients underwent a lateral cervical column radiograph. Patients in the study did not present motor deficits, alterations in the cranial nerves nor severe sensitive alterations or sphincter dysfunction.

None of them presented a plantar extensor reflex. All patients belonged to group I of the Ranawat classification (Table 1).

They were divided into 2 groups according to whether they presented AAS or not. The diagnosis of AAS is established when the distance between the anterior border of the odontoid process and the posterior surface of the anterior arch of the atlas, measured on a lateral, flexed cervical column radiograph, is ≥ 3 mm. All of the patients were submitted for a lateral flexed cervical column radiograph under the same technique. The diagnosis of AAS was established by consensus by at least 2 of the researchers.

For measurements, data was collected concerning the patients gender, age at onset of RA, and time since onset of disease; rheumatoid factor was measured through nephelometry and was considered positive when 20 U/mL or higher in at least 1 determination, at the start or during the evolution of RA.

The presence of radiologically evident erosions was determined through a maximal flexed radiograph of the cervical column, as well as x-rays of the hands and feet; RA was considered to be erosive when at least 1 erosion was seen in a hand or feet x-ray.

All of the patients underwent 2 electrophysiological techniques: SEP and TMS in the neurophysiology lab; the same neurophysiologist carried out all explorations. SEP consists on percutaneous stimulation of the median nerve at the wrist and the detection in the contralateral parietal area (C3-C4, 10-20 system) through surface electrodes (Fz reference) with an average of more than 500 stimuli in 2 series. TMS is done through magnetic stimulation with simple spade Magstim 200 with the detection of ulnar territories (hypothenar) on both sides.

TABLE 1. Ranawat Classification

I. Patients without neurological deficits
II. Patients with paresthesias, hyper-reflexia, and subjective sensation of loss of strength
III. Patients affected by a motor deficit
IIIA. Possibility for moving
IIIB. Impossibility for moving

Determination of central motor conduction was done from an F wave method.

For the statistical analysis a SPSS for windows, version 11 was employed.

To determine the effect of each variable we employed non-parametric testing, Mann-Whitney *U* test for quantitative variables and χ^2 Fisher's exact test for qualitative type variables.

Results

Twenty-nine patients participated in the study, 21 women and 8 men; 12 (9 women and 3 men) did not present AAS and 17 (12 women and 5 men) did.

Of patients with AAS, 11 (64.7%) had erosions, and 12 (70.5%), positive rheumatoid factor; of those without AAS, 8 (66.6%) presented erosive RA and 7 (58.3%) were seropositive (Table 2).

The mean distance (standard deviation) of AAS was 4.9 (1.7) mm and a range of 3-8 mm. Time since onset of RA oscillated between 3 and 35 years; on the other hand, age at onset went from 18 to 66 years.

The results from the electrophysiological testing were as follows: in the group with AAS, 2 (11.7%) patients presented an anomaly in SEP and 7 (41.1%), in TMS; with the particularity that the 2 patients which had an altered SEP were male and the 7 with the diminished TMS were women. In the group without AAS, 2 (16.6%) patients had an altered TMS and none had alterations in SEP. Therefore, 9/17 (52.9%) patients in the group with a radiological alteration of the cervical column had electrophysiologic data compatible with cord damage, while only 2/12 (16.6%) patients of the other group had them (*P*=.06). No patients, with or without AAS, had alterations in both tests.

No significant differences between those positive for rheumatoid factor (RF) or the presence of erosions and atlantoaxial joint abnormalities were found.

There were no differences either between the age at onset or years since onset and AAS. As for the group of patients with electrophysiological abnormalities (SEP and TMS), there were differences, with no statistical significance, regarding gender, because 2 of the patients with an alteration in SEP presented AAS and were male (40% of males with AAS), something that was not altered in any woman. No differences were found between the neurophysiological alterations, years since onset of RA, age at presentation, positivity for RA, and the presence of erosions. No significant differences have appeared between the distance of the AAS and the neurophysiological manifestations

Discussion

Because it is a study with a limited number of patients, results must be interpreted with caution, though they are similar to those described previously.

In our study, patients with AAS had a larger tendency to alterations of the neurophysiological studies than patients without AAS. SEP was normal in all of the patients without AAS and was altered in 2 of the patients with AAS. A slowing of the motor conduction was shown in 7 patients with AAS and also in 2 without AAS. No patients had both electrophysiological tests with alterations. All of our patients belonged to group I of the Ranawat classification; group II and beyond is associated with neurological symptoms that can indicate an alteration in the spinal cord; therefore, patients in group I are those that can benefit more from an early diagnosis. The study shows that 52.9% of patients with AAS have some neurophysiological alteration, compared to 16.6% of the group of patients without AAS; this difference is significant. By carrying out 2 electrophysiological techniques we increased the sensitivity in diagnosis of neurological affection by AAS, because no patients presented alterations in both tests, though it is still to be determined if normality in both tests eliminated that possibility.

