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ORIGINAL ARTICLE

Report on 25 Notalgia paresthetica cases: Clinical features and treatments

Notalgia parestetika tanılı 25 hastanın klinik özellikleri ve tedavileri

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Summary

Objectives: Notalgia paresthetica (NP) is a neuropathic condition that manifests as a chronic itch on the back. The aim of this retrospective study was to examine the characteristics of patients diagnosed with NP.

Methods: A total of 25 female patients, aged 26–64 years (mean±10.67 years; median 47.17 years), were studied to determine the spinal or peripheral origin of NP.

Results: On radiological examination, discopathy was observed in 24% of the patients, arthrosis in 32%, and degeneration in 56%. There was no significant relationship found between dermatological symptoms and magnetic resonance imaging positivity (p=0.188). The patients' treatment programs were based on either physical therapy (44%), local injection (28%), exercise therapy (16%), or physical therapy and kinesiotherapy (12%). Subjective measures for pain were validated with an average visual analog scale (VAS), and the "Douleur Neuropathique 4" (DN4) questionnaire was used to screen for neuropathic pain. The VAS score of the patients before treatment was 7, and after treatment was 2. The mean DN4 score was 7 before treatment and 2 after treatment.

Conclusion: NP is a rare syndrome of unknown etiology. We aim in this study to analyse NP clinical properties and treatment.

Keywords: Itch; neuropathic pruritus; pain; peripheral nerve; pruritus.

Özet

Amaç: Notaljia parestetika (NP), sırtta kronik kaşıntı olarak ortaya çıkan nöropatik bir durumdur. Bu retrospektif çalışmanın amacı, NP tanısı alan hastaların özelliklerini incelemektir.

Gereç ve Yöntem: Notaljia parestetikanın spinal veya periferik kökenini belirlemek üzere, yaşları 26-64 arasında (ortalama±10.67 yıl; medyan: 47.17 yıl) toplam 25 kadın hasta çalışmaya alındı.

Bulgular: Radyolojik incelemede hastaların %24'ünde diskopati, %32'sinde artroz ve %56'sında dejenerasyon gözlendi. Dermatolojik semptomlar ile manyetik rezonans görüntüleme pozitifliği arasında anlamlı bir ilişki bulunamadı (p=0.188). Hastaların tedavi programları fizik tedavi (%44), lokal enjeksiyon (%28), egzersiz tedavisi (%16) veya fizik tedavi ve kinezyoterapi (%12) şeklindeydi. Ağrı için subjektif ölçümler, ortalama bir görsel analog skala (VAS) ile doğrulandı ve nöropatik ağrıyı taramak için "Douleur Neuropathique 4" (DN4) anketi kullanıldı. Hastaların tedavi öncesi VAS skoru 7, tedavi sonrası VAS skoru 2 idi. Ortalama DN4 skoru tedaviden önce 7, tedaviden sonra 2 idi.

Sonuç: NP nadir görülen bir sendromdur. Bu çalışmada NP klinik özelliklerini ve tedavilerini derledik.

Anahtar sözcükler: Ağrı; kaşıntı; nöropatik pruritus; periferik sinir; pruritus.

Introduction

Notalgia paresthetica (NP), first described by the Russian neurologist Astwazaturow, is a neuropathy of the dorsal branches of T2-T6 and is characterized by an itchy hyperpigmented skin lesion accompanied by burning pain, paresthesia, hyperesthesia, and skin tenderness in the scapular region.[1] The clinical presentation of NP ranges from invisible skin lesions to a limited hyperpigmented macule or a hyperpigmented patch. These different clinical findings, such as posterior pigmented itch patches, hereditary localized itch, and macular amyloidosis, are published under different names, but all basically describe the

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same phenomenon.[2] Although the etiology of NP is not yet fully understood, it is thought to be mostly due to compression of the spinal nerves by thoracic spine abnormalities. For example, nucleus pulposus herniation, osteophytes, and more often vertebral pathologies, including degenerative changes, have been described in relation to the dermatomal localization of the NP.[3] In this study, we compiled the characteristics and treatments of 25 patients who we followed up within physiotherapy, rehabilitation, and dermatology outpatient clinics. The main purpose of this two-center study was to examine and correlate multiple clinical, cutaneous, neuroanatomical, and radiological features of NP.

