ECRONICON OPEN ACCESS

EC PAEDIATRICS
Case Report

Unraveling Skin Issues in Children: A Case Report on Prurigo Nodularis

Vilija Bubnaitienė[1] and Agnė Čibirkaitė[2]*

[1]*Doctor, Children's Diseases Department at Lithuanian University of Health Sciences (LUHS), Kaunas, Lithuania*

[2]*Resident Doctor, Children's Diseases Department at Lithuanian University of Health Sciences (LUHS), Kaunas, Lithuania*

***Corresponding Author:** Agnė Čibirkaitė, Resident Doctor, Children's Diseases Department at Lithuanian University of Health Sciences (LUHS), Kaunas, Lithuania.

Received: October 09, 2023; **Published:** October 27, 2023

Abstract

The article describes a clinical case of prurigo nodularis, which is extremely rare in children and therefore poses diagnostic and treatment challenges. An 11-year-old patient with atopic dermatitis (AD) developed prurigo nodularis due to AD complications - impetigo relapses and Malassezia fungal infection, as a result of diseases that appear together with severe itching. The article examines and discusses the peculiarities of the course of the disease, diagnostic considerations, and therapeutic interventions employed in this case.

***Keywords**: Prurigo Nodularis; Prurigo; Chronic Prurigo; Atopic Dermatitis; Children*

Abbreviations

AD: Atopic Dermatitis; IgE: Immunoglobulin E; LUHS: Lithuanian University of Health Sciences; PN (NP): Prurigo Nodularis (Nodular Prurigo); SIT: Specific Immunotherapy; VAS: Visual Analogue Scale

Introduction

Nodular prurigo (NP) or Prurigo nodularis (PN) is an unusual, unknown etiology, difficult-to-treat, chronic skin condition characterized by skin rashes with highly itchy nodules or papules [1]. Nodular prurigo (NP) most commonly occurs in both genders of adults aged 20 to 60 years, particularly rarely in childhood [2]. Patients with NP experience very intense itching, which is challenging to treat. Spontaneous regressions are rare, and relapses are frequent, causing significant physical and psychosocial impact, severely affecting their quality of life. The quality of life of patients with NP is comparable to that of patients with heart failure, diabetes, or even stroke [3]. Since NP is extremely rare in children, this chronic skin condition is sometimes not even considered. Targeted therapy with JAK kinase inhibitor tofacitinib or interleukin-4 and interleukin-13 inhibitor dupilumab is already used in cases of resistant forms in adults, but there are no adapted treatment recommendations for children, leading to challenges in both diagnosis and treatment.

Aim of the Study

To acquaint doctors of various specialties with a clinical case of nodular prurigo, which is exceptionally rare in children. In order to improve the quality of life for children with NP, early diagnosis and appropriate treatment are of utmost importance.

Clinical Case

An 11-year-old patient sought the consultation of a pediatric allergist due to skin lesions on the trunk and limbs that appeared one month ago and have been increasing in number. These lesions were very itchy, causing sleep disturbances and interfering with daily activities. Upon examination, multiple rashes were observed - firm, well-defined reddish-blue plaques with a slightly paler center, and firm hyperpigmented keratotic nodules. There were also some weeping ulcers, and some ulcers were covered with scabs. Abundant excoriations were present, symmetrically distributed on the trunk (chest, abdomen) area, as well as on the extensor surfaces of the hands and legs (See figure 1-3). The intensity of itching was assessed by the patient using the Visual Analogue Scale (VAS), and the patient rated it 10 out of 10.

