

SUCCESSFUL MULTIMODAL THERAPY IN REFRACTORY PRURIGO NODULARIS: A CASE REPORT FROM A TROPICAL SETTING

Laila Tsaqilah¹, Putri Rizki Dwigunasari², Risa Miliawati Nurul Hidayah³, Erda Avriyanti⁴

^{1,2,3,4}Department of Dermatology and Venereology, Faculty of Medicine, Universitas Padjadjaran – Dr.

Hasan Sadikin General Hospital, Bandung, Indonesia

laila.tsaqilah@gmail.com,

putri21056@mail.unpad.ac.id,

risa.miliawati@unpad.ac.id,

erda.avriyanti@gmail.com

*Corresponding Email: laila.tsaqilah@gmail.com

Abstract

Prurigo nodularis is a chronic skin condition characterized by numerous papules, plaques, and nodules, primarily found on the extensor surfaces of the limbs. It is one of the most intensely pruritic dermatological conditions and can significantly impact quality of life. The environmental factors such as heat, humidity, and exposure to insect bites or parasitic infestations can exacerbate or trigger the condition. Various treatments have been proposed for prurigo nodularis, including topical or intralesional corticosteroid and gabapentin. We present a case of a 71-year-old woman who has experienced this condition for two years. She had previously undergone various treatments, including antihistamines and topical and oral corticosteroids. Upon examination, she exhibited multiple erythematous papulonodular lesions with varying degrees of excoriation. The dermatology life quality index (DLQI) questionnaire indicated a score of 12, reflecting a very large effect on her quality of life. The visual analogue scale (VAS) for pruritus was 9 out of 10. Histopathological examination confirmed the diagnosis of prurigo nodularis. The patient was treated with clobetasol propionate 0.05%, gabapentin at a dose of 300 mg daily, and also intralesional triamcinolone acetone 2.5 mg/ml was administered every 4 weeks, along with antihistamine and moisturizer. After two months, there was a marked reduction in pruritus reflected by reduction of VAS for pruritus to 3/10, flattening of the nodules, and an improvement in the DLQI score to 3. Intralesional corticosteroid along with gabapentin showed good effectiveness for PN. Its anti-inflammatory and immunomodulator properties effectively reduce inflammation and mitigate pruritus, making it a valuable option for managing this condition.

Keywords: intralesional corticosteroid, gabapentin, prurigo nodularis, tropical environment

1. INTRODUCTION

Prurigo nodularis (PN) is a chronic, pruritic dermatological condition characterized by multiple hyperkeratotic nodules resulting from persistent scratching.[1] These lesions are intensely pruritic and can affect individuals of various ages.[1],[2] It is estimated that there are around 87,634 cases of PN annually in the United States.[3] However, its prevalence may be underestimated in tropical countries like Indonesia, where environmental factors such as heat, humidity, and exposure to insect bites or parasitic infestations can exacerbate or trigger the condition.[2] These external stimuli may intensify pruritus and scratching behavior, contributing to the chronicity and severity of PN.[4]

The pathophysiology PN remains unclear. However, research suggests that neuroimmune and inflammatory pathways play a role in its development.[5] PN has been associated with various atopic conditions, such as atopic dermatitis, as well as systemic diseases including type 2 diabetes and chronic kidney disease.[6],[7] This condition significantly affects patients' quality of life by causing both physical and psychological distress, interfering with sleep, reducing social engagement, and limiting daily activities.[3],[8]

The goals of PN treatment are to break the itch-scratch cycle, identify and address any underlying conditions, and eliminate existing skin lesions.[9],[10] Various treatments have been proposed for prurigo nodularis, including topical or intralesional corticosteroid and gabapentin. Here we present a case of PN in elderly that showed improvement within two months.

2. METHOD

A 71-year-old Sundanese female patient presented to our Dermatology and Venereology Clinic, Dr. Hasan Sadikin Bandung, Indonesia, with a two-year history of pruritus and erythematous nodules on both forearms and thighs. The pruritus had worsened over time, interfering with sleep and daily activities. The patient initially consulted a general practitioner and attempted self-treatment for the skin lesions, but no improvement was observed. Also, she was referred to a dermatologist and got treated with several therapies, including antihistamines, topical corticosteroids, and a short course of systemic steroids, but

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no significant improvement. The patient is currently unemployed following retirement from her profession as a midwife. Due to the persistent nature of her condition, she experienced psychological distress and feelings of hopelessness. She reported a history of asthma. There was no history of food allergy. She denied any history of eczema. There was no history of similar lesions following scratching or friction. She denied the presence of rapidly enlarging nodules in sun-exposed areas, spontaneous regression of lesions, bullous eruptions, or frequent sun exposure. There was no history of chronic renal failure, liver disease, and diabetes, but the patient had been diagnosed with hypertension and treated with candesartan.

