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ORIGINAL ARTICLE

From a dermatologist point of view, enthesopathy and peripheral neuropathy in psoriasis patients

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Abstract

Background: Investigating psoriasis patients' enthesopathy and peripheral neuropathy, which dermatologists often neglect.

Methods: Seventy-four psoriasis patients' lower limb entheses were evaluated by ultrasonography using Glasgow Ultrasound Enthesitis Scoring Scale (GUESS). Sensory and motor nerve conduction studies in median and ulnar nerve, motor nerve conduction research of peroneal and tibial nerves and sensory conduction study on right sural nerve was performed in 25 patients.

Results: 172 of 730 entheses had ultrasonographic enthesopathy symptoms (23.56%). Enthesopathy was substantially more common in cases involving the nail ($p = 0.004$). The frequency of enthesopathy did not change significantly between symptomatic and asymptomatic patients ($p = 0.408$). Seven of 25 patients (28%) had a pathology in nerve conduction studies. With increasing GUESS scores, bilateral ulnar and right tibial nerve distal motor latencies were shown to become longer ($p = 0.001$, $p = 0.01$, $p = 0.019$), although left ulnar nerve sensory conduction velocity got slower ($p = 0.033$).

Conclusions: Enthesopathy and peripheral nerve dysfunction were frequently observed in psoriasis patients. Dermatologists should be mindful of neuromusculoskeletal disorders in psoriasis patients.

Keywords: Psoriasis, Enthesopathy, Neuropathy, Ultrasound.

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INTRODUCTION

Psoriasis is seen in 2% of the general population, and is accompanied by arthritis in 5-30% of these cases (1). Enthesopathy is inflammation in the area where tendons and ligaments attach to bone. Even though there are studies on the frequency and characteristics of enthesopathy in spondyloarthritis, studies on the entheseal areas of psoriasis patients irrespective of the presence of arthritis are still rare (2). In those studies, psoriasis cases that lacked clinical signs of enthesitis or joint damage were found to have some sort of joint involvement with ultrasonography (USG) (3). Even though larger studies with longer follow-up periods are required in this subject, primary studies indicated that the psoriasis cases with enthesopathy involvement have a greater risk of developing psoriatic arthritis. Regarding this fact, early term diagnosis of enthesopathy presence may be of great assistance in the early diagnosis and treatment of psoriatic arthritis (PsA), a progressive joint damage condition (4). Due to this, we decided to employ Glasgow Ultrasound Enthesitis Scoring Scale (GUESS) in addition to clinical diagnosis to examine entheseal regions using USG (5).

Peripheral neuropathy is an umbrella term used for almost all peripheral nervous system diseases (6). In the previous case studies of psoriasis and PsA patients found in the literature, peripheral neuropathy was reported (7). Even though there are previous studies on the occurrence of polyneuropathy due to pathogenesis or treatment of rheumatologic conditions, only one study has been conducted on this subject in psoriasis patients (7-9). This is the reason why we investigated the presence of polyneuropathy in our cases using electrophysiological methods.

This study aims to investigate the presence and frequency of enthesopathy using GUESS, the frequency of peripheral neuropathy in arm and leg by nerve conduction studies (NCS), the relationship between enthesopathy and clinical parameters, and to compare the frequency of symptomatic and asymptomatic enthesopathy in psoriasis patients.

MATERIALS AND METHODS

Prospectively, seventy-four individuals that are followed in our dermatology clinic, over 18 years of age with chronic plaque type psoriasis and no known musculoskeletal disease, recent trauma, surgery or injection were included in this study. Patients with previously diagnosed polyneuropathy, diabetes mellitus, thyroid disease, chronic kidney failure, autoimmune diseases, pernicious anemia, a history of alcohol abuse, chemotherapy, epilepsy or seizures were excluded from the NCS.

The dermatologist recorded the age, gender, height, weight, body mass index value (kg / m2), age at the diagnosis of psoriasis, duration of the disease, other known diseases, family history of psoriasis, presence of scalp, genital and intergluteal area and nail involvement, PASI ("Psoriasis Area Severity Index") score, and NAPSI ("Nail Psoriasis Severity Index") score. A physical therapy and rehabilitation physician evaluated the presence of pain and / or swelling in the knee and heel joints, as well as pain, tenderness, swelling and restriction of movement in the knee and heel joints. In laboratory exams, C reactive protein (CRP) and erythrocyte sedimentation rate (ESR) values were recorded.