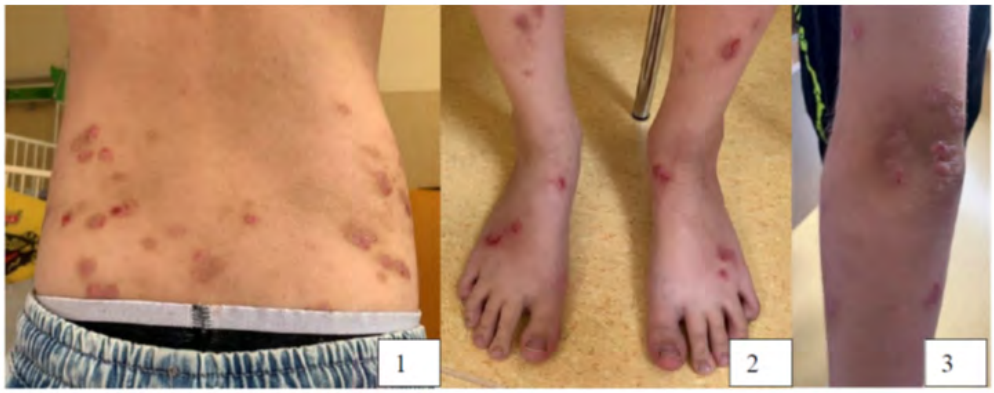

Figure 1-3: *The skin is diffusely dry. In the flexures of the neck and extremities, the skin appears lichenified and pigmented. On the trunk (breast, lower abdomen) and extensor surfaces of the limbs, well-defined dark red nodules with a slightly paler center are visible; there are also weeping ulcers with crusts, and some ulcers are covered with scabs; abundant excoriations are present.*

During infancy and early childhood, the patient experienced rashes typical to atopic dermatitis (AD) on the limbs, trunk, and neck. After an allergological examination, sensitization to certain food products and house dust mites was identified. To manage AD, the patient avoided triggering factors and received comprehensive treatment, including continuous use of emollients, second-generation antihistamines, topical corticosteroids during exacerbations, and topical calcineurin inhibitors during exacerbations and intermittently. This approach led to a remission of AD from the age of 3 to 8 years old.

However, at the age of 8, the appearance of asthma, persistent allergic rhinitis, and hay fever symptoms caused a recurrence of AD symptoms. A molecular 295 allergen test (ALEX2 macroarray) revealed sensitization to 66 allergens and their components: tree pollen (class 4), grass pollen (class 3), weed pollen (class 2), house dust mites (class 3), legumes (class 3), cereals (class 1), spices (class 1), vegetables (class 2), fruits (class 4), nuts and seeds (class 4), meat (class 1), domestic animals (class 4), and animals (class 4) (0 - negative or questionable, 1 - low, 2 - moderate, 3 - high, 4 - very high IgE concentration).

Due to the difficult-to-control course of AD, with symptoms worsening particularly in spring during tree pollen season, the patient began subcutaneous specific immunotherapy (SIT) with tree pollen allergens at the age of 9. However, during the second course of subcutaneous SIT, an anaphylactic reaction occurred, leading to the discontinuation of SIT with tree allergens.

From the age of 10, the patient experienced recurring secondary skin infections, with impetigo diagnosed six times until the age of 11 years old. Ambulatory treatment with oral antibiotics was provided, but impetigo would quickly recur after antibiotic therapy.

At the age of 11, due to impetigo and inadequate response to oral antibiotic treatment, the patient was hospitalized and treated in the Children's Diseases Department at Lithuanian University of Health Sciences (LUHS) Hospital (See figure 4-6).

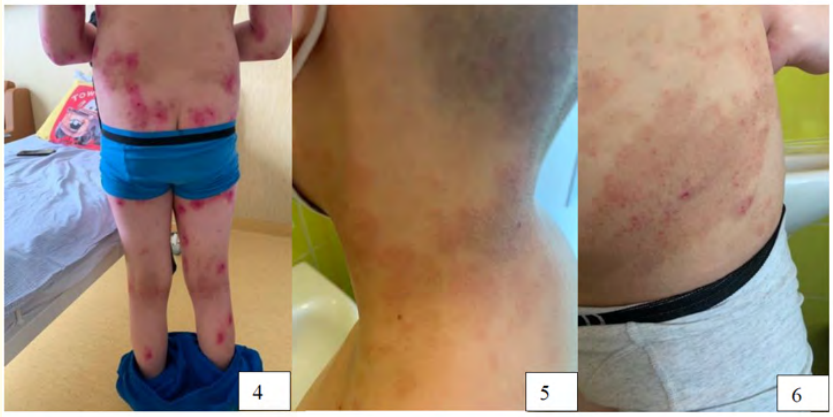

Figure 4-6: *The skin is diffusely dry. The neck, neck base, trunk, back, abdomen, and limb skin show signs of scratching, scales, and remnants of impetigo rashes. There are areas of hyperpigmentation on the neck and lower back.*

