

Dermatology Online Journal

Volume 13 Number 3

[DOJ](#)

[Contents](#)

Netherton's syndrome: the importance of eyebrow hair

Lobna Boussofara MD, Nadia Ghannouchi MD, Najet Ghariani MD, Mohamed Denguezli MD, Colandane Belajouza MD, Rafia Nouira MD

Dermatology Online Journal 13 (3): 21

Department of Dermatology, Farhat Hached Hospital, 4002 SOUSSE, TUNISIA

Abstract

Netherton's syndrome (NS) is a rare autosomal recessive disease associated with variable expressions: congenital ichthyosiform erythroderma, ichthyosis linearis circumflexa, specific hair shaft defects (trichorrhexis invaginata) and atopic diathesis. We report the case of 14-year-old non-identical twins whose diagnosis of NS was established on light microscopy of eyebrow hairs. The sisters consulted for a severe episode of atopic dermatitis. Skin examination revealed an ichthyosiform eruption with generalized, polycyclic erythematous plaques with fine double-edged scaling. The flexural creases were lichenified and multiple eczematoid patches were noted. Blood investigation revealed eosinophilia and high IgE level. Microscopy of scalp hair of the twins was repeatedly normal, but the one of the eyebrows revealed typical trichorrhexis invaginata. The presence of trichorrhexis invaginata is necessary to make the diagnosis of NS, but its identification can be difficult because this defect is variable in time and localization. The examination of eyebrow hairs is especially beneficial for patients first seen in late childhood and adults.

Netherton's syndrome (NS) is a rare autosomal recessive disease that is associated with variable expressions, including congenital ichthyosiform erythroderma, ichthyosis linearis circumflexa, specific hair shaft defects (trichorrhexis invaginata), and atopic diathesis.

The trichorrhexis invaginata is pathognomonic of Netherton's syndrome and its presence confirms the diagnosis. But, its identification can be difficult because not all hairs show the particular finding termed *bamboo nodes*.

We report the case of 14-year-old non-identical twins whose diagnosis of NS was established on light microscopy of eyebrow hairs.

Clinical synopsis

The 14-year-old non-identical twin born of nonconsanguineous parents consulted for a severe episode of atopic dermatitis. The parents, who were of normal appearance, reported that their daughters were born at term with generalized scaly erythroderma. This eruption quickly evolved to multiple itching erythematous patches considered to be atopic dermatitis. The twins were treated with topical corticosteroids and emollients. The sisters had also a history of food intolerance to peanuts.

Skin examination revealed an ichthyosiform eruption of the trunk with brown scale on the limbs. She had generalized, polycyclic erythematous plaques with fine double-edged scaling. She had also lichenification of flexural creases with presence of eczematoid patches of the trunk.

Scalp examination revealed diffuse scaling with mid-length blistering and brittle hairs. The eyebrow hair was sparse, especially at the outer third. This change was more evident in one twin than the other.



Figure 1



Figure 1

Figure 1. Generalized xerosis and ichthyosiform eruption with brown scale

Figure 2. Characteristic ichthyosis linearis circumflexa with polycyclic erythematous patches surrounded by serpiginous double-edged scales



Figure 3



Figure 4

Figure 3. Lichenification of flexural creases

Figure 4. Eczematoid patches of the trunk



Figure 5



Figure 6

Figure 5. Sparsity of eyebrow hairs

Figure 6. Light microscopy of eyebrow hair revealed typical trichorrhexis invaginata. the distal portion of the shaft is invaginated into the proximal portion.

Blood investigation revealed: eosinophilia with absolute eosinophil count of 0.9 and 1.2×10^3 cell per mm^3 (normal $< 0.4 \times 10^3$ cell per mm^3), high IgE level of 840 and 970 IU/mL (normal < 160 IU/mL).

Microscopy of scalp hair of the twins was repeatedly normal, but eyebrow hair examination revealed typical trichorrhexis invaginata. The diagnosis of Netherton's syndrome was established.

Treatment with acitretin (0.5 mg/Kg/Day) and mid-potency topical corticosteroids was associated with reduction in erythema, scaling, and itching.

Discussion

Comel Netherton syndrome is a rare autosomal-recessive ichthyosis that was first described by Comel in 1949 [1] and later by Netherton in 1958 [2]. This disease is characterized by the triad of ichthyosis linearis circumflexa, trichorrhexis invaginata, and an atopic diathesis [3]. The skin lesions appear at birth or within the first month of life as a congenital ichthyosis erythroderma of variable expressions with at the most a collodion baby phenotype.

This erythroderma gives place after 1-2 years to ichthyosis linearis circumflexa (ILC) which consists of erythematous migratory polycyclic patches surrounded by serpiginous double-edged scales. Ichthyosis linearis circumflexa is variable and episodic evolving with recurrent acute attacks lasting a few weeks [4, 5, 6]. Patients with NS have abnormal hair with sparse, dry, short, spiky and brittle hair [5, 6]. The diagnosis of NS is definitely established by demonstration on light or scanning electron microscopy of trichorrhexis invaginata (TI). Other hair anomalies such as pili torti, trichorrhexis nodosa, and helical hairs can be found but aren't specific of NS [6, 7].

From 30 to 75 percent of patients with NS develop atopic manifestations such as atopic dermatitis-like skin lesions, urticaria, angioneurotic edema, asthma, allergic rhinitis, food allergy (particularly allergy to peanuts, egg and fish), peripheral eosinophilia, and elevated serum IgE level. Other associated manifestations of NS include aminoaciduria, failure to thrive, mental and neurological retardation, and immune abnormalities [3, 4, 7].