Material and Methods

A literature search was performed using PubMed. The search term was "NP;" the language was English, and the date range was 1990–2020. Patients who were diagnosed with NP and could attend regular follow-up visits were included in this study. Pediatric patients <18 years of age, patients with uncontrolled diabetes, hypertension, and cardiovascular patients with a history of malignancy and progressive neurological disease were excluded.

We recruited 25 patients who were diagnosed with NP and subsequently attended Physical Medicine and Rehabilitation and Dermatology outpatient clinics for a 1-year period between January 2019 and January 2020. Patients were analyzed retrospectively (Table 1). The analyzed parameters included demographic data, history, and localization of NP, dermatological investigation, pruritus characteristics, spinal pathologies, and treatment. Informed consent forms were obtained from all patients before starting treatment. All of our patients were female (100%, n=25). According to the International Physical Activity Questionnaire (short), 28% (n=7) of the patients were in desk jobs, 60% (n=15) were in jobs requiring moderate physical activity, and 12% (n=3) were working in heavy jobs. Regarding the lesion locations,72% (n=18) of the patients had lesions on the right or left side (unilateral), and 28% (n=7) had bilateral lesions. Skin biopsy was performed in 8 of 25 patients for histopathological examination.

Etiologically, 16% (n=4) of the patients had myofascial pain syndrome, 32% (n=8) had cervical arthrosis, 24% (n=6) had cervical/thoracic discopathy, and 28% (n=7) had posture disorder (Table 1).

Table 1. The clinical features of the 25 patients with NP

NP features	n	%
Dermatological findings		
Skin lesion	25	100
Region		
Neck	6	24.0
Dorsum	16	64.0
Lumbar	3	12.0
Side		
Unilateral	18	72.0
Bilateral	7	28.0
Comorbidity		
Discopaty	6	24.0
Arthrosis	8	32.0
Myofascial pain syndrome	4	16.0
Postural disorders	7	28.0
Skin biopsy		
Absent	17	68.0
Present	8	32.0
MRI positivity		
Absent	11	44.0
Present	14	56.0
Pruritus		
Absent	10	40.0
Present	15	60.0

NP: Notalgia paresthetica; MRI: Magnetic resonance imaging.

To measure pain and pruritis intensity, the visual analog scale (VAS) is used to improve NP management and research. The VAS consists of a straight line with endpoints that define extreme boundaries such as "no pain, no pruritus" and "pain as bad as possible." Patients were asked to mark the level of pain and itchy on the line between the two extremes, and these levels were scored as follows: low 0 to <3 points, moderate ≥3 to <7 points, severe itching ≥7 points.

The Douleur Neuropathique 4 (DN4) questionnaire has been recommended as a screening questionnaire for neuropathic pain. It consists of four questions about the characteristics of pain and itching, and questions are answered with a yes (1) or no (0). Symptoms such as itching, burning, alodynia, hyperesthesia, or hypoesthesia for needle sticking were evaluated and pa-

