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Case Report

Netherton Syndrome in a 9-Month-Old Child: Unraveling a Complex Dermatologic Disorder

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Abstract

Netherton syndrome is a rare autosomal recessive disorder caused by mutations in the *SPINK5* gene, leading to LEKTI protein dysfunction, impaired skin barrier function, and immune dysregulation. It manifests as a triad of ichthyosiform erythroderma, trichorrhexis invaginata (bamboo hair), and atopic diathesis, often mimicking other inflammatory dermatoses. We report a 9-month-old Javanese Indonesian male infant presenting with extensive erythematous, scaly skin lesions and severe pruritus. Laboratory tests revealed elevated eosinophil count and high serum immunoglobulin E levels. Trichoscopic examination identified trichorrhexis invaginata, confirming clinical suspicion of Netherton syndrome. A skin biopsy further supported the diagnosis of this disease. The patient initially responded to topical corticosteroids, but symptoms recurred upon tapering. Systemic therapy with low-dose methotrexate was introduced, leading to a marked improvement in skin lesions and pruritus. This case highlights the importance of early recognition of the syndrome to initiate

appropriate treatment and prevent misdiagnosis. Comprehensive management should address skin barrier restoration, inflammation control, and allergy management. Early multidisciplinary intervention can significantly improve the quality of life and reduce the risk of complications in affected patients.

Keywords
Netherton syndrome; *SPINK5*; trichorrhexis invaginata; methotrexate

1. Introduction

Netherton syndrome is a rare form of ichthyosis that is inherited in an autosomal recessive manner [1]. This condition results from genetic mutations, primarily affecting the *SPINK5* gene located on chromosome 5q32, which leads to a dysfunctional lymphoepithelial Kazal-type-related inhibitor (LEKTI) protein [2, 3]. The absence of functional LEKTI disrupts epidermal protease regulation, causing impaired skin barrier function and dysregulated immune responses [2]. The incidence of Netherton syndrome is estimated to be 1 in 200,000 births, with a prevalence ranging from 1 to 9 per million individuals [1, 4, 5].

This syndrome is characterized by chronic epidermal inflammation and excessive desquamation, which can often be fatal during the perinatal period [1]. The clinical triad of Netherton syndrome includes ichthyosiform dermatitis, trichorrhexis invaginata (bamboo hair), and atopic diathesis with elevated IgE levels and eosinophilia [2]. Early diagnosis is crucial to ensure appropriate management for affected patients [4]. Patients with Netherton syndrome are highly susceptible to complications arising from impaired skin barrier function, including recurrent cutaneous and systemic infections, dehydration with electrolyte imbalance, metabolic disturbances, failure to thrive, growth retardation, and an increased risk of allergic disorders and sepsis. These complications contribute to the significant morbidity and mortality associated with the condition and underscore the importance of early diagnosis and comprehensive care [2, 4]. The treatment of Netherton syndrome is primarily supportive, focusing on symptom control and complication prevention [2].

This paper describes a case of Netherton syndrome in a 9-month-old child, emphasizing the importance of early recognition and appropriate management to improve patient outcomes.

2. Case Report

A 9-month-old Javanese Indonesian male infant was referred to the dermatology clinic with complaints of extensive erythematous patches and peeling skin covering almost the entire body. The skin changes initially appeared as red patches in the neck folds and progressively spread to the trunk, arms, and legs over five months. The child exhibited severe pruritus, leading to persistent scratching. The condition worsened over time, with increased scaling and inflammation. Two months before hospital admission, the parents sought medical treatment at a local healthcare center, but initial therapy failed to produce any improvement. The patient was subsequently referred to a tertiary care hospital for further evaluation.

There was no history of similar skin conditions in family members, consanguinity, or other hereditary disorders. The child was born full-term via vaginal delivery, with no reported perinatal

complications. The parents denied any history of drug or food allergies. At 9 months of age, the patient's weight was 7.8 kg (between –1 SD and –2 SD WHO growth standards), while his length was 65 cm (below –2 SD), indicating growth retardation. Routine skincare included commercial baby bath soap and oil-based emollients.

