Netherton syndrome

V. Dragoš and A. Godič

ABSTRACT

The authors present the case of a boy with a typical Netherton syndrome (NS). In the first year of life his skin appeared erythrodermic and he suffered from hypernatremic dehydration and failure to thrive, as well as from several bacterial infections without impaired cellular or humoral immunodeficiency. Total IgE and IgE specific for cow milk were elevated, but his condition did not improve in spite of a strict diet. After the first year of life erythroderma slowly disappeared and migratory circinate plaques typical of ichthyosis linearis circumflexa (ILC) became evident. Histopathology of skin revealed psoriasiform changes. At the age of five, eczematoid skin lesions appeared in the flexural areas, and an atopic dermatitis was additionally diagnosed. At that time total IgE levels were elevated and allergy to house mite, grass pollen, and tree pollen was found. Ultrastructural analysis of hair showed pili torti. To all above-mentioned findings the diagnosis of a NS was made. To our knowledge this is the first report of NS where the atopy was evidently manifested with atopic dermatitis.

KEY WORDS

Netherton syndrome, ichthyosis linearis circumflexa, atopy, atopic dermatitis, pili torti, child, boy

Introduction

Netherton syndrome (NS) is a rare autosomal recessive hereditary ichthyosiform disease (1). The classical triad of clinical features includes ichthyosis, hair shaft abnormalities, and atopic diathesis. The syndrome is named either as Netherton or as Comel and Netherton. In 1949 Comel described ichthyosis linearis circumflexa (ILC), which consists of congenital migratory erythema and pathognomonic double-edged scales. In 1958, Netherton described a patient with erythroderma and hair shaft abnormality (2). A generalized erythroderma is present at birth or soon after. Later, in the second year of life, skin manifestations can be present either as ILC or less frequently as congenital ichthyosiform erythroderma (CIE). Two-thirds of patients have various atopic manifestations and elevated immunoglobulin class E (IgE), though serum immunoglobulin levels are usually normal (3,4). Hair shaft abnormalities include trichorrhexis invaginata, pili torti and/or trichorrhexis nodosa (5,6,7). In addition, a variant mode of impaired cellular immunity, aminoaciduria, recurrent infections, delayed growth and development, as well as mental retardation have also been described (8,9,10).

Case report

The boy was born at term of a normal pregnancy and delivery. Neither the parents of the boy nor close relatives had any atopic manifestation or skin disease. In the third week of life generalized papular exanthema appeared, which was gradually progressing to erythroderma and scaling, especially on the scalp, face, neck, ears, perigenital and gluteal regions. The lower extremities and trunk were less involved. Soon a bilateral recurrent otitis media and externa appeared with mastoiditis in the right ear. In addition, conjunctivitis, tonsillopharyngitis and acute enterocolitis, the last due to an *Escherichia coli infection* were also present at that time. In the discharge from the ears, nose and throat *Staphylococcus aureus* and *Pseudomonas aeruginosa* were isolated. The boy also had suffered from a septic coxitis and had to be operated because of an incarcerated inguinal hernia. The whole skin gradually appeared erythrodermic with extensive scaling, a hypernatremic dehydration developed as well. At that time a skin biopsy was done which revealed psoriasiform changes so the working diagnose was erythrodermic psoriasis. Because of the dystrophy, poor weight gaining and recurrent otitis media an immune deficiency was suspected. Although immunoglobulins were in the normal range, there were slightly elevated specific IgE against the egg white and against cow milk. We also detected a slightly decreased T4/T8 index, although relative and absolute values of T lymphocytes were in the normal range. The patient was treated with different locally applied steroids, a hypoallergenic diet, parenteral rehydration and antibiotics. As results of the treatment were not encouraging, the mother decided to take the boy home. We saw the boy again at the age of 5 when numerous, partly confluent gyrate lesions with double-edged scaling become evident (Fig. 1, 2) on the skin of the entire body. Lichenification of the flexural areas, which is a symptom of atopic dermatitis also became evident. Total IgE levels were elevated and allergy to house mite, grass pollen, and tree pollen was found. At the age of 9 we found pili torti on the scalp (Fig. 3). At that time the diagnosis of NS was made.

