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Original article

Sensory disturbance and polyneuropathy in rheumatoid arthritis patients with foot deformity

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ABSTRACT

Introduction: Our aim in this study was to present the results of sensory evaluation tests and electrophysiological evaluations in rheumatoid arthritis (RA) patients with foot deformity and to determine their relation with general health status and lower extremity functionality.
Materials and methods: Fifty-one patients with RA diagnosis and foot deformity were included in the study. Demographic and disease characteristics of the patients were recorded, and a detailed neurological examination was performed. Superficial sensation, pain, heat, vibration, and two-point discrimination sensation were evaluated in each foot, and their sum was used to determine the sensory deficits index (SDI) of 0–10. The presence of polyneuropathy was evaluated with electrophysiological methods. The Health Assessment Questionnaire and mobility and walking subscales of the Arthritis Impact Measurement Scales-2 were used to assess general health status and lower extremity functionality, respectively. According to the sensory examination and electromyography results, patients were compared in terms of their general health status and lower extremity functional status.
Results: Sensory disturbance was detected in 39 patients (74%) during the examination; however, 27 patients (52.9%) had polyneuropathy determined electrophysiologically. In patients with sensory deficits, statistically significant deterioration was detected in general health and foot functionality, including mobility and walking, when compared to patients with a normal sensory evaluation.
Conclusions: Even in the presence of normal electrophysiological tests, sensory dysfunction alone seems to be associated with severe disability in general health status and foot functionality when compared to patients with a normal sensory examination.

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Perturbações sensitivas e polineuropatia em pacientes com artrite reumatoide com deformidade do pé

Palavras-chave:
Artrite reumatoide
Pé
Polineuropatia
Aspecto funcional

RESUMO

Introdução: O objetivo deste estudo foi apresentar os resultados dos testes de avaliação sensitiva e exame eletrofisiológico em pacientes com artrite reumatoide (AR) com deformidade do pé e determinar a sua relação com o estado geral de saúde e aspecto funcional dos membros inferiores.

Materiais e métodos: Foram incluídos no estudo 51 pacientes com diagnóstico de AR e deformidade do pé. Foram registradas as características demográficas e da doença de cada indivíduo, e foi realizado um exame neurológico detalhado. Foi avaliada a sensibilidade superficial, sensibilidade dolorosa, sensibilidade térmica, sensibilidade vibratória e aplicado o teste de discriminação de dois pontos em cada um dos pés, e a soma dos escores foi usada para determinar o índice de déficits sensitivos (IDS) de 0-10. A presença de polineuropatia foi avaliada com métodos eletrofisiológicos. Foi utilizado o Health Assessment Questionnaire e as subescalas mobilidade e deambulação da Arthritis Impact Measurement Scales-2 para avaliar o estado geral de saúde e o aspecto funcional de membros inferiores, respectivamente. De acordo com os resultados dos exames de eletromiografia e de sensibilidade, os pacientes foram comparados em relação ao seu estado geral de saúde e estado funcional de membros inferiores.

Resultados: Foram detectados distúrbios sensitivos em 39 pacientes (74%) durante o exame; contudo, 27 deles (52,9%) tinham polineuropatia determinada eletrofisiologicamente. Em pacientes com déficits sensitivos, foi detectada deterioração estatisticamente significativa no estado geral de saúde e no aspecto funcional do pé, inclusive na mobilidade e deambulação, quando comparados aos pacientes com uma avaliação sensitiva normal.

Conclusão: Mesmo na presença de testes eletrofisiológicos normais, a disfunção sensitiva isolada parece estar associada a incapacidade grave no estado geral de saúde e no aspecto funcional do pé em comparação a pacientes com um exame sensitivo normal.