On physical examination, the patient's vital signs were within normal limits. A dermatological examination revealed erythematous plaques with scaling on the face, chest, abdomen, back, and all four extremities (Figure 1). Laboratory tests indicated marked eosinophilia (13.2%) and significantly elevated IgE levels (2500 IU/mL). IgE testing was ordered due to the persistence of widespread dermatitis refractory to standard treatment, recurrent skin infections, and growth retardation, raising suspicion for an underlying immunologic or genetic disorder rather than routine evaluation of chronic eczema. Peripheral blood smear findings suggested a hypersensitivity reaction rather than hematologic malignancy. Trichoscopic examination was performed due to clinical suspicion of hair shaft abnormalities, independent of the IgE result, and revealed trichorrhexis invaginata (bamboo hair), a hallmark feature of Netherton syndrome (Figure 2). Histopathological examination showed orthokeratosis with a basket weave pattern, focal parakeratosis, hypogranulosis, spongiosis with neutrophilic exocytosis, and mild acanthosis. There was also a neutrophil collection (abscess) in the corneal layer. Inflammatory infiltration consisting of lymphocytes, neutrophils, and eosinophils was observed in the dermis, primarily in the perivascular region (Figure 3). These findings confirmed the diagnosis of Netherton syndrome. Genetic mutation testing was not performed due to resource limitations.

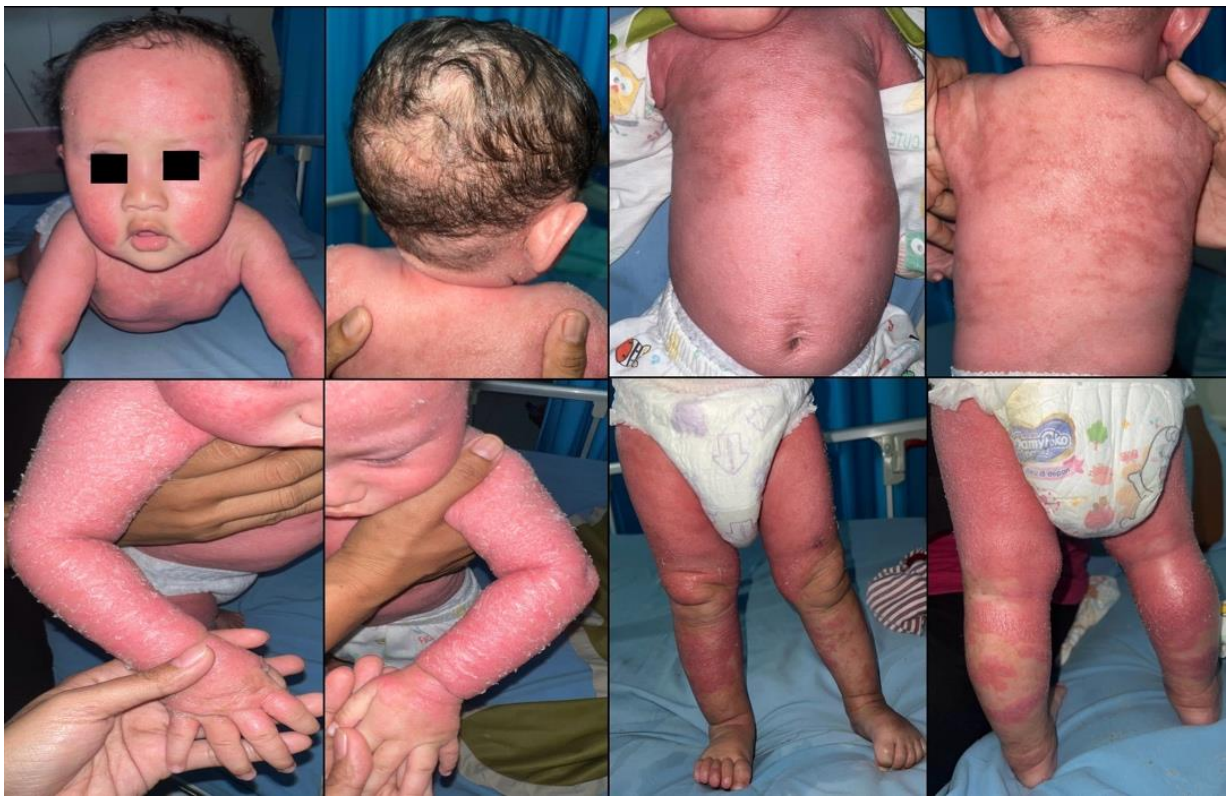

Figure 1 Erythematous plaques with scaling on the face, chest, abdomen, back, and all four extremities.

