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Prurigo nodularis: what do patients and their skin have to tell us?

Prurigo nodular: o que o paciente e a sua pele têm a nos dizer?

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ABSTRACT

Prurigo nodularis (PN) is a chronic skin disease characterized by pruritic lesions that can severely affect quality of life, impacting daily activities, sleep, mental health, and social relationships. Its pathogenesis involves a complex neuroimmune feedback loop. The case of a young patient illustrates the suffering caused by PN, which led to school dropout, social isolation, and depressive symptoms. After failure of treatment with corticosteroids and methotrexate, dupilumab treatment and psychological and psychiatric support were initiated. The management of PN requires humanized care and personalized strategies to minimize the impact of the disease and improve quality of life.

Keywords: Pruritus, quality of life, chronic disease.

RESUMO

O Prurigo Nodular (PN) é uma doença crônica da pele caracterizada por lesões pruriginosas que afetam gravemente a qualidade de vida, com impacto em atividades diárias, sono, saúde mental e relações sociais. Sua patogênese envolve um ciclo neuroimune complexo. O caso de uma jovem paciente ilustra o sofrimento causado pelo PN, que levou ao abandono escolar, isolamento social e sintomas depressivos. Após falhas terapêuticas com corticoides e metotrexato, iniciou tratamento com dupilumabe e suporte psicológico e psiquiátrico. O manejo do PN exige cuidado humanizado e estratégias personalizadas para minimizar o impacto da doença e melhorar a qualidade de vida.

Descritores: Prurigo, qualidade de vida, doença crônica.

Introduction

The term “prurigo” derives from the Latin “pruire,” which means “itching,” and was coined by Ferdinand von Hebra in 1850, in Vienna, when describing papules and nodules accompanied by intense pruritus. However, some authors attribute to Robert Willan, more than 200 years ago, the first description of pruritic papules under the term “prurigo.”

Prurigo is a reactive hyperplastic skin condition that manifests clinically as isolated or multiple papules, plaques, and/or nodules with intense pruritus. Some authors classify prurigo based on different criteria, such as type (acute, subacute, or chronic), clinical form, or causative agent/associated disease.[1]

All information and concepts are widely available in the main studies and literature reviews on prurigo. However, it is crucial that we focus on the particularities of each patient and the major impact that the disease has on their lives. For this reason, we chose not to present a traditional case report from the physician’s perspective, but rather to share the patient’s own perspective. This case, full of particularities, suffering, and pain, illustrates the reality that we can encounter in

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our daily practice as allergists and immunologists. Our objective is to encourage deep and comprehensive reflection that will inspire others to search for all the necessary tools to offer the best support to patients.

Case report from the patient's perspective

"Doctor, I am 17 years old and have suffered from recurring wounds on my body since I was a child. Although treated with dermatological ointments, the wounds always returned, marking my childhood with trips to the doctor's office. Starting in 2021, the frequency and severity of the wounds increased, even with the continued use of ointments. In 2023, the boils on my leg and lesions became so severe that I was unable to wear a bra due to a lesion on my back. I saw a dermatologist and was diagnosed with atopic dermatitis. The initial treatment lost its effectiveness over time, and the lesions began to affect my social and personal life to the point that I could not get dressed for school. The shame of my body, intensified by the bullying I suffered at school, being called 'scabby' and 'mangy,' led me to drop out of school, something I had always loved. There were days when I could not wash my hair because of the painful wounds on my arm. I needed my aunt's help for simple everyday tasks. Taking a shower was a pain because my body ached from the water and the prescribed soaps. The search for medical help, with visits to several specialists and the use of different medications, was unsuccessful. The disease prevents me from doing the things I love, because I feel ashamed of my body and fear judgment from others. I avoid wearing clothes that expose my wounds, which leads me to isolate myself at home. Even when I go out, I wear clothes that hide me. I would like to go back to playing volleyball and attending school normally. My romantic relationships are also affected. Last year, I had an online relationship that I ended by putting off meeting in person for fear of being judged. I believe my condition contributed to the end of the relationship. Recently, the disease has worsened, with the appearance of nodules and lesions on my face and flaking on my scalp. This has made me extremely sad. At the beginning of the year, I sought help from a family member and, since then, my mother has been providing me with psychological support. I feel like I lost half of my teenage years because of the pain and lack of motivation caused by the disease. I wish I could go back to living the way I used to, but the pain and wounds prevent me from doing so. I really need your help."

Prurigo nodularis (PN) is a chronic skin disease, present for more than 6 weeks, characterized by history and/or signs of repeated pruritus and the presence of multiple pruritic lesions of the nodular type, which may be localized or generalized (see diagnostic criteria in Table 1). A Japanese consensus[2] classified the types of prurigo according to the underlying cause, as shown in Table 2.