One week after their initial evaluation, all patients underwent USG for their knee and ankle joints at the Hacettepe University Physical Therapy and Rehabilitation clinic. A specialist conducted the study in a dark room using a 7-12 MHz linear probe (Logiq 5, GE Medical systems) without being informed of the clinical severity of the patients. With the patient supine and the knee flexed 30°, the superior pole of the patella (quadriceps tendon insertion), the inferior pole of the patella (patellar ligament origin) and the patellar ligament insertion at the tibial tuberosity was examined. The Achilles tendon and the plantar aponeurosis were evaluated with the patient supine and the feet at 90° of flexion over the edge of the examination table. In GUESS, the quadriceps tendon, patellar tendon (attachment areas to the lower pole of the patella and tibial tuberosity), Achilles tendon and plantar aponeurosis are evaluated in grey scale for tendon thickness, the presence of bursitis, erosion and enthesophyte. Bursitis was described as a well circumscribed, localized anechoic or hypoechoic region at the site of an anatomical bursa that was compressible by the transducer. Bony erosion was described as a cortical fracture with a step down contour defect, whereas an enthesophyte was defined as a step up bony prominence at the end of the normal bone contour. The maximum thickness of the ligament, aponeurosis, and tendon was measured proximal to the bony insertion.

The following criteria were used to determine abnormal structure thickness: quadriceps tendon thickness >6.1 mm, proximal and distal patellar ligament thickness >4 mm, Achilles tendon thickness >5.29 mm, plantar aponeurosis thickness >4.4 mm. Total GUESS score ranges from 0-36 (5).

Electromyography (EMG) and NCS tests were performed without the use of needles on patients without an underlying cause for polyneuropathy such as a pre-existing illness or history. According to Oh, the latency and conduction velocities (NCV) of patients were measured (10). The median and ulnar nerves of the upper extremities were measured for sensory and motor NCV, the peroneal and tibial nerves of the lower right extremities were measured for motor NCV, and the sural nerve was measured for sensory NCV. Another physician performed the procedure at the Hacettepe University Physical Therapy and Rehabilitation Clinic using a 5-channel EMG instrument (Medelec Synergy TECA machine; Oxford Instruments Medical, Surrey, United Kingdom) at room temperature, while the skin temperature was over 30° C.

All statistical reviews were performed using SPSS 15.0 for Windows. The Kolmogorov-Smirnov test was used to determine if the numerical data were normally distributed or not. The "significance test of the difference between the two means" was used to compare normally distributed numerical variables between two groups, and the "Mann-Whitney U test" was used to compare non-normally distributed numerical variables. In the comparison of more than two independent groups, the Kruskal-Wallis test was used for data that did not meet the parametric test assumptions, but the "One-way Analysis of Variance (ANOVA)" or "Welch ANOVA" tests were used for data that satisfied the parametric test assumptions. To establish the link between categorical variables, a Chi-square test (Pearson Chi-square, Yates Corrected Chi-square, or Fisher-Exact Chi-square) was employed. As descriptive statistics, parametric tests provided mean±standard deviation, while non-parametric tests provided median (minimum-maximum). Spearman's rho coefficient was used to analyze correlations between variables. P values below 0.05 were considered as statistically significant.

The study was conducted with the approval of the Ethics Committee of Hacettepe University Faculty of Medicine Clinical and Pharmaceutical Research Local Ethics Committee with decision number HEK 12/70.

RESULTS

Using USG, 740 entheses from 74 patients (39 female (52.7%), 35 male (47.3%)) were evaluated. Due to extremely thick psoriasis plaques on the skin, ten enthesis regions from 3 patients (bilateral patellar ligament proximal and distal entheses in 2, left patellar ligament proximal and distal entheses in 1 patient) could not be seen. In 55 of 74 patients (74.32%), at least one enthesopathy finding was present in 172 of the 730 entheses (23.56%). Achilles' enthesis was the most common area where enthesopathy was diagnosed (59 / 730) (8.08%). The most prevalent symptom was enthesophytes (95 / 730) (13.01%) and the most common site of enthesophyte was the calcaneus posterior pole in Achilles tendon enthesis (26 / 74 patients, 50/730 entheses). Table 1 shows the findings of USG.