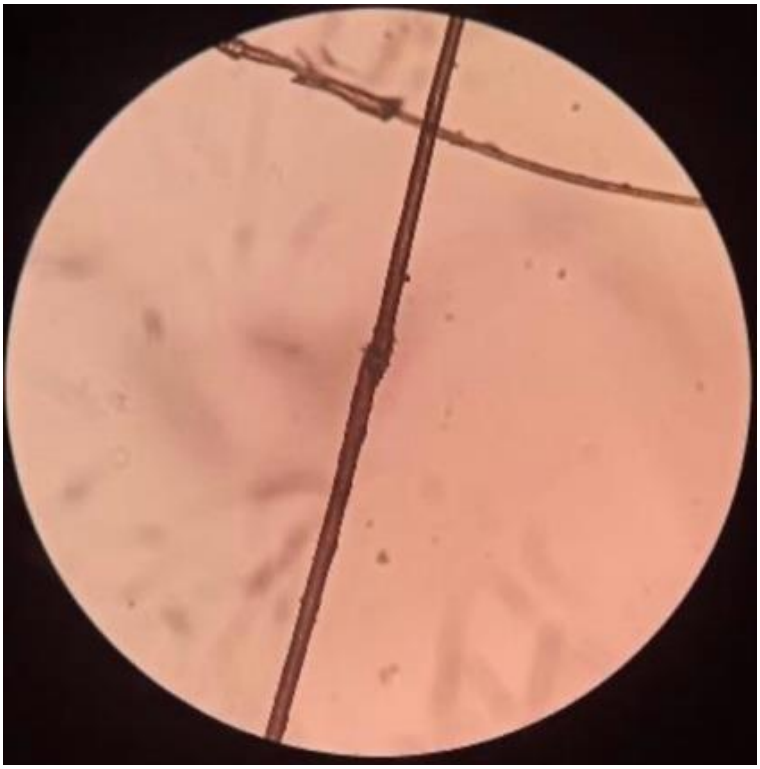

Figure 2 Trichoscopy examination: Trichorrhexis invaginata (bamboo hair).

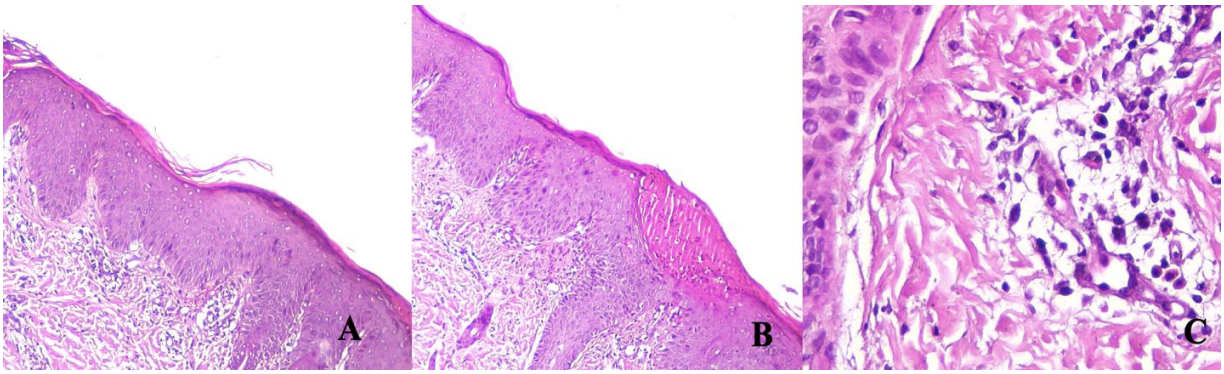

Figure 3 Histopathological findings with H&E Staining (A) Orthokeratosis with a basket weave pattern, focal parakeratosis, focal hypogranulosis, spongiosis, and mild acanthosis. (B) Neutrophil aggregation (abscess) in the corneal layer. (C) Patchy inflammatory cell infiltration consists of lymphocytes, neutrophils, and eosinophils, primarily in the perivascular area.

