# Vulvovaginal involvement in Netherton syndrome: A case report

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***Key words:*** genodermatosis; Netherton syndrome; vulvovaginal.

## INTRODUCTION

Netherton syndrome (NS) is an autosomal recessive, rare genodermatosis and ichthyosiform disease caused by loss-of-function mutations in the SPINK5 gene on chromosome 5q32,[1,2] a gene thought to be implicated in epidermal cell growth and differentiation.[3] The identification of this gene mutation makes a definitive diagnosis, but NS can also be diagnosed clinically. The incidence is estimated to be around 1 case per 200,000 individuals.[2-4] It presents at birth or shortly after with a classic triad of atopic diathesis with elevated serum immunoglobulin E (IgE), pathognomonic hair shaft anomalies (trichorrhexis invaginata), and ichthyosis linearis circumflexa.[1,2,4] This disease mainly affects the skin, by desquamation of the stratum corneum and impairment of the skin barrier, but it also disturbs the hair and the immune system.[1] Treatment is unfortunately not curative and relies on conservative options.[2,4] A combination of therapies aiming to restore the skin barrier and modulate the immune response is thought to be most effective.[2] There have been some case reports about this disease and its potential association with genital clinical presentation such as papillomatous skin tumors and bacterial vaginosis, without describing vulvar and vaginal manifestations and how to address the problem. We therefore report a case of a female patient with difficult to treat vulvovaginal involvement of NS.

*Abbreviations used:*

IgE: immunoglobulin E
NS: Netherton syndrome

## CASE REPORT

A 27-year-old woman with NS was referred to our clinic for chronic and severe vulvovaginal symptoms. She presented with the classic manifestations of NS including ichthyosis linearis circumflexa, trichorrhexis invaginata, and multiple known allergies to eggs, animals, and seasonal allergies. She was also a smoker. She was born to nonconsanguineous parents and had no family history of skin disorder. From the age of 13, the patient presented with episodes of thick white discharge that was abundant at times. She also suffered significantly from NS vulvar involvement. Through the years, on physical examination, the patient consistently had widespread erythematous plaques with double-edged scales that showed maceration under the breast (Fig 1, *A*), in the groin area and on the vulva (Fig 1, *B*). These plaques were occasionally associated with significant edema of labia minora. Vaginal examination showed normal vaginal walls and cervix and significant white discharge with normal pH (Fig 2).

Wet smears of vaginal discharge showed normal flora and abundant normal epithelial cells, emphasizing the desquamative nature of vaginal involvement. On 3 separate occasions, vaginal discharge was milky and grey and showed an elevated pH, positive swift test, and clue cells on wet smear. The patient was treated for bacterial vaginosis on those occasions. Vulvar and vaginal cultures occasionally

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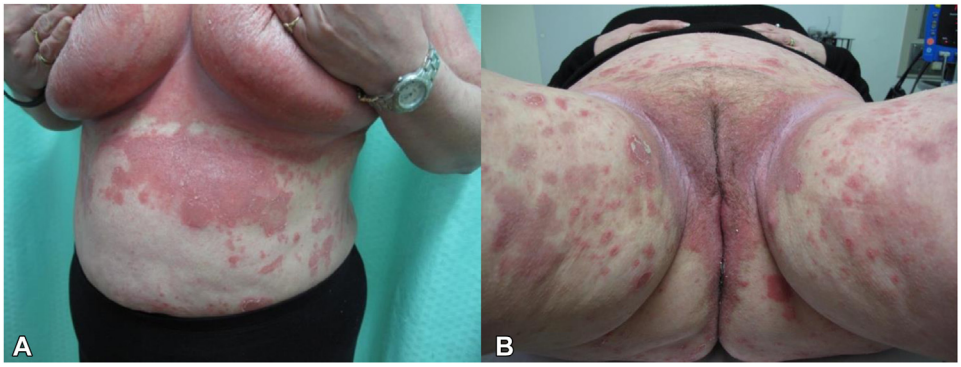


**Fig 1.** Erythematous confluent plaques with double-edged scales in Netherton syndrome. **A,** under the breast and on the abdomen. **B,** in the groin area and on the vulva with intertriginous maceration.