The diagnosis of NS was delayed in our patients because the neonatal manifestations were moderated and transient and they were not explored, their atopic manifestations were predominant, and light microscopy of scalp hair was repeatedly negative. The pathognomonic TI was later found in eyebrow hair.

The occurrence of TI is necessary to make the diagnosis, but its identification can be difficult. This defect occurs in scalp, eyebrow, eyelash, axillary, and pubic hair, however its presence is inconsistent and it can be found in some areas and not in others. In some cases, sparsity of hair makes the examination difficult.

On the other hand, TI does not become evident until after the first year of life and can also completely regress in adulthood. Sometimes, only the eyebrow hair may be affected in adults [4, 5, 6, 7]. Powell demonstrated in NS patients that density of abnormalities was greater in eyebrow than in scalp hair [8]. For that reason, examination of eyebrow hair is recommended for patients in whom NS is suspected, especially those first seen in late childhood and adults.

The gene, SPINK5, responsible for this disease is mapped to chromosome 5q 31-32 and encodes for a serine protease inhibitor with antitrypsin activity termed *lymphoepithelial kalsin type inhibitor* (LEKTI). This LEKTI is expressed in epithelial and lymphoid tissues and may play an important role in anti-inflammatory and antimicrobial effects [9]. More recently, other SPINK5 gene polymorphisms were identified in the pathogenesis of asthma and atopic dermatitis [10].

Various therapeutic options have been attempted in NS with variable success. Topical and low-dose oral corticosteroids are inconsistently successful with a high risk of adverse effects especially systemic absorption and infections. Systemic and topical retinoids may be sometimes harmful. Other options have been used like PUVA therapy, cyclosporine, 12 percent lactic acid lotion [4, 5, 6, 7]. Recent reports suggest the efficiency of topical tacrolimus and picrolimus in NS but close control of blood drug levels is recommended [11, 12].

The prognosis of NS depends on perinatal complications dominated by recurrent skin and systemic infections, hypothermia and hypernatremic

dehydration. Severe forms with high perinatal mortality justify making a prenatal diagnosis [13].

Our cases illustrate the clinical variability of the NS and the importance of examination of eyebrow hairs by light microscopy in order to confirm the diagnosis.

References

1. Comèl M. Ichtyosis linearis circumflexa. *Dermatologica* 1949;98: 122-136.
2. Netherton EW. A unique case of trichorrhexis nodosa – "Bamboo hairs". *AMA Arch Derm.* 1958 Oct;78(4):483-7. [PubMed](#)
3. Greene SL, Muller SA. Netherton's syndrome. Report of a case and review of the literature. *J Am Acad Dermatol.* 1985;13(2 Pt 2):329-37. [PubMed](#)
4. Plantin P, Delaire P, Guillet MH, Labouche F, Guillet G. Syndrome de Netherton. Aspects actuels. A propos de 9 cas. *Ann Dermatol Venereol* 1991;118(8):525-30. [PubMed](#)
5. Judge MR, Morgan G, Harper JJ. A clinical and immunological study of Netherton's syndrome. *Br J Dermatol* 1994;131(5):615-21. [PubMed](#)
6. Sun JD, Linden KG. Netherton syndrome: A case report and review of the literature. *Int J Dermatol* 2006;45(6):693-7. [PubMed](#)
7. Smith DL, Smith JG, Wong SW, deShazo RD. Netherton's syndrome: A syndrome of elevated IgE and characteristic skin and hair finding. *J Allergy Clin Immunol.* 1995;95(1 Pt 1):116-23. [PubMed](#)
8. Powell J, Dawber RP, Ferguson DJ, Griffiths WA. Netherton's syndrome: increased likelihood of diagnosis by examining eyebrow hairs. *Br J Dermatol* 1999;141(3):544-6. [PubMed](#)
9. Chavanas S, Bodemer C, Rochat A, Hamel-Teillac D, Ali M, Irvine AD, Bonafe JL, Wilkinson J, Taieb A, Barrandon Y, Harper JJ, de Prost Y, Hovnanian A. Mutations in SPINK 5, encoding a serine protease inhibitor cause Netherton syndrome. *Nat Genet.* 2000;25(2):141-2. [PubMed](#)
10. Walley AJ, Chavanas S, Moffatt MF, Esnouf RM, Ubhi B, Lawrence R, Wong K, Abecasis GR, Jones EY, Harper JJ, Hovnanian A, Cookson WO. Gene polymorphism in Netherton and common atopic disease. *Nat Genet.* 2001;29(2):175-8. [PubMed](#)
11. Saif GB, Al-Khenaizan S. Netherton syndrome: Successful use of topical tacrolimus and pimecrolimus in four siblings. *Int J Dermatol (OnlineEarly Articles).* doi:10.1111/j.1365-4632.2006.02956.x
12. Mégarbané H, Tomb R, Klein-Tomb L, Mégarbané A. Erythrodermie congénitale desquamative. *Ann Dermatol Venereol.* 2004;131(2):211-2. [PubMed](#)
13. Bitoun E, Bodemer C, Amiel J, de Prost Y, Stoll C, Calvas P, Hovnanian A. Prenatal diagnosis of a lethal form of Netherton syndrome by SPINK5 mutation analysis. *Prenat Diagn.* 2002;22(2):121-6. [PubMed](#)