Initial treatment included topical emollients enriched with a provitamin D3 lotion (5000 IU) and antihistamines to alleviate pruritus. As symptoms progressed, oral corticosteroids were introduced, with methylprednisolone (4 mg daily, corresponding to approximately 0.51 mg/kg/day for a body weight of 7.8 kg) providing temporary improvement. However, prolonged corticosteroid therapy led to disease recurrence upon tapering. The treatment was subsequently switched to oral methotrexate (5 mg once weekly), administered together with daily folic acid supplementation (1 mg/day, except on the methotrexate day), and continued antihistamines. This modification resulted in significant clinical improvement, characterized by a reduction in erythema and scaling over the subsequent months (Figure 4).

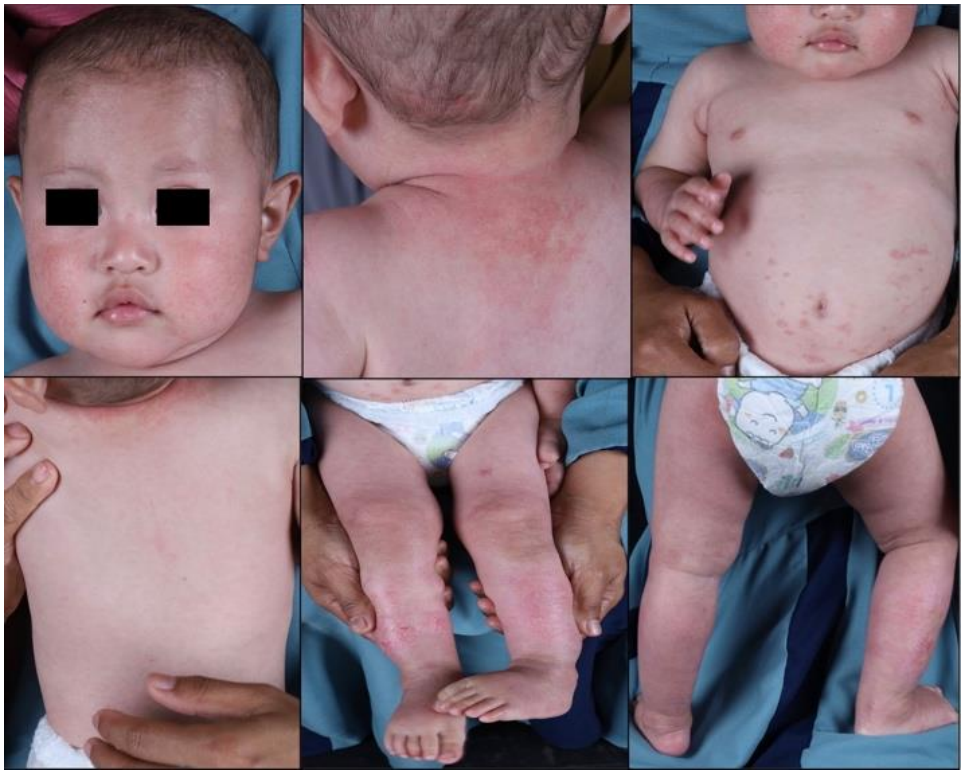

Figure 4 Erythematous plaques without scaling on the face, chest, abdomen, back, and all four extremities.

At the six-month follow-up, the patient maintained a marked reduction in erythema and scaling, with improved pruritus and growth parameters. Methotrexate was continued for six months with regular laboratory monitoring (complete blood count and liver function tests) and clinical assessments, without clinically significant adverse events.

2.1 Ethics Statement

Written informed consent for publication, including the use of clinical images, was obtained from the patient's legal guardian. Ethical standards were maintained throughout the patient's evaluation and treatment.