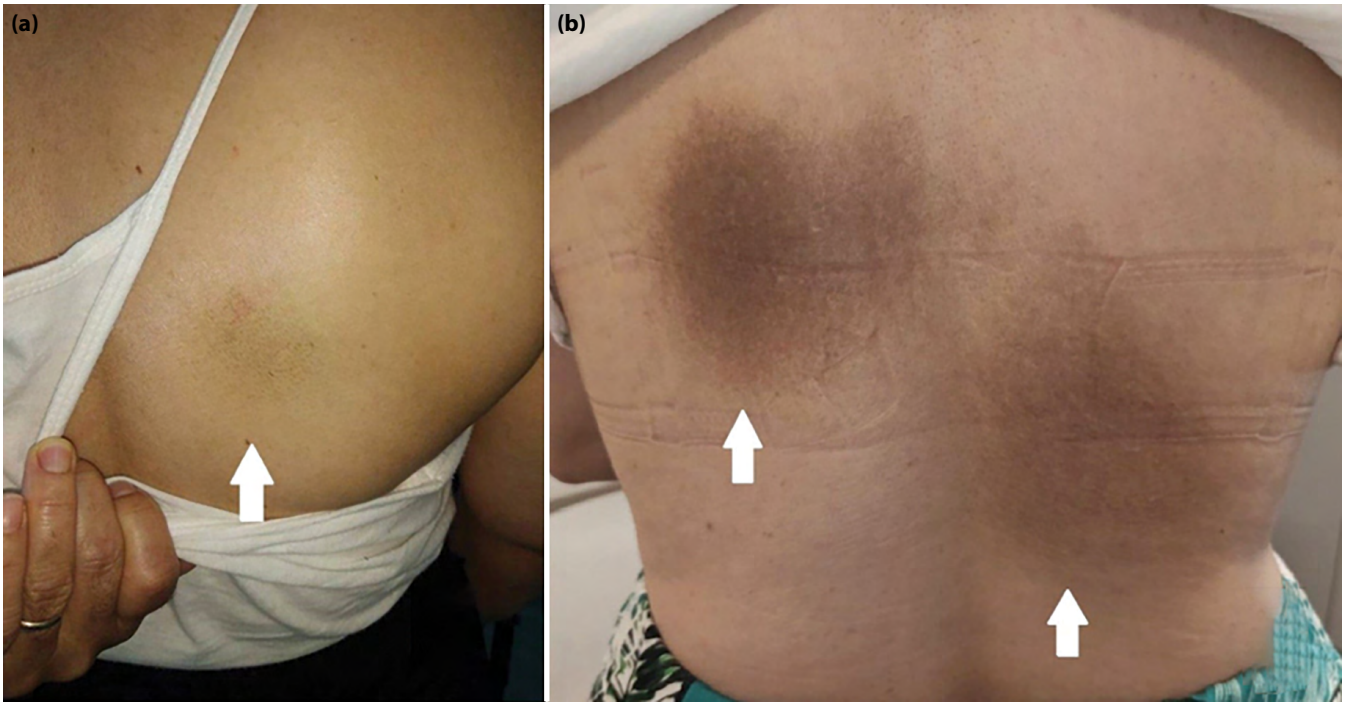

Figure 1. (a) Unilateral 2x3 cm hyperpigmented brownish patch in the scapular area in 42 years old female patient **(b)** Bilateral hyperpigmentation in the back area in 49 years old female patient.

tients completed the questionnaire before and after treatment. The total score was calculated as the sum of ten items, and the cut-off value for the diagnosis of neuropathic pain was a score of 4 or greater.

Statistical Analyses

All analyses were performed using SPSS v21 (SPSS Inc., Chicago, IL, USA). For the normality check, the Shapiro Wilk test was used. Data are given as mean±standard deviation or median (1^{st}–3^{rd} quartile) for continuous variables according to the normality of distribution and frequency (percentage) for categorical variables. Normally distributed variables were analyzed with an independent samples t-test and analysis of variance. Non-normally distributed variables were analyzed with the Mann Whitney U and Kruskal Wallis tests. Categorical variables were evaluated using the Chi-square test or Fisher's exact test. The continuous variables from different times were analyzed with the Wilcoxon signed-rank test. Values of $p<0.05$ were accepted as statistically significant results. Statistical analysis revealed that VAS and DN4 scores were independent of the age and skin type of the patient.

Results

Dermatological Findings

Skin findings were distinguished by the presence of hyperpigmentation and/or scratch lesions (Fig. 1a). Pruritus was a common symptom. All patients (100%) showed a hyperpigmented patch and mild lichenification with skin lesions (Fig. 1a). In regional classification, lesions were most commonly localized to the dorsal region (n=16, 64%), followed by the neck (n=6, 24%), and then the lumbar region (n=3, 12%). Dermatomal involvement was mostly unilateral in 18 patients (72%) and bilateral in 7 patients (28%) (Table 1). The DN4 score of those with dermatological symptoms (pruritus) was higher than that of those without dermatological findings (p=0.010) (Table 2).