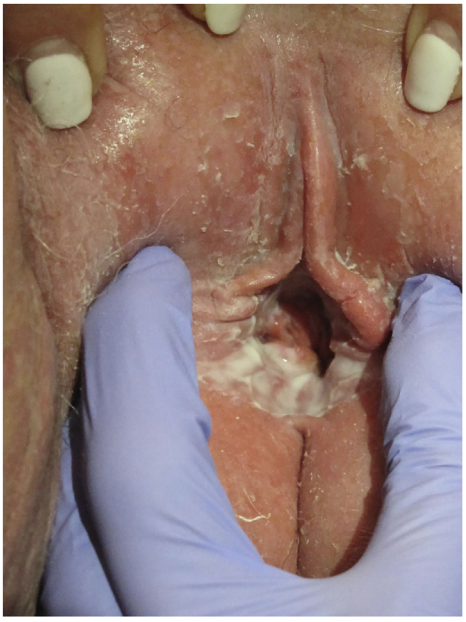

**Fig 2.** Significant *white* vaginal discharge.

showed bacterial growth for group B streptococcus and staphylococcus aureus. Cultures were consistently negative for yeast. On one occasion, she was treated for a suspected pelvic inflammatory disease although sexually transmitted disease tests were negative. Through the course of her follow-up, she developed vulvar lichen simplex chronicus and vestibulodynia for which she was treated and was also diagnosed with hidradenitis suppurativa which presented itself with inflammatory nodules and sterile abcesses in her groin and axillae.

Different treatments were tried to treat her Netherton syndrome-associated cutaneous and vulvovaginal issues, including systemic and topical antibacterial and antifungal treatments, topical corticosteroids, pimecrolimus and crisaborole, emollients, zinc oxide paste, one course of oral prednisone, intravenous and subcutaneous immunoglobulins, dupilumab and oral contraceptives. To this day, her disease has improved. However, her condition continues to flare premenstrually and following sun exposure. Continuous oral contraceptives helped with discharge as well as vulvar and generalized skin involvement (Fig 3).

## DISCUSSION

Netherton syndrome (NS) is a rare genodermatosis with an atopic predisposition. Only a few cases of vulvar and vaginal involvement have been reported in the literature, such as papillomatous genital lesions associated with bacterial infection and human papillomavirus infection.[5-8] One case of recurrent bacterial vaginosis in a female patient with NS was reported in 1999.[9] The authors proposed that patients with NS might have a lower tolerability towards bacterial cytotoxins associated with bacterial vaginosis, thus increasing vulvovaginal desquamation and transudation.[9] The SPINK5 gene encodes a reversible serine protease inhibitor called LEKTI expressed in stratified epithelium such as the skin and the vaginal mucosa,[2] which could explain the susceptibility to vulvovaginal symptoms in NS patients. The immune system dysfunction associated with this syndrome predisposes to skin infections predominantly with *Staphylococcus aureus*.[2,9] Cutaneous barrier disruption enables pathogen penetration and promotes inflammation,[2] which we observed with our patient. However, none of the reviewed articles mentioned how to manage these vulvovaginal chronic symptoms. Since NS is characterized by scaling erythroderma on most parts of the body,[10] the genital area could easily be forgotten and overlooked. Our case emphasizes the complexity of treating vulvovaginal lesions in

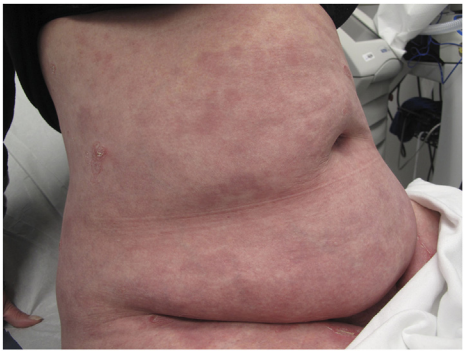

**Fig 3.** Improvement under treatment.

NS patients, with oral contraceptives providing significant relief for our patient. Furthermore, we did not find any report relating hidradenitis suppurativa to Netherton syndrome.

## CONCLUSION

Our case highlights vulvovaginal involvement in a female patient with a long history of NS, and the multiple treatments that were tried with only a few providing substantial improvement of symptoms. Though many treatments such as intravenous immunoglobulins, anti-TNF-alpha, anti-IL-17A, and gene therapy are promising,[2] NS vulvovaginal involvement could also benefit from continuous oral contraceptive use. Lubricants for sexual activities and zinc oxide paste for skin fissures in intertriginous areas should also be proposed to patients. Physicians should think of NS in the presence of hair shaft anomalies and profound scaly erythroderma that does not respond to usual atopic dermatitis treatment, but they should also be aware that these signs can be present on any part of the body including vulvovaginal areas. To prevent distress associated with genital NS presentation, we want to emphasize the importance of dermatologists asking their NS female patients about vulvovaginal symptoms for a better long-term treatment outcome.

### Conflict of interest

None disclosed.

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