Prurigo in general, and PN in particular, can be extremely debilitating for patients. Indeed, prurigo represents a significant public health burden, contributing to a large number of years lived with disability. It is a major source of morbidity globally,

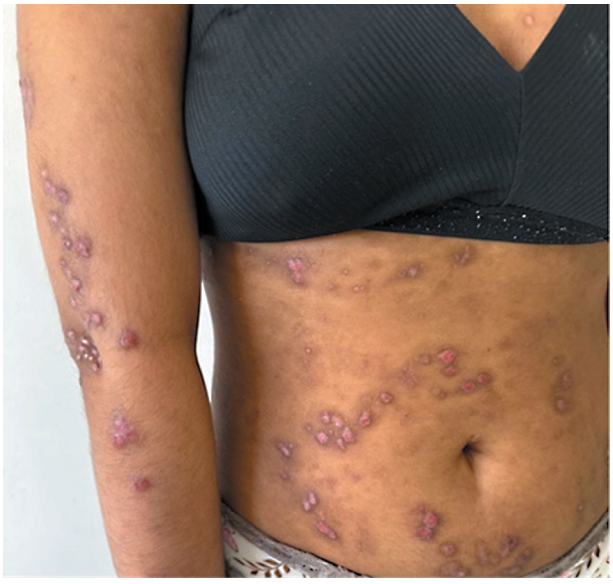

Figure 1
Numerous infiltrated and excoriated hyperkeratotic nodules on the right arm and abdomen

compared even with other chronic diseases such as anxiety disorders and diabetes mellitus. PN has a profound impact on individual health, affecting sleep, resulting in school and/or work absenteeism, compromising mental health and quality of life, and increasing the need for care. Substantial impacts on quality of life have been demonstrated in other pruritic skin conditions, such as atopic dermatitis (AD) and chronic urticaria.[3] However, there are conflicting data on the specific impact of PN on quality of life. In a systematic review and meta-analysis of studies that assessed symptom and quality-of-life burden in patients with PN, Janmohamed et al. evaluated 13

studies and concluded that quality of life is negatively impacted in PN.[4] They recommend that clinicians be aware of the burden of disease on their patients, monitor their quality of life, and incorporate this information into treatment decision-making.[5]

The pathogenesis of PN is associated with a self-sustained itch-scratch vicious cycle. Although recent research has partially elucidated the complex interactions of the cutaneous neuroimmune network, the underlying mechanism is still not fully understood. Several mediators play a crucial role in pruritus amplification in PN. These include a number of pro-inflammatory and pruritogenic mediators, such as cytokines (IL-4, IL-13, IL-31, oncostatin M, IL-17, IL-22, and TSLP), neuropeptides (substance P, calcitonin gene-related peptide [CGRP], cortistatin), neutrophins (nerve growth factor [NGF]), extracellular matrix proteins (periostin), vasculogenic substances (vascular endothelial growth factor [VEGF], endothelin-1 [ET-1]), ion channels, and intracellular signaling pathways

Table 1
Diagnostic criteria for chronic prurigo

Major criteria
i. Chronic pruritus (≥ 6 weeks)
ii. History and/or signs of repeated pruritus
iii. Presence of multiple localized or generalized pruritic lesions[a]
Associated criteria
i. Signs: Pruritic lesions: symmetrically distributed, rarely affecting the face and palms Signs of scratching: excoriation, scars, lichenification
ii. Diversity of clinical manifestations Papular type Nodular type Plaque type Umbilicated type Linear type
iii. Symptoms Usually pruritic lesions develop after the onset of pruritus Quality: pruritus, burning, pain, or stinging Signs of chronicity: great intensity of pruritus, allokinesis, hyperkinesia, continuous increase in the number of lesions Impaired quality of life, loss of sleep, days of absenteeism from work, and/or obsessive-compulsive behavior
iv. Emotions Depression Anxiety Anger Disgust Shame Hopelessness

[a] Definition of pruritic lesions: excoriated papules and/or nodules and/or desquamative and crusted plaques, often with a whitish or pink center and hyper-pigmented border.

Adapted from Satoh T. et al.[1]

Table 2
Classification of chronic prurigo according to the underlying cause

Symptomatic prurigo (associated with underlying systemic or cutaneous conditions)
Prurigo in atopic dermatitis
Prurigo in diabetes mellitus
Prurigo in renal failure
Prurigo in liver failure
Prurigo in internal malignancy
Prurigo in hematological malignancy
Prurigo associated with eczematous diseases
Prurigo in HIV infection/pruritic-papular eruption of HIV (prevalence of 24% to 36%)
Prurigo in pregnancy/Prurigo gestationis (special form: polymorphic eruption of pregnancy)
Prurigo in allergy to drugs
Prurigo in allergy to metals
Prurigo in psychiatric diseases
Idiopathic prurigo (undetermined cause)
Insect bite reaction

Adapted from Satoh T. et al.[1].

(members of the Janus kinase [JAK] family: JAK1, JAK2, JAK3, and TYK2). A deeper understanding of the mechanism of action of these mediators will be critical for the development of new targeted antipruritic agents.