Histological Findings

Histopathological examination was performed in 8 of 25 patients. Skin biopsies stained with haematoxylin eosin and congo red were evaluated under light microscopy. In five patients, dermal hyperpigmentation, post-inflammatory melanosis, hyperkeratosis, and an inflammatory melanophage dermal infiltrate histopathology were found to be compatible with NP (Fig. 2). In three patients, hyperpigmentation, necrotic keratinocytes, and amyloid deposits were prominent. Although histopathology did not fully support the diagnosis in these three patients, clinical and radiological findings were consistent.

Radiological Findings

Radiological investigations showed arthrosis in eight patients (32%), postural degeneration in seven pa-

Table 2. VAS and DN4 scores of patients according to clinical features

Treatment features	VAS	p	DN4	p
Treatment				
Physical therapy	6 (5–7)		7±1.55	
Exercise	6.5 (5–7.5)		7±1.83	
Dry needling	7 (6–9)	0.074	7.14±1.07	0.970
Kinesiotherapy	9 (9–9)		7±1	
Physical activity				
Low	6 (5–7)		6.14±1.21	
Moderate	7 (5–9)	0.374	7.4±1.24	0.109
High	8 (7–8)		7.33±1.53	
Dermatological symptoms				
Absent	6 (5–9)	0.531	6.3±1.06	0.010
Present	7 (6–8)		7.53±1.3	

VAS: Visual analog scale; DN4: Douleur neuropathique 4.

tients (28%), discopathy in six patients (24%), and myofascial pain syndrome in four patients (16%) (Fig. 3). Magnetic resonance imaging (MRI) findings could be correlated with the exact clinical dermatomal localization of the NP, but there was no significant relationship between dermatological symptoms and MRI positivity (p=0.188).

The 25 participants completed the DN4 questionnaire. Most of the patients (75%) were classified as having mild-to-moderate impairment, and patients (25%) obtained scores that revealed severe impairment.

The treatment protocols were as follows: 44% (n=11) of the patients undertook a physical therapy program (15 sessions over 3 weeks) consisting of hot pack (20 min), transcutaneous electrical nerve stimulation (TENS) (conventional 70–100Hz, 20 min) and ultrasound therapy (1w/cm 2, 5 min); 28% (n=7) of the patients had dry needle therapy (5 times over 3 weeks); 12% (n=3) of the patients had kinesiotherapy (5 times over 3 weeks); and 16% (n=4) of the patients undertook a home exercise therapy program (stretching and resistance exercises). Patients were re-evaluated 3 months after treatment.

The average VAS score of the patients before treatment was 7, and after treatment was 2. The mean DN4 scores were 7 before treatment and 2 after treatment. When the distribution of the patients' prognostic scores before and after treatment was examined, it was observed that the VAS (p=0.001) and DN4 (p=0.001) scores significantly decreased (Table 3).

In addition, it was observed that the DN4 scores of those with dermatological findings changed more than the scores of those without dermatological findings (p=0.016) (Table 4).