Introduction

Rheumatoid arthritis (RA) is a chronic, systemic and inflammatory disease with involvement of the peripheral joints, and its etiology cannot be understood completely despite the many new developments. It causes joint destruction, decreased life quality and shortened life expectancy.[1]

The joints of the hand are the most frequent and initially affected in arthritis; thus, studies in the literature have focused mostly on hand deformities and hand disabilities. While foot involvement at the onset of the disease has been reported in 16–20% of patients, this ratio may increase to approximately 95% over the course of the disease.[2,3]

Synovial hypertrophy and capsular tension generated by hyperplasia, ligamentous laxity, muscular imbalance, and ultimately joint subluxation and dislocation play a role in the development of foot deformities in RA. Further, with the direct effect of inflammation, destruction occurs in the cartilage and pericapsular structures.[4] Due to all these changes, the loading on joints causes different deformities and constitutes a severe disability in the patient's mobility and functional independence.[5,6]

Nervous system involvement in RA is often in the form of peripheral involvement.[7] Entrapment neuropathies, mononeuropathies, and sensory and sensorimotor axonal polyneuropathies are considered in this context. In clinical practice, superficial touch, pain, heat, and vibration senses with the two-point discrimination test, muscle strength measurement, deep tendon reflexes tests, and electrophysiological methods are used for the assessment of the peripheral nervous system. Studies investigating the presence of neuropathy in RA patients have frequently used electrophysiological methods in their evaluations.[7–10]

Although sensory evaluation tests are often subjective tests, in recent years, it is reported that the involvement of the other nerve fibers can be shown with these tests.[11]

While in some studies they were reported that a correlation between deterioration in quality of life and functionality, and foot complaints in RA,[12,13] there is no study comparing the sensory examination and electrophysiological assessment findings or evaluating the relationship between these and the patient's general health status and lower extremity functionality.

Foot deformities in patients may be only visible part of the iceberg and much more its below. Even if effective treatment was given for the patient's deformity, functionality and quality of life may not be enough improvement due to nervous system involvement.

We thus aimed in this study to present the results of the electrophysiological evaluation and sensory evaluation tests and to determine their relationship with lower extremity

functionality and general health status in RA patients with foot deformity.

Material and methods

Study population

This study was conducted by the Physical Medicine and Rehabilitation clinic in Ankara Diskapi Yildirim Beyazit Education and Research Hospital in Ankara, Turkey.

Fifty-one patients aged 35–65 years with foot deformity and diagnosed as RA according to the American College of Rheumatology (ACR) 1990 classification criteria were included in this study.

Only housewives and female patients with no salaried employment were included because of foot involvement in RA was reported as 89–90% in almost equal rates in both genders[14] and to ensure homogeneity in terms of functional status of patients.

Exclusion criteria of the study were as follows: age under 16 years and over 65 years, male gender, lower extremity trauma and/or history of operation, diabetes mellitus, acute and/or chronic liver and kidney disease, severe heart failure, hypo/hyperthyroidism, amyloidosis, malignancy, vitamin B12 deficiency, additional connective tissue disease, such as Sjögren's syndrome, and/or vasculitis symptoms, previously diagnosed peripheral nervous system involvement, and positive pathological reflexes. Also excluded from the study were patients using more than 7.5 mg corticosteroid over the last six months or biologic therapy.

Our patients on biologic therapy represented late-period disease and also fit other exclusion criteria, such as mostly high-dose corticosteroid use and diabetes mellitus.

At baseline, patients were informed about the study and their written informed consent was obtained. The approval of the hospital's local ethics committee was received before the study. The study was conducted in accordance with the Helsinki Declaration.

For the evaluation of demographic and disease characteristics of the patients, age, education, marital status, duration of the disease and of morning stiffness, medications used, number of tender and swollen joints, quality of life (QOL) level, erythrocyte sedimentation rate (ESR) (mm/h), and rheumatoid factor (RF) (IU/ml) were recorded. Disease activity score-28 (DAS-28) was calculated by using tender and swollen joint counts, QOL level assessed on the visual analog scale of 0–100 mm, and ESR.

A detailed neurological examination of patients was performed. On the lower extremity sensory assessment, superficial sensation, pain, heat, vibration, and two-point discrimination senses were evaluated in each foot, and with the sum of these, the sensory deficits index (SDI) of 0–10 was obtained. For superficial senses, 5.07 Semmes-Weinstein monofilament was applied perpendicular to the plantar surface of the distal phalanx of the foot thumb. Pain sensation was evaluated with needle insertion into the plantar surface of the distal phalanx of foot thumb. The patient was queried regarding distinction between blunt and sharp tip, and in the presence of correct answers to 8 of 10 questions, pain sensation was accepted as preserved. Ice cubes were applied for 3 s to the plantar surface of the distal phalanx of foot thumb to determine heat sensation. Vibration sensation was evaluated on the dorsal surface of the metatarsal joint of foot thumb with a 256 Hz tuning fork. Two-point discrimination test was evaluated as static. Distance between the two needles applied to the plantar side of the distal phalanx of the foot thumb less than 0.5 cm was evaluated as normal.

