

# Netherthon syndrome revealed by recurrent skin infections: a case report

---

## ABSTRACT

Netherthon syndrome (NS) is a rare autosomal recessive disorder characterized by a triad of symptoms including a scaly skin condition known as circumflex linear ichthyosis, hair shaft abnormalities known as trichorrhexis invaginata, and an atopic terrain which predisposes patients to allergic reactions and asthma.

The disorder is caused by mutations in the SPINK5 gene which encodes for a serine protease inhibitor called LEKTI. This leads to a disruption in the skin's natural barrier function and a hyperactive immune response, resulting in the characteristic symptoms of NS.

Newborns with NS may have a poor prognosis, with possible life-threatening complications and high postnatal lethality. However, the symptoms can improve with age and growth, and management of the disorder is aimed at controlling the symptoms and preventing complications such as infections. Symptomatic treatment for cutaneous xerosis and management of infections are commonly used. Additionally, topical emollients and systemic immunoglobulin therapy may be used to help manage the condition.

We present a clinical case that can help raise awareness about rare diseases such as Netherthon syndrome and improve early diagnosis and management. It is important for healthcare providers to be familiar with the clinical and etiological characteristics of these conditions to ensure that patients receive appropriate care and treatment.

The reported case is an infant of 3 months old, who presents from the age of 2 months a cutaneous xerosis under the care of a dermatologist, and managed by symptomatic treatment. Based on the clinical presentation and examination (The hair trichoscopy), the infant have Netherthon syndrome with a superimposed bacterial infection leading to ichthyosis linearis circumflexa superinfected.

*Key words: netherthon syndrome, genodermatosis, ichthyosis, trichoscopy.*

## 1. INTRODUCTION:

Netherthon syndrome (NS) is a rare autosomal recessive genodermatosis with an incidence of 1 case per 200,000 newborns. It is characterized by a triad of symptoms including circumflex linear ichthyosis, trichorrhexis invaginata which may be absent in the first years of life [1], and an atopic terrain. In 2000 the involvement of the SPINK5 gene in Netherthon syndrome was established [2].

The prognosis of Netherthon syndrome can be severe in newborns, with possible life-threatening complications and high postnatal lethality. The skin manifestations and hair shaft abnormalities persist throughout life, but the symptoms can decrease with age and the growth often improves during the second year of life. The severity of the disease varies widely, even within the same family. Some individuals may have a milder form of the disease, while others may have more severe symptoms that require more aggressive management.

## 2. PRESENTATION OF CASE:

We present a clinical case with the written consent of the patient. The reported case is an infant of 3 months old, female sex, from a consanguineous marriage, with an asthmatic father. The pregnancy was followed up, full term. The mother had a caesarean section for breech presentation, the birth weight was 2900 g (6400 pounds). There was no neonatal respiratory

distress, the umbilical cord fell off at 7 days of life, the patient is correctly receiving her vaccines, and has a correct psychomotor evolution for the age.

She presents from the age of 2 months a cutaneous xerosis under the care of a dermatologist, and managed by symptomatic treatment (skin emollient and hydrocortisone cream).

The infant is presenting at the emergency department for a fever resistant to the antipyretic treatment, The clinical examination of the child showed a patient in good general condition, active and reactive, Febrile (39 degrees), well hydrated. A failure to thrive was noted (-2 major growth percentiles; weight: 3500 g, height: 55 cm, PC: 41 cm).

The patient has a severe form of ichthyosis linearis circumflexa that has become superinfected, resulting in purulent pustules. The lesions are predominantly located on the face and neck skin and are characterized by thick yellow-brown scaly patches on a serpiginous erythematous base. The eyebrows are sparse, particularly on their lateral parts, with short, brittle hair in the frontal and lateral regions [Fig. 1]. The rest of the body has an erythematous squamous skin.



**Fig.1: An ichthyosis linearis circumflexa superinfected predominant on the face and neck skin.**

The patient was hospitalized, paraclinical exploration found a neutrophil hyperleukocytosis at  $20.8 \times 10^3/\mu\text{l}$  with a hypereosinophilia at  $1800/\mu\text{l}$ , a C-reactive protein at 160 mg/l, with an elevated level of IgE. A congenital and acquired immune deficiency exploration was realized without finding any deficit. The hair trichoscopy revealed the presence of bamboo hairs: the trichorrhexis invaginata [Fig. 2].

The patient's laboratory results suggest an inflammatory process, as evidenced by the neutrophil hyperleukocytosis, hypereosinophilia, and elevated C-reactive protein. The elevated IgE level is also consistent with atopic dermatitis, which is commonly seen in Netherton syndrome. The fact that no congenital or acquired immune deficiency was found suggests that the patient's symptoms are likely related to Netherton syndrome.



**Fig.2: Trichorrhexis invaginata (bamboo hair) revealed by the hair trichoscopy.**

Skin biopsy revealed a hyperkeratosis, an acanthosis and a focal hypergranulosis with a superficial perivascular lymphocytic infiltrate.

The patient got intravenous antibiotics (amoxicillin and clavulanic acid) for 15 days and intravenous Immunoglobulins. She also got topical medications including low potency corticosteroids and emollients. The clinical evolve was good: afebrile within 48 hours with desquamation and progressive healing of the lesions [Fig. 3].



**Fig.3 (a,b): Desquamation and progressive healing of the predominantly facial and neck lesions.**

Based on the clinical presentation and examination, the infant have Netherton syndrome (NS) with a superimposed bacterial infection leading to ichthyosislineariscircumflexa superinfected. The sparse and brittle hair and erythemasquamous skin are consistent with the characteristic hair shaft abnormality (trichorrhexisinvaginata) and atopic terrain seen in Netherton syndrome. The patient's family history of consanguinity and asthma in the father are also consistent with an autosomal recessive inheritance pattern for Netherton syndrome. It is important to continue close monitoring and management of the patient's symptoms, including infection control, topical treatment, and potential use of systemic immunomodulatory therapies.