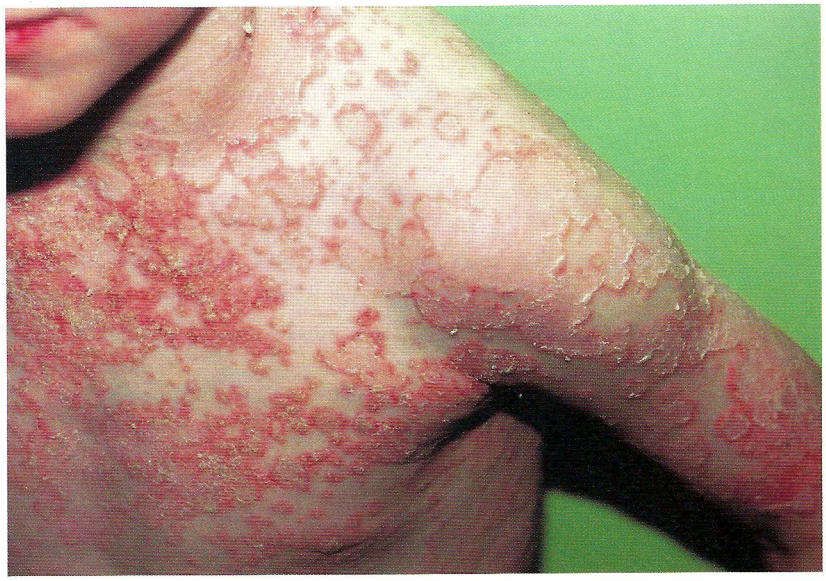
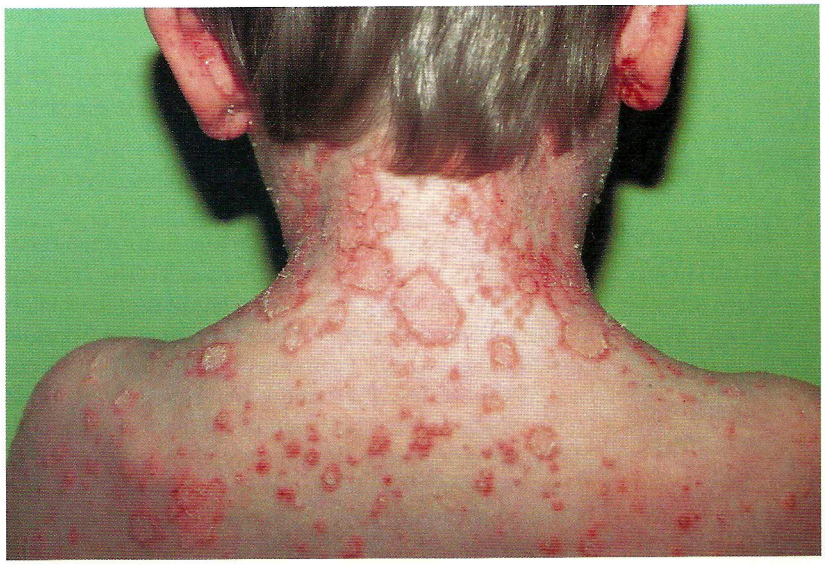


Figure 1. Gyrate lesions with double-edged scaling at the age of five years.

Discussion

NS is a rare autosomal recessive genodermatosis consisting mostly of ichthyosis linearis circumflexa, trichorrhexis invaginata and/or pili torti, and atopic predisposition. The exact genetic defect is still unknown but it appears to be of an autosomal recessive mode (2). During the first months of life erythroderma predominates with hypernatremic dehydration and failure to thrive. Erythroderma can be caused by multiple factors: immunodeficiency, metabolic disease like acrodermatitis enteropathica, ichthyosis, atopic dermatitis, psoriasis, seborrhoic dermatitis, but sometimes the origin remains unknown. The specificity of clinical and histopathological features is low in neonates so it usually takes a long period before the final diagnosis is established. Erythrodermic neonates are at risk to get sepsis, hypernatremic dehydration, malnutrition, failure to thrive, and are at risk to die from life threatening condition.

Figure 2. Gyrate lesions with double-edged scaling at the age of five years.