Approximately half of patients with PN also have AD or atopic predisposition, suggesting a possible overlap in the pathogenesis of the two diseases. Although both diseases feature type 2 inflammation, recent transcriptomic studies have clearly differentiated PN from AD. PN does not exhibit the strong type 2 response pattern that is typically found in AD, but it is characterized by stromal remodeling and neurovascular dysregulation.[5,6]

The therapeutic approach to PN is currently based on case series and clinical experience. Treatment can be challenging due to recurrence of lesions, often associated with underlying diseases, or the limitation of the use of systemic medications in patients susceptible to adverse effects. Table 3 lists a series of approaches reported in the literature, both pharmacological and non-pharmacological. However, treatment success relies heavily on the correct diagnostic classification and identification of underlying conditions.[7]

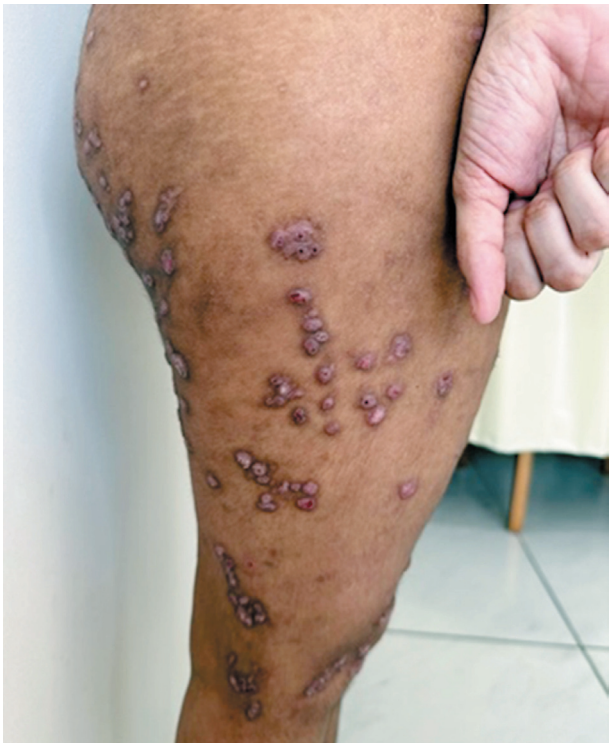

Figure 2
Numerous infiltrated and excoriated hyperkeratotic nodules on the lateral portion of the right thigh and buttock

After analyzing the patient's report, the impact of the disease on several areas of her life is enormous, including daily activities, school performance, interpersonal relationships, and social and leisure activities, as is the number of years lived with disability. The Dermatology Life Quality Index (DLQI) showed a score of 30, indicating an extreme effect on the patient's quality of life. In addition to PN, the patient has a diagnosis of AD, allergic rhinitis, and asthma, comorbidities that also contribute to the impairment of her quality of life. The patient's treatment history includes multiple cycles of oral corticosteroids, with negative consequences for her health, and methotrexate for 3 months, discontinued due to adverse gastrointestinal effects. Treatment with dupilumab was initiated 1 month ago, and the patient was referred for psychiatric support due to depressive symptoms and advised to continue psychological therapy. Monthly follow-up was suggested to monitor and evaluate the effectiveness of the proposed therapies.

In conclusion, PN exerts a negative impact on the personal, professional, and social life of patients. Providing a space for these patients to express their feelings regarding the disease is the first step in the treatment process. Therefore, it is essential to raise this issue, seeking a global assessment of these individuals to establish a more comprehensive, effective, and personalized therapy. As the physician, professor, researcher, and writer from Minas Gerais, Celmo Celeno Porto, wisely expressed: *"We must have compassion for our patients. Compassion is*

Table 3
Treatments indicated for prurigo

Topical treatments
Emollients
Topical corticosteroids [a]
Calcineurin inhibitors (tacrolimus/pimecrolimus)
Intralesional corticosteroids [a]
Topical capsaicin [a]
Systemic treatments
UV phototherapy (narrow band UVB)
H1 antihistamines
Gabapentin, pregabalin [a]
Antidepressants (e.g., mirtazapine) [a]
Cannabinoids
Immunosuppressants (methotrexate, cyclosporine A) [a]
Thalidomide [a]
Neurokinin 1 antagonist (NK1 - aprepitant) [a]
μ-opioid receptor antagonist (naloxone, naltrexone) [a]
JAK inhibitors (abrocitinib, tofacitinib, upadacitinib) [a]
Anti-IL-4/13: dupilumab [a]
Anti-IL-31: nemolizumab [a]
Anti-oncostatin anti-receptor (OSMRb/IL-13): vixarelimab [a]
KIT anti-receptors (CDX-0159) [a]

[a] Indicated in chronic prurigo.
Adapted from Satoh T. et al.[1].

understanding the patient's suffering, whatever it may be, not just the pain, and doing everything in your power to eliminate or reduce it."

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