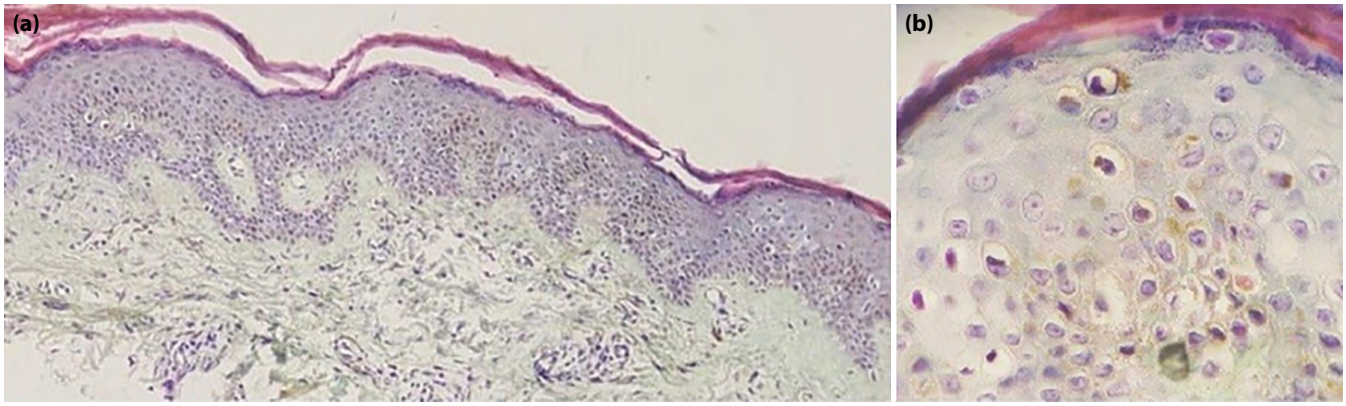

Figure 2. (a, b) Post-inflammatory melanosis, hyperkeratosis, and an inflammatory melanophage dermal infiltrate (H&E x100).

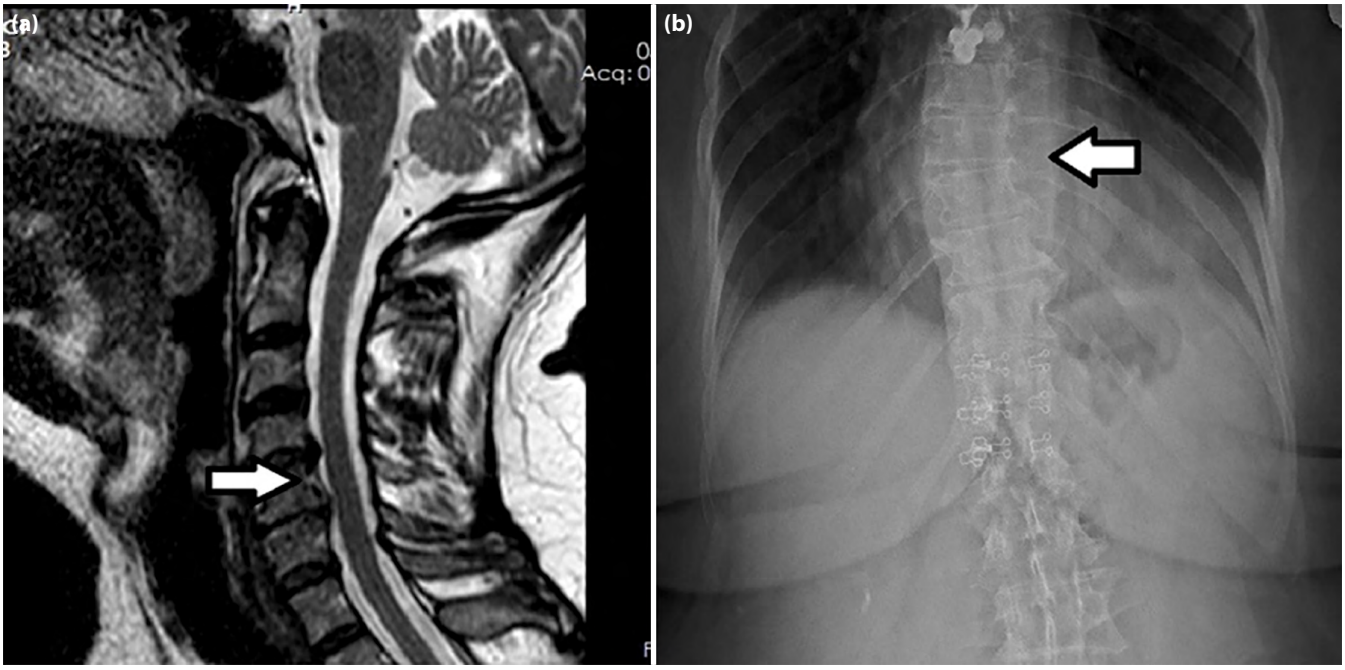

Figure 3. (a) T1 weighted sagittal dorsal spine MRI image demonstrated with arthropathy C4-C5. **(b)** Thoracic hernia and mild scoliosis on x-ray imaging.