3. Discussion

Netherton syndrome is a multisystem disorder characterized by skin barrier dysfunction, immunological abnormalities, and hair shaft defects. The primary pathogenic mechanism involves mutations in the *SPINK5* gene, which encodes the LEKTI protein [2, 4]. This protein regulates epidermal serine proteases, including kallikreins, which are responsible for the controlled desquamation of the stratum corneum [3]. In the absence of functional LEKTI, excessive protease activity leads to premature corneocyte detachment, resulting in chronic inflammation, impaired barrier function, and increased transepidermal water loss [2, 4, 6].

The syndrome manifests early in life, often presenting as congenital ichthyosiform erythroderma. Infants with Netherton syndrome are highly susceptible to dehydration, infections, and metabolic imbalances due to compromised skin integrity [7, 8]. The condition frequently mimics other

inflammatory dermatoses, including psoriasis and atopic dermatitis, necessitating a thorough diagnostic workup [9]. In this case, differential diagnoses included psoriatic erythroderma and erythroderma secondary to atopic dermatitis [10]. However, the presence of trichorrhexis invaginata was a distinguishing feature favoring Netherton syndrome. Histopathology is a valuable diagnostic tool, typically showing a psoriasis-like epidermal hyperplasia, a diminished stratum granulosum, and a superficial perivascular lymphocytic infiltrate. Laboratory findings often reveal eosinophilia and elevated IgE levels, indicative of underlying atopic diathesis [8]. DNA sequencing of the *SPINK5* gene is the gold standard for diagnosis, though it may not always be available in clinical settings [3].

The management of Netherton syndrome is mainly supportive, focusing on restoring the skin barrier, controlling inflammation, and minimizing allergic reactions. Topical emollients and moisturizers play a crucial role in reducing transepidermal water loss. Anti-inflammatory agents, such as topical corticosteroids and topical calcineurin inhibitors, are used to manage flares, though long-term steroid use can lead to complications [8, 11]. Systemic therapies, including methotrexate, cyclosporine, and intravenous immunoglobulin, have been employed in severe cases with varying degrees of success [8].

In this case, initial systemic corticosteroid therapy with oral methylprednisolone provided symptomatic relief but was associated with disease recurrence upon discontinuation. The transition to oral methotrexate (5 mg once weekly) resulted in sustained clinical improvement, highlighting its potential as a steroid-sparing agent. The patient has been followed for six months, showing marked improvement with no significant adverse events. Although methotrexate use in infants is off-label and not curative, it was considered in this case due to severe disease, poor response to conventional therapy, and significant impact on quality of life. Treatment duration remains individualized, with close monitoring and multidisciplinary management.

4. Conclusion

This case highlights the diagnostic and therapeutic challenges of Netherton syndrome in infancy. Early recognition, supported by clinical features, trichoscopy findings, and histopathology, is essential for timely intervention. While no definitive cure exists, a multidisciplinary management approach, including systemic immunomodulation and intensive skincare, can significantly improve patient outcomes. Awareness of this rare condition among dermatologists and pediatricians is crucial for early diagnosis and optimal treatment strategies.

Author Contributions

Dwinanda Almira Rizkiani was responsible for patients' data collection, drafted the case report manuscript, and reviewed and approved the final version for publication. Erliana Tantri Harsono assisted in drafting the manuscript and reviewed and approved the final version for publication. Raden Roro Rini Andayani assisted in drafting the manuscript and reviewed and approved the final version for publication. Hanggoro Tri Rinonce contributed to the histopathological evaluation and interpretation of the skin biopsy findings, providing essential input for establishing the final diagnosis. Niken Trisnowati contributed to the interpretation of clinical data, assisted in drafting the manuscript, and reviewed and approved the final version for publication. Retno Danarti was responsible for providing oversight and guidance in case report preparation, assisting in interpreting

clinical data, revising the manuscript critically for intellectual content, and finalizing and approving the manuscript for submission and publication. All authors have read and approved the published version of the manuscript.

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Competing Interests

The authors have declared that no competing interests exist.

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