On physical examination, she was found to have grade I hypertension and a pruritic score of 9/10. Nutritional status was classified as Obesity Class I. Dermatological examination revealed multiple papules, plaques, and dome-shaped nodules with hyperkeratotic surfaces on both forearms and lower legs (Figure 1 and 2). Workup for the patient was done, including complete blood count, liver and renal function tests, and blood glucose within the normal limit. A skin biopsy with punch in size of 6 millimeter was taken from the left forearm lesion. Histopathological examination showed hyperkeratosis, parakeratosis, acanthosis, and collagen bundles in the dermis and perivascular lymphocytes (Figure 3). The Dermatology Life Quality Index (DLQI) was 12 (very large impact). The patient was diagnosed with prurigo nodularis PN.

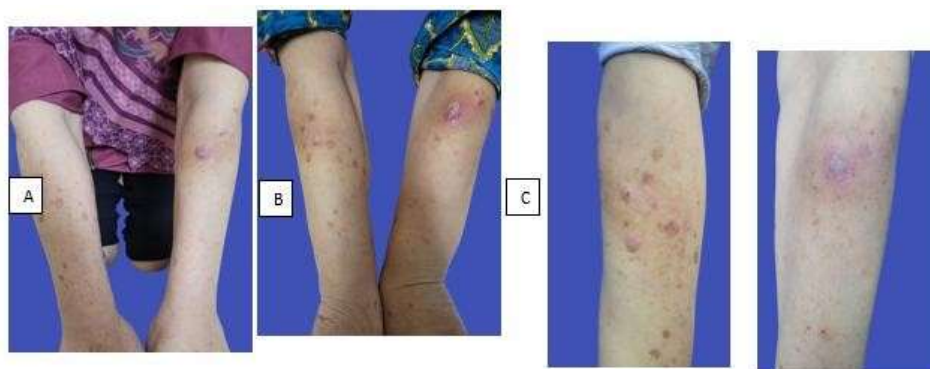


Figure 1. Clinical manifestation of PN. Multiple scaly and hyperkeratotic nodules on the both forearm. (A) Before therapy; (B) One month after initiating therapy; (C) two months after initiating therapy



Figure 2. Clinical manifestation of PN. Multiple scaly and hyperkeratotic nodules on the both thighs. (A) Before therapy; (B) One month after initiating therapy; (C) two months after initiating therapy.

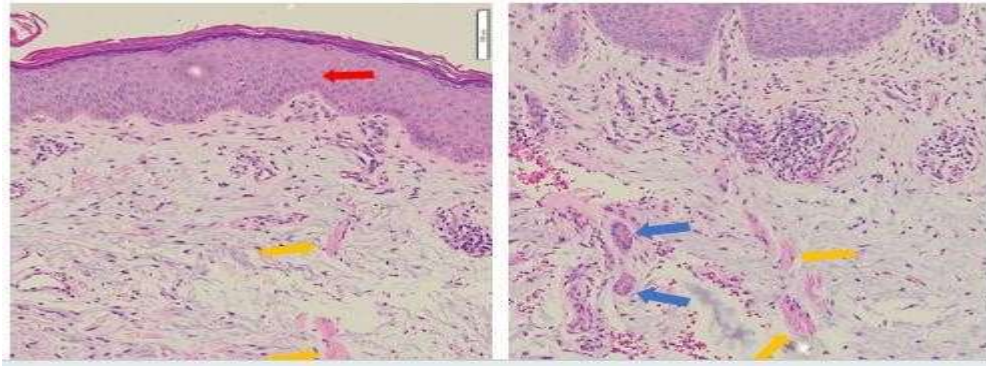


Figure 3. Histopathological findings of PN showed hyperkeratosis (red arrow), parakeratosis, acanthosis, and collagen bundles (yellow arrow) in the dermis and perivascular lymphocytes (blue arrow). (Hematoxylin & eosin, x100)

Following the diagnosis of PN, the patient was initiated on vaseline album, clobetasol propionate 0.05%, gabapentin at a dose of 300 mg daily, and also intralesional triamcinolone acetonide 2.5 mg/ml was administered every 4 weeks. However, the patient declined to undergo cryosurgery. In addition, cetirizine was continued as an antihistamine therapy. Two months after initiating therapy, the patient showed clinical improvement, as evidenced by a reduction in pruritus score to 3/10, flattening of the nodules, and an improvement in the DLQI score to 3.