Table 1. USG findings of entheses

	Quadriceps enthesis (n = 148)	Proximal Patellar enthesis (n = 143)	Distal Patellar enthesis (n = 143)	Achilles enthesis (n = 148)
Tendon thickness*	2	2	1	1
Bursitis	19	0	3	6
Bone erosion	2	7	29	5
Enthesophyte	34	5	3	50
Inflammation	21	2	4	7
Chronic Symptoms	36	12	32	55

*Quadriceps tendon ≥ 6.1 mm, proximal patellar ligament ≥ 4 mm, distal patellar ligament ≥ 4mm, Achilles tendon ≥ 5.29 mm, plantar aponeurosis tendon ≥ 4.4 mm
n = Enthesis number

The mean GUESS score was determined to be 2.51 ± 2.49 (0 - 13). Nineteen patients had a GUESS score of 0, while the remaining 55 scored at least 1. There was no statistically significant correlation between the GUESS score and gender, disease onset age, disease duration, family history, scalp involvement, intergluteal / perianal area involvement, genital area involvement, PASI, NAPSI, body mass index, ESR and CRP values, knee and / or heel symptoms ($p > 0.05$). This link was statistically significant ($p = 0.022$, $r = 0.266$): as age increased, so did the GUESS score. Patients with nail involvement had substantially higher GUESS scores when compared to patients without nail involvement ($p = 0.004$, $r = 0.338$), although there was

no statistically significant difference in age between the two groups (p = 0.309). Table 2 depicts the relationship between the GUESS score and demographic and clinical data, and Figure compares the GUESS scores of patients with and without nail involvement.

Table 2. The relationship between the GUESS score and demographic and clinical data

	GUESS score Median (minimum-maximum)	p
Gender		
Female (N = 39) Male (N = 35)	2 (0 - 7) 2 (0 - 13)	0.721
Family history		
No (N = 55) Yes (N = 19)	2 (0 - 13) 1 (0 - 7)	0.187
Scalp involvement		
No (N = 15) Yes (N = 59)	2 (0 - 7) 2 (0 - 13)	0.589
Intergluteal/perianal involvement		
No (N = 48) Yes (N = 26)	2 (0 - 13) 2 (0 - 7)	0.633
Genital area involvement		
No (N = 44) Yes (N = 30)	2 (0 - 7) 2 (0 - 13)	0.45
Nail involvement		
No (N = 30) Yes (N = 44)	1 (0 - 5) 3 (0 - 13)	**0.004**
Knee and/or heel symptom		
No (N = 45) Yes (N = 29)	2 (0 - 13) 2 (0 - 7)	0.408

When 29 patients with symptoms on the knee and/or heel were compared with 45 patients without symptoms, no significant difference was found between these two groups in terms of GUESS score (p = 0.408). 25 of 74 patients went under NCS. 7 of the 25 patients (28%) were diagnosed with a pathology. As a result of NCS, 1 patient (4%) had decreased motor NCV in the peroneal nerve, 1 patient (4%) had increased motor latency in right tibial distal nerve, 1 patient (4%) had decreased left median sensory NCV, 2 patients (8%) had decreased sensory NCV in bilateral median nerve, and 2 patients (8%) were diagnosed with right carpal tunnel syndrome. Right ulnar (p = 0.001), left ulnar (p = 0.01) and right tibial nerve distal motor latency (p = 0.019) increased as GUESS scores went up, while left ulnar NCV decreased (p = 0.033). Other clinical and laboratory parameters were not found to correlate with latency and conduction velocities.

DISCUSSION

Psoriasis is a chronic, recurrent, inflammatory dermatosis accompanied by 5-30% PsA. In the seronegative spondyloarthritis (SpA) group, PsA is clinically characterized by joint, tendon and entheses involvement. It is hypothesized that the inflammation in spondyloarthropathies starts at the first entheses and subsequently spreads to the adjacent joint (3). The early detection of enthesopathy using USG can be a very useful method in the early diagnosis and treatment of PsA, a progressive disease characterized by joint destruction (4).

In one study that employed GUESS scores to investigate subclinical enthesis involvement in psoriasis patients, 62.5% of the patients were reported to have enthesopathy (11), and in another study, at least one symptom of enthesopathy was observed in 32.9% of 450 entheses evaluated (12). 62% of psoriasis patients in a recent study using the MASEI (Madrid Sonography Enthesitis Index) score (an enthesis score which contains power doppler and upper limb examinations in addition to GUESS score) for enthesis evaluation had at least one entheseal abnormality (13). These results are similar to our study.