Some studies show neurophysiological testing as methods for the early detection of cervical neurological affection due to RA.^{12,15,16} It is important to reach an early diagnosis because clinical neurological signs appear late in the course of the disease and can overlap with other RA manifestations (interosseus muscle atrophy, peripheral neuropathy, hand rigidity, etc). We must keep in mind that all of the patients were asymptomatic at the moment of the study, both in the anamnesis of pain as in the physical examination directed to the detection of neurological deficits, both motor and sensitive.

We know that MR is the most specific method to evaluate cervical morphology, mainly in the spinal cord, and is very

TABLE 2. Characteristics and Results From the Study*

Characteristics	AAS (12)	Without AAS (17)	<i>P</i>
Women	12 (70.6%)	9 (75%)	.98
Erosions	11 (64.7%)	8 (66.6%)	.61
Rheumatoid factor	12 (70.5%)	7 (58.3%)	.69
Years with rheumatoid arthritis	12.9 (7.5)	9.5 (5.2)	.17
Age at onset	50.4 (12.6)	52.4 (8.2)	.79
SEP altered	2 (11.7%)	0	.49
TMS altered	7 (41.1%)	2 (16.6%)	.23
Total altered	9 (52.9%)	2 (16.6%)	.06

*Values expressed as mean (standard deviation) for continuous variables or n (%) for categorical variables. TMS indicates transcortical magnetic stimulation; SEP, somesthetic evoked potentials; SAA, atlantoaxial subluxation.

sensitive to detect abnormalities in these zones,¹⁴ though it does not study the functionality of the neuronal pathways. Other diagnostic tests of cord lesions due to AAS can be tridimensional computed tomography of the cervical column¹⁷ and echo-Doppler of the supraaortic trunks in positions of extreme movement of the cervical column.¹⁸ Electrophysiologic tests do not substitute MR, and it is possible for both tests to be complementary and provide a better evaluation of the neuronal pathways, because one must take into account the fact that pathologic alterations can appear both in x-rays as in MR (including lesions of the spinal cord) without functional alterations, or viceversa; therefore, the radiological evaluation can be complemented by electrophysiologic tests.^{12,14,15}

Neurological alterations can present themselves even when not caused by a subluxation (ie, spinal cord vasculitis, granulation tissue, synovial pannus, etc).^{14,16,18,19}

An early diagnosis is desirable because treatment, both conservative and surgical, can improve the neurological clinical signs and reduce progression.^{9,18,20-23}

We found no significant differences regarding gender, erosions, age at onset, years since onset of RA (which was discreetly higher in AAS, without achieving significance). Though we know that patients with AAS have more erosions and a higher prevalence for RF seropositivity than those without AAS^{2,3,5-7}; these differences were non significant in our study.

The difference with other studies is owed, certainly to the fact that our group of patients was very small and the design of the study did not set out to characterize patients according to their cervical pathology; for this objective, a larger sample is needed. We consider that the homogeneity of both groups, regarding age, age at onset of RA and years since onset, positivity to RF, and the presence of erosions, discards interference with other variables, besides there existing AAS or not.

We found no relationship between the neurophysiological alterations and the distance of the AAS. Some authors have shown similar data of neurophysiological alterations in AAS affected and non affected patients,¹⁹ in contrast to others who do show a higher prevalence in patients with AAS,²⁴ making the neurophysiologic tests for the diagnosis of AAS more specific, though less sensitive (similar to our results).

It is interesting to note that both of the patients that had an alteration in the SEP were male, because this fact has not been described previously though it could be due to the sample size or something random.

In summary, we believe the fact of the appearance of neurophysiologic alterations in patients with AAS and RA without any clinical signs to be interesting. The difference in the prevalence of neurophysiological alterations between patients with and without AAS is clear, and it cannot be explained by other clinical or radiological variables. Though the sample is limited and no definite conclusions can be extracted, the results are

in agreement with most of the previous studies.^{12,14} The sum of both studies seem to increase their diagnostic power, mainly due to the fact that there are no patients that have pathology in both tests.

Because we did not do a MR to these patients, we do not know the correlation between this and complementary testing, because RM is the best imaging technique to define a possible anatomical on the cervical cord in patients with RA.

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