3. RESULT AND DISCUSSION

Prurigo nodularis (PN) is a chronic skin disease that present with severe pruritic, multiple hyperkeratotic papules, nodules, and/or plaques.[1] Most individuals diagnosed with PN are between 51 and 65 years old, although occurrences have also been reported in other age ranges.[11] PN affects both males and females, but it tends to occur more frequently in women.[12] PN is often linked with various dermatological, systemic, and psychological disorders. Among the dermatological associations, atopic dermatitis and xerosis cutis are commonly reported. Systemic conditions that have been connected to PN include renal insufficiency, thyroid dysfunction, liver failure, hepatitis B and C, hematologic malignancies, diabetes mellitus, and hypertension.[12],[9] Research indicates that individuals with an atopic predisposition generally experience an earlier onset of PN.[9] In this case report, the patient is a 71-year-old female with a history of atopic disease and hypertension.

Indonesia is an archipelago country with a tropical climate. The temperature and humidity are relatively uniform throughout the year.[13] PN is characterized by a persistent itch-scratch cycle, which not only defines the condition but also exacerbates it.[14] The warm, humid conditions often found in tropical environments may worsen itching and potentially contribute to the development or worsening of PN in susceptible individuals.[2] While not directly caused by tropical environments, PN can be influenced by factors prevalent in such settings, like insect bites, heat, and humidity. Furthermore, PN is often associated with underlying conditions that may be more common or exacerbated in tropical climates.[15] The pathogenesis of PN is involve a complex interplay of three main processes: immune dysregulation, neural dysregulation, and a fibrotic response.[10],[16] Immune dysregulation is characterized by an increased infiltration of immune cells—such as T lymphocytes, mast cells, and eosinophils—within the dermis of affected skin. These cells release various pro-inflammatory mediators, including interleukin (IL)31, histamine, prostaglandins, eosinophil cationic protein (ECP), tryptase, and neuropeptides, which contribute to chronic inflammation and severe pruritus.[9],[10] Notably, T helper 2 (Th2) cells produce IL-31, a key cytokine implicated in the sensation of itch.[9] Neural dysregulation in PN is evidenced by dermal neuronal hyperplasia, with increased expression of neural markers such as protein gene product (PGP) 9.5 and nerve growth factor (NGF).[3] Immunohistochemical analyses have shown significantly higher levels of NGF and PGP receptors in PN lesions compared to normal skin, suggesting a role in the exaggerated neural response associated with pruritus.[3],[4] Additionally, the fibrotic process in PN involves the activation of fibroblasts and endothelial cells, promoting angiogenesis, fibrosis, and excessive

deposition of extracellular matrix components, ultimately leading to the thickened and scarred appearance of the skin lesions.[9],[10]

Early manifestations of prurigo nodularis commonly appear as erythematous papules, frequently featuring a centrally located hypopigmented macule encircled by peripheral hyperpigmentation.[10] Pruritus in PN may present as persistent, paroxysmal, or episodic in nature,[11] although some patients may also endorse burning or stinging pain.[17] Chronic and forceful scratching of the affected sites contributes to the development of excoriations, hyperkeratotic changes, and lichenification, which eventually progress to nodule formation.[10],[12] The condition predominantly involves areas that are easily reached during scratching, particularly the extensor surfaces of the limbs, and typically symmetrical distribution.[11],[9],[10]

Prurigo nodularis often reduces patients' quality of life.[9] The condition can cause sleep disturbances, limit daily functioning, and raise cosmetic concerns, all of which negatively affect a patient's psychological health.[11],[9] Individuals with PN are at higher risk of developing depression, anxiety, obsessivecompulsive disorder, and other mental health conditions.[9] A study by Kwatra et al.[18] in 2023 involving 311 PN patients in the United States reported a mean DLQI score of 17.5, indicating a very large impact on quality of life. Similarly, a 2020 systematic review of 13 studies found a mean DLQI score of 13.5, also suggesting a substantial reduction in quality of life.[8] The patient in this case had an initial DLQI score of 12, which decreased to 3 following treatment.