Electrophysiologic tests

Polyneuropathy in patients was evaluated with Medelec Synergy 10-channel electroneuromyography (ENMG) (Oxford, U.K.) device and the protocol described by Oh et al.[15] Accordingly, bilateral sural sensory nerve conduction studies and bilateral peroneal and tibial nerve motor conduction studies were carried out. For identification of the polyneuropathy, right median, ulnar motor and sensory nerve conduction studies were added. Bilateral tibial and common peroneal nerve F waves were studied. Entrapment neuropathy was ruled out by applying the lateral and medial plantar nerve conduction studies in patients without polyneuropathy. To identify the presence of polyneuropathy, pathophysiological assessment was performed as axonal or demyelinating at the affected motor and sensory nerve fiber.

Clinic tests

For the assessment of the functional status of patients, the Health Assessment Questionnaire (HAQ) was used.[16]

Mobility and walking subscales of the Arthritis Impact Measurement Scales-2 (AIMS-2) were used for assessing lower extremity functionality.[17] Scoring was from 0 to 10, with 0 indicating the best and 10 indicating the poorest health status.

Comparisons

Patients were divided into groups according to SDI scores and electrophysiological evaluation as SDI score 0 (group 1a), SDI score $\geq$1 (group 1b), normal electrophysiological evaluation (group 2a), and polyneuropathy (group 2b). Groups were compared with HAQ in terms of their general health status and with the mobility and gait subscales of AIMS-2 for the assessment of their lower extremity functional status.

Statistical analysis

For data analysis, the Statistical Package for the Social Sciences 15.0 (SPSS Inc., USA) program was used. Descriptive statistics were displayed with chi-square test for continuous variables as mean $\pm$ standard deviation and median and for nominal variables as a percentage. Shapiro–Wilk test was used to examine whether the continuous variables were distributed normally. Because there are non-normally distributed continuous variables, the significance of differences between the groups with respect to the variables was investigated with

Mann–Whitney *U*-test. A value of $p < 0.05$ was considered statistically significant.

Results

The average age of the 51 patients in the study was 54.0 years, disease duration was 13 years, and morning stiffness duration was 30 min. The distribution of demographic and disease characteristics of the patients are shown in Table 1.

The mean number of foot deformities was 8.00 (7.49 ± 4.24). There were 17 patients (33.3%) with hammer toe, 15 (29.4%) with claw toe, 25 (49%) with cock-up deformity, 32 (62.7%) with hallux valgus, 21 (41.2%) with metatarsophalangeal subluxation, 11 (21.6%) with ankle contracture deformity, 29 (56.9%) with pes planus, and 6 (11.8%) with pes cavus deformity.

The results of the sensory examination are presented in Table 2.

Sensory disturbance was detected in 39 patients (76.4%). The average level of SDI was found to be 4.00. Polyneuropathy was detected in 27 patients (52.9%) with electrophysiological evaluation. In all patients, there was sensorimotor axonal polyneuropathy with sensorial predominance. At least one sensory evaluation test was impaired in all patients.

Table 1 – The distribution of demographic and disease characteristics of the patients.

	$n = 51$ mean ± SD, *n* (%)
Age (year)	54.72 ± 10.98
Education level	
Illiterate	10 (19.6)
Only literate	12 (23.5)
Primary school graduate	24 (47.1)
Secondary school graduate	3 (5.9)
High school graduate	1 (2.0)
University graduate	1 (2.0)
Marital status	
Married	42 (82.4)
Single	3 (5.9)
Divorced	6 (11.8)
Disease duration (year)	14.91 ± 9.41
Morning stiffness period (min)	74.01 ± 65.45
Drugs used	
NSAID	51 (100)
Sulfasalazine	39 (76.5)
Methotrexate	42 (82.4)
Leflunomide	12 (23.5)
Hydroxychloroquine	14 (27.5)
QOL (0–100 mm)	59.21 ± 26.00
DAS-28 score	5.50 ± 1.36
RF (IU/mL)	109.19 ± 184.69
HAQ (0–3)	1.53 ± 0.68
Mobility level (AIMS-2) (0–10)	5.27 ± 2.25
Walking level (AIMS-2) (0–10)	6.77 ± 2.61

SD, standard deviation; min, minute; NSAID, non steroidal anti-inflammatory drug; QOL, quality of life; DAS-28, disease activity score-28; RF, rheumatoid factor; HAQ, health assessment questionnaire; AIMS-2, arthritis impact measurement Scale-2.