In the skin culture, *Staphylococcus aureus* and later Malassezia fungus were detected. Due to recurrent skin infections, primary immunodeficiency was suspected, and an immune system examination was performed. An increased concentration of immunoglobulin E (IgE) was found - 983.8 kU/l (age-normal range 0 - 150 kUl), which is typical for atopy; however, the concentrations of other immunoglobulins (IgA, IgM, and IgG), lymphocyte subpopulations, and the activity of monocytes' and granulocytes' phagocytosis were within normal limits.

The treatment included oily emollients, topical antiseptics (0.4% aqueous Fuchsin solution), oral second-generation antihistamines (Bilastine), intravenous antibiotic (Cefazolin) administered for 14 days, and oral antifungal treatment (Itraconazole) started when a Malassezia fungus infection was suspected in the neck and hip areas, was continued for 20 days. With this comprehensive treatment, the skin condition significantly improved (See figure 7-9), but despite the improvement, intense itching persisted (VAS 8-9).

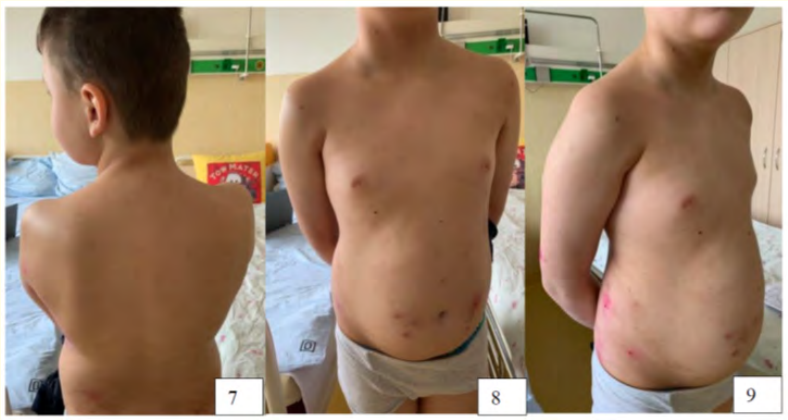

Figure 7-9: *The skin condition has improved during the course of treatment.*

A few weeks after the hospital treatment and continuing the home treatment with emollients, second-generation oral antihistamines, a rash with itchy nodules appeared and increased on the trunk and limbs (See figure 1-3). Due to this, the patient sought consultation with a pediatric allergologist and was readmitted to LUHS Hospital Children's Diseases Department.

The consulting dermatologist at the Children's Diseases Department initially diagnosed pyoderma and later suspected scabies. However, considering the patient's medical history, the course of the disease, and the nature of the rash, the scabies diagnosis was ruled out, and nodular prurigo was suspected. A skin biopsy was taken for histopathological examination, which revealed superficial and deep perivascular dermatitis, supporting the diagnosis of nodular prurigo, especially in its early stages.

The treatment included continued use of oily emollients, Fucicort (Betamethasone with Fusidic Acid) cream, later replaced by Dermovate (Clobetasol) cream. The second-generation antihistamine Opexa (Bilastine) was administered in double doses. Additionally, the patient received Doxepin, a tricyclic antidepressant with antagonist effects on alpha-adrenergic, muscarinic, and histaminic receptors, to control itching. To further alleviate itching, the patient was advised to wear socks and gloves during the night. An antiseptic cleanser "Octenisept" was used for bathing.

With this treatment approach, the patient's skin condition significantly improved, and the intensity of itching decreased (VAS 1-2) (Figure 10-12).