### **3. DISCUSSION:**

Netherton syndrome is a rare genetic disorder that affects the process of skin cell formation. It is inherited in an autosomal recessive manner. In 2000 [2], the involvement of the SPINK5 gene in Netherton syndrome was established. Mutations in this gene are known to be associated with the condition, and coding polymorphisms of SPINK5 have also been linked to atopic dermatitis and asthma [3].

NS can be diagnosed clinically by the presence of the characteristic triad of symptoms including circumflex linear ichthyosis, trichorrhexisinvaginata, and an atopic terrain, the genetic testing can confirm the diagnosis by identifying mutations in the SPINK5 gene [4].

Atopic manifestations are common in NS and can include asthma, allergic rhinitis, and eczema. These manifestations are thought to be related to the underlying genetic defect affecting the skin barrier function and immune system [1].

The ichthyosislineariscircumflexais a particular variety of the hereditary ichthyosis, with autosomal recessive transmission. It starts at the birth or after a free interval of a few weeks, with an erythemasquamous state often associated with hypotrichosis, then taking on the appearance of erythematokeratotic lesions with a circinate arabesque arrangement and a double border of desquamation [5].

Trichorrhexisinvaginata, also known as "bamboo hair," is a hair shaft abnormality characterized by nodular thickenings and longitudinal splitting of the hair shaft. It is a diagnostic feature of NS and is often accompanied by hair shaft fragility and hair loss [6]. The hair is short, weak, sparse and dull, the trichoscopy examination on the hair or better on the eyebrows [6], reveals the pathognomonic sign called trichorrhexisinvaginata, which may be absent in the first years of life [1].

Netherton syndrome can be complicated with various symptoms, including allergic manifestations, chronic non-infectious diarrhea, neurological deficits, hypernatremic dehydration, impaired thermoregulation, growth retardation, and infections/sepsis. These complications can have significant effects on the patient's overall health and quality of life. It is important to monitor and manage these symptoms to improve the prognosis [7, 8, 9].

It is important to note that topical therapy is the first line of treatment, with emollients and antiseptics being recommended for daily use. Topical corticosteroids and calcineurin inhibitors may be used in the short term and for localized areas during flares. Narrow band UVB phototherapy is also a possible option. In cases of superinfection, an antistaphylococcal antibiotic may be necessary. Additionally, regular dermatological examinations are recommended due to the increased risk of skin cancer [10]. Management of NS is primarily supportive, with emphasis on maintaining skin hydration and preventing infections.

### **4. CONCLUSION:**

Early diagnosis of Netherton syndrome is important for appropriate management and improving the short and long term prognosis. The diagnosis may be delayed due to similarities with atopic dermatitis and other skin disorders, but histological examination of the hair (trichoscopy) can aid in making a definitive diagnosis.

With early diagnosis, patients can receive tailored treatment including topical emollients, low potency corticosteroids, and systemic immunomodulators, and can be monitored for potential complications such as hypernatremic dehydration, recurrent infections, and malabsorption.

It's important for the patient to continue regular follow-up with a dermatologist to monitor for any relapses or complications. Long-term management of Netherton syndrome may involve a combination of topical therapy, systemic therapy, and supportive care for associated manifestations.

## 5. REFERENCES:

1. Fartasch M, Williams ML, Elias PM. Altered lamellar body secretion and stratum corneum membrane structure in Netherton syndrome: differentiation from other infantile erythrodermas and pathogenic implications. *Arch Dermatol* 1999; 135:823–32.
2. Chavanas S, Bodemer C, Rochat A, et al. Mutations in SPINK5, encoding a serine protease inhibitor, cause Netherton syndrome. *Nat Genet* 2000; 25:141–2.
3. Walley AJ, Chavanas S, Moffatt MF, et al. Gene polymorphism in Netherton and common atopic disease. *Nat Genet* 2001; 29:175–8.
4. MeltemAkkurt Z, Tuncel T, Ayhan E, Uçmak D, Uluca U, Uçak H. Rapid and easy diagnosis of Netherton syndrome with dermoscopy. *J Cutan Med Surg*. 2014 Jul–Aug; 18(4):280–2.
5. NETHERTON EW. A unique case of trichorrhexisnodosa; bamboo hairs. *AMA Arch Derm* 1958; 78:483.
6. Powell J, Dawber RP, and Ferguson DJ, et al. Netherton's syndrome: increased likelihood of diagnosis by examining eyebrow hairs. *Br J Dermatol* 1999; 141:544–6.
7. Sun JD, Linden KG. Netherton syndrome: a case report and review of the literature. *Int J Dermatol*. 2006 Jun; 45(6):693–7.
8. Bellon N, Hadj-Rabia S, Moulin F, Lambe C, Lezmi G, Charbit-Henrion F, et al. The challenging management of a series of 43 infants with Netherton syndrome: unexpected complications and novel mutations. *Br J Dermatol*. 2020 Jun.
9. Roda Â, Mendonça-Sanches M, Travassos AR, Soares-de-Almeida L, Metze D. Infliximab therapy for Netherton syndrome: a case report. *JAAD Case Rep*. 2017 Nov; 3(6):550–2.
10. Mazereeuw-Hautier J, Hernández-Martín A, O'Toole EA, Bygum A, Amaro C, Aldwin M, et al. Management of congenital ichthyoses: European guidelines of care, part two. *Br J Dermatol*. 2019 Mar; 180(3):484–95.