Table 2 – The results of the sensory examination.

	Right foot ($n = 51$) *n* (%)	Left foot ($n = 51$) *n* (%)
Sensory evaluation		
Disturbance of superficial sensation	29 (56.9)	30 (58.8)
Disturbance of pain sensation	14 (27.5)	14 (27.5)
Disturbance of temperature sensation	13 (25.5)	13 (25.5)
Disturbance of vibration sensation	34 (66.7)	34 (66.7)
Disturbance of two-point discrimination sensation	16 (31.4)	15 (29.4)

The comparisons between general health status and foot functionality evaluations in patients with and without sensory deficit and also in those with and without polyneuropathy are shown in Table 3.

In patients with sensory deficits, a statistically significant deterioration was detected in general health status and foot functionality, including mobility and walking ($p = 0.044$, $p = 0.005$, $p = 0.006$, respectively) when compared to patients with a normal sensory evaluation.

There was no statistically significant difference in terms of general health status, mobility and walking functions when patients with polyneuropathy were compared to patients with normal electrophysiological findings ($p = 0.871$, $p = 0.532$, $p = 0.866$, respectively).

Discussion

In patients with RA, several extra-articular systems, including the nervous system, are involved, and more commonly, the peripheral nervous system, and these cases are reported as entrapment neuropathies, mononeuropathies, and sensory and sensorimotor axonal polyneuropathy.[7] The incidence of peripheral nervous system involvement in RA has been shown in studies to range widely, from 18% to 75%.[7–9,18–20] This wide range can be attributed to the fact that in patients without clinical neuropathy, subclinical peripheral nervous system involvement is detected during electrophysiologic studies and autopsies. In these patients, the mechanism of involvement of the peripheral nervous system is explained by the inflammation and immune complex-mediated injury of myelinated nerve fibers as well as soft tissue swelling, bone deformities, and mechanical compression due to nodules.[9] Further, comorbidities and the drugs used by these patients may cause secondary involvement of the peripheral nervous system.[7]

In RA patients with foot deformity, there is a special focus on entrapment neuropathies.[21] In older studies, polyneuropathy was often associated with the presence of vasculitis.[22] However, more recently, sensory-predominant polyneuropathy has emerged as the most frequently reported peripheral neuropathy in RA patients independent of vasculitis.[21] Additionally, in some studies, a higher rate of polyneuropathy has been observed in patients with RA compared to healthy subjects.[23,24]

Table 3 – Comparison between general health and foot function evaluation in patients with and without sensory deficit and with and without polyneuropathy.

	General health level mean ± SD	Mobility level mean ± SD	Walking level mean ± SD
Sensory examination			
Normal sensation ($n = 12$)	0.18 ± 0.72[a]	3.75 ± 1.86[a]	4.33 ± 2.38[a]
Sensory deficits ($n = 39$)	1.64 ± 0.64	5.74 ± 2.16	6.91 ± 2.68
Polyneuropathy			
Normal electrophysiology ($n = 24$)	1.52 ± 0.62	5.06 ± 2.35	6.83 ± 2.45
Polyneuropathy ($n = 27$)	1.55 ± 0.76	5.46 ± 2.18	6.70 ± 2.82

SD, standard deviation.
[a] $p < 0.05$.

Some studies have investigated the presence of polyneuropathy in RA. Disease duration, disease activity and RF positivity have been reported to be associated with neuropathic involvement, but have shown no association with foot deformities and joint damage.[7,10,23] These results are in conflict with the studies reporting much more foot deformity development in patients with long-term illness and high disease activity.[14] Therefore, the primary purpose of this study was to exclude entrapment neuropathies due to mechanical compression caused by foot deformity and to evaluate the peripheral nervous system involvement, including possible polyneuropathy, using sensory examination as well as electrophysiological methods. According to the results of our study, there was impairment in at least one of the sensory examination tests in 76.4% of patients. On electrophysiological studies, sensorimotor axonal neuropathy was found in 52.9% of patients.