Discussion

NP is still a mysterious disease, as there are no representative cohort studies. It may be a dermatological sign of an underlying systemic disease. There is no single clinical finding or laboratory test that allows a definitive diagnosis of NP to be made.[4,5]

Multiple possible mechanisms have been proposed for NP. Many studies report radiographic findings, with T2 to T6 posterior thoracic polyradiculopathy reported as the primary cause in some patients. Radiological examinations mostly reveal cervical and thoracic degenerative changes.[6] Savk et al.[7] used MRI to evaluate spinal pathologies in 43 patients with NP and found degenerative disc hernias in 24.6% of cases, degenerative changes in the thoracic vertebrae in 32.8%, and thoracic disc hernias in 3.3%.Consistent with the literature, 56% of our patients had spinal pathologies (detected by MRI) and showed evidence of cervical/dorsal spinal pathologies in radiological imaging at the thoracic level corresponding to the NP. Another hypothesis on the etiology of NP focuses on the dermal sensory innervation and sensory neuropathy of the posterior branches of peripheral nerves. Wang et al.[8] reported thoracic nerve damage leading to serratus anterior dysfunction as the cause of NP in four patients. These reports highlight a hypothesis that NP has a peripheral, not spinal, origin. For example, one patient developed NP after neuralgic amyotrophy; electromyography showed no spontaneous activity in the muscles, while radiography of the spine was normal.[9] In our study, 42% of the patients had myofascial pain and postural disorders, supporting this hypothesis.

Regarding the genetic origin of NP, several cases have been associated with multiple endocrine neoplasia type IIA (MEN 2A), and RET codon 634 mutations have been reported. Hence, this can be considered an early clinical marker. In fact, histopathological examination of NP does not reveal amyloid deposits, but melanin usually increases in the basal layer and dermis.[10,11]

NP is typically reported in older females and can last for months to years. All of our patients were women, which supports the findings in the literature. The most common NP sites are the shoulder blades and the upper back. The area may be limited to only one side of the back, or it may occur in the middle of the upper back above the spinal bones. In general, cases

Table 3. Distribution of patients' pre- and post-treatment (after 3 months) prognostic scores

Pain scale	Pre-treatment	Post-treatment	p
VAS	7.00 (6.00–8.00)	2.00 (1.00–2.00)	0.001
DN4	7.00 (6.00–8.00)	2.00 (1.00–2.00)	0.001

VAS: Visual analog scale; DN4: Douleur neuropathique 4.

Table 4. Prognostic score changes three months after treatment

	VAS change	p	DN4 change	p
Treatment				
Physical therapy	−5 (−6−−3)		−5 (−6−−4)	
Exercise	−5 (−7.5−−3)		−5.5 (−7.5−−3.5)	
Dry needling	−6 (−6−−4)	0.060	−6 (−7−−6)	0.604
Kinesiotherapy	−8 (−9−−8)		−5 (−6−−4)	
Physical activity				
Low	−4 (−5−−3)		−5 (−6−−3)	
Moderate	−6 (−7−−3)	0.101	−6 (−7−−4)	0.249
High	−7 (−8−−6)		−6 (−8−−4)	
Dermatological symptoms				
Absent	−5.5 (−8−−3)	0.849	−4.5 (−5−−3)	0.016
Present	−6 (−7−−4)		−6 (−7−−5)	

VAS: Visual analog scale; DN4: Douleur neuropathique 4.

have unilateral distribution, but up to 10% of cases are bilateral.[7] NP sometimes occurs without any obvious changes in the skin. This condition can often be delayed or even overlooked because patients are primarily referred to dermatology clinics for itching complaints. If skin changes occur, there may be well-defined dark hyperpigmentation in the affected area. Although periodic itching is the main symptom, which is observed in ≤30% of patients, some people describe pain, tingling, or a change of sensation.[12]