The diagnosis of PN is primarily clinical, based on the identification of characteristic skin lesions in typical locations. However, the definitive diagnosis is achieved through histopathological examination.[9] Histopathological features of PN include hyperkeratosis with parakeratosis, acanthosis, hypergranulosis, and inflammatory cell infiltration in the perivascular dermis.[9],[19] Notably, there is often an increase in collagen arranged vertically, particularly in the dermal papillae, accompanied by dermal fibrosis. Additionally, vascular hyperplasia may also be observed.[9] The histopathological findings in this patient support the diagnosis of PN. For measuring pruritic intensity, monodimensional tools like the Visual Analog Scale (VAS) have demonstrated strong reliability and concurrent validity. The VAS consists of a 10 scale, with "0" representing "no itch" and "10" indicating the "worst imaginable itch." [20],[21] In this case, the patient's initial VAS score was 9, indicating severe itching.

Current treatments for PN focus on interrupting the itch-scratch cycle[9] and include a variety of topical medications such as steroids including intralesional, calcineurin inhibitors, and capsaicin, and ketamineamitriptyline-lidocaine.[22] The use of emollients is considered a first-line treatment in prurigo nodularis, both in typical and recalcitrant cases.[23] However, topical treatments alone often prove ineffective, necessitating the use of systemic therapies. These systemic options include, oral antihistamines for itch relief, neuromodulators like gabapentin and pregabalin, and phototherapy.[22],[23] For more severe cases, immunosuppressive drugs such as thalidomide, mycophenolate mofetil, azathioprine, methotrexate, and cyclosporine are used, though they can have significant side effects and varying levels of success. [9],[11]

According to IFSI guideline on chronic prurigo, topical or intralesional corticosteroid is classified as step 2 therapy, whereas gabapentin is considered part of step 3 treatment.[23] Topical corticosteroids with potent to super potent strength remains the first-line topical treatment for prurigo nodularis. They help reduce inflammation and itching by modulating T cells and cytokine activity, as well as by affecting neuropeptides such as substance P.[24] Triamcinolone acetonide, in concentrations of 10–20 mg/mL injected intralesionally, has been shown to flatten lesions and provide relief from pruritus.[2] In contrast to Elmariah et al.,[11] the recommended concentration of triamcinolone is 5–20 mg/mL, administered at a volume of 0.05–0.1 mL per prurigo nodularis lesion. In this patient, we administered clobetasol propionate 0.05% cream twice daily and intralesional triamcinolone acetonide 10 mg/mL.

Gabapentin is an anticonvulsant drug with additional analgesic effects that has been utilized in managing chronic pruritus in modern clinical practice.[22] It works by targeting the spinal cord, potentially disrupting the transmission of nociceptive signals to the brain and thereby helping to suppress pruritus.[25] A study by Kouwenhoven et al.,[26] reported that gabapentin, at a dose of 900–1800 mg/day, was able to reduce pruritus from a median average score of 7 to 5.5 after four weeks of treatment. Dereli et al.[27] (2008) reported a case of prurigo successfully treated with gabapentin, initiated

at a dose of 300 mg/day and titrated up to 1200 mg/day. The treatment resulted in complete resolution of pruritus and disappearance of lichenified papules and plaques, leaving only mild residual hyperpigmentation.[27]

4. CONCLUSION

This case underscores the importance of a comprehensive and multidisciplinary treatment strategy tailored to the individual, particularly in patients with recalcitrant PN. Furthermore, environmental and psychological factors, especially in tropical settings like Indonesia, may influence the severity and chronicity of PN, necessitating contextual clinical management. Future studies are needed to explore longterm outcomes and optimize therapeutic combinations for refractory cases. **Ethic Statement**

The publications of images were included in the patient's consent for publication of the case.

Institutional approval has been obtained to publish the case details

Consent Statement

Written informed consent was obtained from the patients for the publication of case details and images. Approval has been obtained from Dr. Hasan Sadikin General Hospital to publish the case details.

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Disclosure

The authors report no conflicts of interest in this work.

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