In our investigation, there was no statistically significant correlation between GUESS score and disease period or PASI scores. This outcome is consistent with previous studies (2,12,13,14). Nail involvement is a risk factor for developing PsA. Future PsA development is 2.24 times more likely in patients with nail involvement (15). In a study comparing psoriasis patients with and without nail involvement, Ash et al. found that patients with nail involvement had a significantly higher USG mean score than those without nail involvement. In addition, this study demonstrated that USG scores increase with the severity of nail involvement (14). Similarly, in our study, patients with nail involvement had higher GUESS scores (p = 0.004, r = 0.338), however there was no significant relationship between GUESS scores and the severity of nail involvement (p = 0.224). Regardless of the level of nail involvement we discovered a substantial correlation

between nail involvement and enthesitis formation in psoriasis patients. Therefore, all psoriasis patients with nail involvement should be reviewed for enthesopathy presence, regardless of the severity of nail involvement.

Only 3-8% of early-stage PsA patients exhibit articular symptoms (4). Using GUESS scores, Gisondi et al.'s study on 30 patients without articular symptoms revealed at least one enthesopathy finding in every patient (2). De Simone et al.'s study about the review of Achilles tendon alterations using USG reported that 53.6% of 41 asymptomatic psoriasis patients had some kind of pathology in USG (16). De Filippis et al. found that 33% of 24 asymptomatic patients had developed enthesopathy (17). Comparing 29 symptomatic patients to 45 asymptomatic patients in our study revealed no significant difference in GUESS scores ($p = 0.408$). However, during USG review, 75.5% of 45 patients displayed at least one symptom of enthesopathy. These results support the idea that psoriasis patients with no musculoskeletal symptoms or signs frequently have enthesopathy.

Due to the fact that autoimmune collagen tissue diseases can directly affect the nerves, cause nerve entrapment secondary to arthritis and synovitis, or be caused by the medications used to treat these conditions, peripheral neuropathy can be observed in these conditions. In case reports from previous studies in the literature, neuropathy coexisted with psoriasis and psoriatic arthritis patients (18,19). 7 out of 25 NCS patients (28%) were diagnosed with pathological disorders, with 2 (8%) of them being diagnosed with right carpal tunnel syndrome. In a study of peripheral nerve dysfunction in 32 psoriasis patients, Chroni et al. did not identify any patients with a pathological condition (7). In another study comparing Ankylosing spondylitis (AS) patients and healthy control groups, AS patients had a 46% rate of peripheral neuropathy whereas in the healthy control group this rate was 3.3% (9). Furthermore, epidemiological studies revealed that peripheral neuropathy was observed in 7% of the elderly population and in 10% of patients with connective tissue disease (20,21). In this regard, our research is groundbreaking since it demonstrates that psoriasis and peripheral nerve involvement are connected. To more precisely identify this relationship more clearly, further controlled studies are necessary.

According to the findings of this study, bilateral ulnar and right tibial nerve distal motor latencies appear to increase when GUESS scores are higher. There is no evidence in the published literature of a correlation between enthesopathy and peripheral neuropathy. Entrapment of nerves between joint structures swollen with edema, rheumatoid synovitis, nodules and calcified ligaments is one of the peripheral neuropathy mechanisms in rheumatologic illnesses (9). In enthesopathy, increased tendon thickness, edema, and newly developed bony structures known as enthesophytes can also cause nerve compression. In our study, we only examined lower extremity entheses, however, we found a correlation between GUESS scores and ulnar nerve measurements (direct proportion with right ulnar latency ($p = 0.001$) and left ulnar latency ($p = 0.01$), opposite proportion with left ulnar nerve sensory NCV ($p = 0.033$)). Similar changes may occur in the upper extremity entheses as they do in the lower extremities. In conclusion, our study is the first to suggest a possible relationship between enthesopathy and peripheral nerve dysfunction. To clarify this relationship's etiology, more controlled studies with more patients are necessary.

Our study was limited by the absence of a control group, the small number of patients who underwent NCS, and the analysis of only the lower extremity entheses with USG.

CONCLUSION

Our findings indicate that nail involvement and enthesopathy are closely related, that psoriasis is associated with a significant prevalence of asymptomatic enthesopathy, and that enthesopathy may be associated with peripheral nerve dysfunction. Dermatologists should keep in mind the neuromusculoskeletal disorders in psoriasis patients.

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Declarations

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