Common treatments that provide patients with variable relief include topical corticosteroids, topical capsaicin, and local anesthetics such as lidocaine. Many patients treated with capsaicin reported burning, tingling, and pain after treatment, and most patients experienced a relapse of symptoms within a month.[13] Anti-seizure drugs such as oxcarbazepine (Trileptal and others) and gabapentin (Gralise, Neurontin, Horizont, and others) have been used in the treatment of NP. These drugs block nerve pathways and have beneficial effects in patients with other neuropathic conditions. The tricyclic antidepressant amitriptyline has also been used to treat NP with variable results.[14] Botulinum toxin A (BTX-A) may have beneficial effects on local itching by preventing the release of substance p that causes pain and itching, and it was also found to suppress the release of glutamate and noradrenaline. BTX-A treatment was used in five cases; there were variable results, and none of the patients completely recovered from itching. Since the number of cases in these studies is limited, more comprehensive studies are required on BTX-A therapy.[15] In our study, there was no patient in whom we used botulinum toxin.

Fortunately, current therapeutic approaches are proving successful for the treatment of patients with NP. Examples of these non-invasive methods include physical therapy techniques, physiotherapy, manipulative therapy, analgesic electric currents, and traction. These techniques were selected for inclusion in this study based on reports in the literature of their success as NP treatment options. Patients who have nostalgia parestetica and have undertaken an exercise program with the McKenzie method for three weeks have experienced pain relief within 1–3 weeks. Studies have shown that pain is relieved in a significant number of individuals within 1–3 weeks when regularly completing these exercises.[16] In two cases, the exercises and stretches used for pain relief had a similar effect on the sensation of itch. In a study that investigated the effect of simple stretching exercises for 12 patients over 12 weeks, 11 patients achieved a satisfactory improvement in their symptoms with no side effects.[17] In our study, patients experienced statistically significant improvements with these exercises.

In an earlier report, 15 NP patients with a relevant spinal pathology underwent ten sessions of conventional TENS therapy. As a result, differences between their pre-treatment and post-treatment VAS and DN4

scores were statistically significant.[18] In our study, when TENS therapy was used as a treatment, patients reported serious decreases in their pain levels. Kinesiology taping is another method increasingly used in recent years in the treatment of musculoskeletal diseases. The effectiveness of this method is explained by different mechanisms, such as increasing the blood and lymphatic circulation due to the increase of subcutaneous interstitial area by lifting the skin and regulating the superficial and deep fascia functions. In one study, eight sessions of dry needling and kinesiology taping were applied to one patient, two days a week. After the treatments, the patient's pain and paresthesia complaints were greatly reduced.[19] In this study, significant success was achieved with kinesiology taping in nine patients.

One of the biggest challenges in our study was randomizing the groups because there were large differences in the measurement of symptoms between patients and even at different time points for the same patient. VAS scores were also used to convert a subjective symptom into numerical information to facilitate analysis of treatment response. After treatment, patients showed a significant improvement, indicated by a decrease in mean VAS scores for pruritus and pain.

Generally, the diagnosis of neuropathic itching is based on the presence of clinical signs, abnormal sensations, neurological symptoms, and/or localization along the dermatomes. Often, it is simple to grade. As a result, five questions of our Neuropathic Pruritus tool can be asked to help diagnose NP as a DN4 score. Two or more positive criteria favor NP, with 76% sensitivity and 77% specificity.[20] Therefore, the DN4 questionnaire was selected for use in this study. Our results confirmed test-retest reliability and internal consistency. We noticed that pain and itchiness, which can be very disturbing problems for patients receiving treatment for NP, decreased markedly, and this test was used to monitor treatment success.

Conclusion

In conclusion, NP is a rare syndrome of unknown etiology, and the lack of studies makes it difficult to optimize indications and recommendations to guide treatment. The aim of our study was to retrospectively analyze a group of patients with NP against the background of existing hypotheses about the cause and contributing factors of NP. Consequently, we have drawn attention to the multiple clinical, histological, and radiological parameters of NP that are related to different disciplines and have analyzed various current treatments. It is worthwhile to note that, in agreement with previous reports, the application of non-invasive physical therapy appeared to be the most promising treatment method.

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