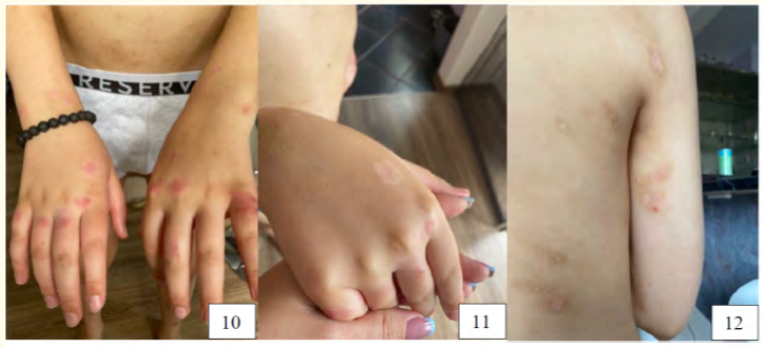

Figure 10: *1 week after the treatment.* ***Figure 11 and 12:*** *2 weeks after the treatment.*

Discussion

Prurigo nodularis (PN) is a chronic skin condition characterized by the formation of intensely itchy nodules or papules. This condition commonly affects individuals with chronic itching and is often associated with atopic dermatitis (AD) [1].

PN is more frequently diagnosed in older age, and it is very rare in childhood. Analyzing 108 clinical cases, the average age of PN was found to be 62 years [4]. The prevalence of PN does not statistically differ between men and women, and its incidence is slightly higher in developing countries [5].

The exact prevalence of PN varies depending on the region. In the UK, a retrospective analysis of articles published from 2008 to 2018 found a prevalence of 3.27/10,000 individuals (95% confidence interval) [6]. In the United States, the prevalence of PN was reported to be slightly higher at 7.2/10,000 individuals in 2016 [2]. However, data on PN frequency in children is not available. In our patient's case, PN was diagnosed at the age of 11, about 1.5 months after the onset of the condition. This is one of two cases of PN in children treated at

our clinic over 20 years. Every year in the Children's Diseases Department at Lithuanian University of Health Sciences (LUHS) Hospital we treat about 4500 inpatients and about 40000 outpatients aged from 1 month to 18 years with allergic, gastrointestinal, respiratory, urinary, cardio-rheumatological, oncological, and hematological diseases, both acute and chronic.

The exact cause of PN is unknown, but it is believed to be influenced by a combination of genetic, immunological, and environmental factors. While PN can develop in individuals with no prior history of skin problems, about 50% of cases are associated with various skin conditions that cause chronic and intense itching, most commonly with an atopic predisposition [7]. Certain systemic diseases (chronic kidney disease, cardiovascular diseases, diabetes, celiac disease, hepatitis C) and psychiatric disorders (anxiety, depression, emotional stress) increase the risk of developing PN [7,8]. There are three main hypotheses about the pathogenesis of PN. The first hypothesis suggests that PN develops in individuals whose bodies produce an increased amount of nerve growth factor due to genetic reasons, leading to an increased number of nerve fibers in the skin. Another possible cause of PN may be small fiber neuropathy of the skin, leading to the onset of intense itching. The last hypothesis examines the role of T-helper cells, their increased activity, and enhanced cytokine production. With constant scratching, firm nodules start to form [8]. In our clinical case, the patient's key risk factors were atopy and complications of atopic dermatitis, such as impetigo and Malassezia fungus-induced dermatitis, accompanied by intense itching.

PN is typically diagnosed based on medical history and objective examination findings. The number of itchy nodules can vary from a few to several hundred. The nodules can be skin-colored, brown, or even black. The extensor surfaces of the limbs are most commonly affected, but various areas of the body can be affected. Less frequently affected areas include the face, soles, palms, and upper back [9,10]. While skin biopsy is not a routine diagnostic test for PN, it can be helpful in cases of unclear diagnosis or when the response to first-line treatment is inadequate. Histopathological features characteristic of PN include epidermal hyperplasia, keratosis, and nonspecific dermal infiltration of lymphocytes, eosinophils, neutrophils, and macrophages [11]. In our patient's case, PN was diagnosed based on objective examination findings, and the histopathological examination revealed superficial and deep perivascular dermatitis, which is consistent with the diagnosis of PN.