In our study, the presence of polyneuropathy in RA patients was consistent with the rate of 18–90% reported in the literature.[18–20] In these studies, particularly in patients with over 2–5 years' disease duration, observed polyneuropathy was associated with disease duration, RF positivity and disease activity, irrelevant of joint deformities and radiographic damage. In our study, in accordance with reports in the literature, patients had much longer duration of disease (13 years) and higher levels of disease activity and RF levels.

In our study, disturbance in terms of polyneuropathy detected by sensory evaluation tests was much greater than the polyneuropathy (76.4%) detected by electrophysiological studies. To our knowledge, there is no study in the literature evaluating sensory tests in RA patients specifically. However, in RA patients with polyneuropathy, some studies used sensory tests including superficial touch, pain, heat, and vibration senses as well as electrophysiological assessment and reported disturbance in the sensory evaluation tests.[20,22,25,26] One other study compared electrophysiological methods and sensory evaluation tests. However, the study conducted Ajena et al.[25] reported that 12% of patients who were determined normal electrophysiologically had small fiber neuropathy.

Electrophysiological methods only examine the thick myelinated fibers, and do not show the dysfunction of unmyelinated and thinly myelinated fibers. In sensory evaluation tests, superficial touch, pain and temperature senses are conducted with unmyelinated C and thinly myelinated A delta fibers, while vibration and two-point discrimination tests are conducted with thick myelinated A beta fibers.[27] In two studies in patients with diabetes mellitus, a high correlation was reported between the vibration sense and electrophysiological methods, but it does not reflect the involvement of small fibers.[28,29] In another study comparing the electrophysiological methods and sensory evaluation tests, with the clinical examination of pain and heat senses, small fiber neuropathy can be detected in electrophysiologically normal patients.[30] This may explain why more disturbance was detected using sensory examination tests than with the electrophysiological methods in our study. Thus, we think that a limitation of our study is not verifying the possible existence of small-fiber neuropathy with a diagnostic procedure such as skin biopsy.

However, another possible cause of this result may be changes in foot sensitivity to two-point discrimination, touch, pain, and temperature senses due to hyperkeratosis in abnormal regions due to foot deformities. Studies of the feet in RA patients have reported altered pressure zones and decreased sensory sensitivity when compared to healthy subjects.[31] Another limitation is that our study did not include a quantitative gait analysis. Larger studies are needed in this regard.

It was also found in this study that general health status and foot functionality are worse in patients with sensory disturbance than in patients with a normal sensory examination, but there was no statistically significant difference between the patients with and without polyneuropathy according to ENMG.

There are no studies in the literature evaluating the relationship between disturbance in sensory tests in RA patients and general health status and foot functionality. Furthermore, the results reported in studies of RA patients with polyneuropathy are conflicting.[20,27]

In the study of Bayrak et al.[27] polyneuropathy in RA patients was associated with the general health status as assessed by HAQ, and disability was much greater in patients with polyneuropathy than in patients without polyneuropathy. On the other hand, Agarwal et al.[19] study with 108 patients reported no association between polyneuropathy and

general health status assessed by HAQ. Unlike our study, patients in those studies had a shorter duration of illness (mean 5.5 years), and the study was performed in patients without foot deformities. We believe that there is not necessarily an electrophysiological abnormality in all patients with sensory disturbances. The statistically significant difference between the patients with and without sensory disturbance in terms of general health status and foot functionality supports this prediction. As discussed above, sensory disturbance overlaps with the possibility of the presence of small fiber neuropathy; however, more comprehensive studies are needed.

Conclusion

Finally, sensory disturbance was detected in 76% of RA patients with foot deformities with sensory evaluation tests. Although those patients had electrophysiologically detected polyneuropathy, this method should not be assessed alone especially in terms of general health status and foot functionality. Further, even if electrophysiological tests are normal, it should be taken into consideration that the presence of sensory dysfunction alone may lead to severe disability in general health status and foot functionality when compared to patients with a normal sensory examination.

Conflicts of interest

The authors declare no conflicts of interest.

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