PN is associated with intense itching that significantly affects the quality of life. It is believed that the quality of life of individuals with PN is comparable to that of patients with heart failure, diabetes, or those who have experienced a stroke [3]. Selecting the most suitable, individually tailored treatment is crucial. Although PN significantly impairs the quality of life, there is no universally recognized specific treatment for PN. In many cases, the choice of treatment relies on the physician's individual judgment [7]. During PN, intense scratching leads to skin trauma and the formation of nodules. Managing itching is one of the most important aspects. Basic treatment for alleviating itching includes oral antihistamines, tricyclic antidepressants (e.g., Doxepin, Amitriptyline), and antiepileptic drugs (e.g., Gabapentin, Pregabalin). In milder cases with a few nodules, topical corticosteroids, calcineurin inhibitors, and vitamin D analogs are commonly prescribed. In cases where large areas of the skin are affected, phototherapy is recommended, which is used in children from the age of 16. Treatment with immunosuppressive agents (e.g., Methotrexate, Cyclosporine) or biological therapy (JAK kinase inhibitor Tofacitinib or interleukin-4 and interleukin-13 inhibitor Dupilumab) may be considered [8]. In our patient's case, Doxepin significantly reduced itching and, in combination with previously prescribed AD treatment, controlled the course of PN, significantly improving the patient's skin condition and quality of life.

Conclusion

1. While nodular prurigo is an extremely rare chronic skin condition, its onset, although uncommon, should be considered in any patient complaining of intensely itchy nodular rash.
2. For our patient, the main factors that triggered PN were atopic dermatitis and it's complications – skin infections, such as impetigo and Malassezia fungus-induced dermatitis, accompanied by intense itching.

3. The pathogenesis of nodular prurigo is not clearly understood, but it is associated with chronic inflammation in the skin, leading to intense scratching, skin trauma, and the formation of nodules. Therefore, managing itching is one of the most important ways to control PN and should be individually tailored for each patient.
4. Our examined case demonstrates the importance of not forgetting atypical cases in children when diagnosing skin diseases. Such cases may more commonly manifest in young age. Accurately identifying the diagnosis is crucial for controlling the course of the disease.

Bibliography

1. Williams KA., *et al*. "Prurigo nodularis: Pathogenesis and management". *Journal of the American Academy of Dermatology* 83.6 (2020): 1567-1575.
2. Huang AH., *et al*. "Real-World Prevalence of Prurigo Nodularis and Burden of Associated Diseases". *Journal of Investigative Dermatology* 140.2 (2020): 480-483.e4.
3. Whang KA., *et al*. "Health-related quality of life and economic burden of prurigo nodularis". *Journal of the American Academy of Dermatology* 86.3 (2022): 573-580.
4. Iking A., *et al*. "Prurigo as a symptom of atopic and non-atopic diseases: aetiological survey in a consecutive cohort of 108 patients". *EADV: European Academy of Dermatology and Venereology* 27.5 (2013): 550-557.
5. Boozalis E., *et al*. "Ethnic differences and comorbidities of 909 prurigo nodularis patients". *Journal of the American Academy of Dermatology* 79.4 (2018): 714-719.e3.
6. Morgan CL., *et al*. "Epidemiology of prurigo nodularis in England: a retrospective database analysis". *British Journal of Dermatology* 187.2 (2022): 188-195.
7. Frølunde AS., *et al*. "Non-Atopic Chronic Nodular Prurigo (Prurigo Nodularis Hyde): A Systematic Review of Best-Evidenced Treatment Options". *Dermatology* 238.5 (2022): 950-960.
8. Watsky Kalman. Prurigo nodularis (2022).
9. Kwon CD., *et al*. "Diagnostic Workup and Evaluation of Patients with Prurigo Nodularis". *Medicines* 6.4 (2019): 97.
10. Elmariah S., *et al*. "Practical approaches for diagnosis and management of prurigo nodularis: United States expert panel consensus". *Journal of the American Academy of Dermatology* 84.3 (2021): 747-760.
11. Weigelt N., *et al*. "Prurigo nodularis: systematic analysis of 58 histological criteria in 136 patients". *Journal of Cutaneous Pathology* 37.5 (2010): 578-586.

Volume 12 Issue 11 November 2023