In the second year of life in patients with NS erythroderma slowly disappears and migratory gyrate lesions with double-edged scaling become evident. Some patients can remain severely affected with erythrodermic flares or have erythroderma with pustules (11). In patients with NS atopy is usually manifested as angioedema, allergic rhinitis, asthma, urticaria and elevated IgE (3, 4). Beside lesions typical for ILC we observed in our patient lichenification in flexural areas which appeared in the fifth year of life. According to our knowledge this seems to be the first description of atopic dermatitis in a patient with NS. Total IgE levels were elevated and allergy to house mite, grass pollen, and tree pollen was found. Hair shaft abnormalities on patient's scalp manifested as trichorrhexis invaginata, pili torti and/or trichorrhexis nodosa (5). In our patient ultrastructural analysis of the hair disclosed pili torti.

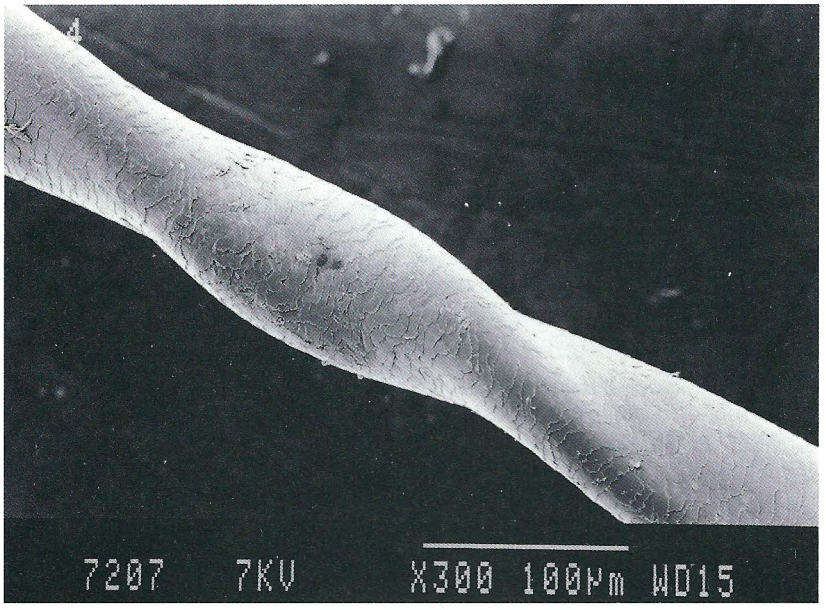


Figure 3. Pili torti in our patient (scanning electron microscopy).

Histologically, combined characteristics of both psoriasis and atopic dermatitis are expressed in patients with NS (11), which makes a correct diagnosis difficult. Ultrastructural analyses of skin in patients with NS, congenital ichthyosiform erythroderma, and erythrodermic psoriasis can be of great value in establishing a correct diagnosis (12). Ultrastructural analyses of skin in patients with NS show (using postfixation with osmium tetroxide and ruthenium tetroxide) replacement of stratum corneum with parakeratotic cells. Distinctive features as premature secretion of lamellar bodies and foci of electron dense material in the intercellular spaces of stratum corneum, which are not observed in other erythrodermic disorders, appear to be frequent and relatively specific markers for NS. Ultrastructural analyses of the skin of patient with NS may facilitate the early diagnosis of NS (13). Patients with NS usually have normal values of serum immunoglobulin levels but selective antibody deficiency to bacterial polysaccharide antigens can be found, so it is important to evaluate the functional antibody response to both protein and bacterial polysaccharide (10). Our patient suffered from several bacterial infections in the first year of life, therefore above mentioned diagnostic procedures should be performed. Patients with NS may suffer from gastrointestinal involvement (8), which could be the reason for a dystrophy and a poor weight gaining in early childhood of our patient. In some patients with NS an intermittent aminoaciduria has been observed (9).

The therapy of patients with NS includes emollients, topical steroids, tars, PUVA, and oral vitamin A derivatives, with moderate and temporary effects (5, 14). A long-term treatment with topical tacalcitol was tried in few cases with good results and without severe side effects, but its effect should be additionally proved on a larger group of patients.

Conclusions

The early diagnosis of the NS is usually difficult due to erythroderma in the first months of life, which later slowly disappears, and lesions typical for ichthyosis linearis circumflexa become evident. Some patients may remain erythrodermic, even with pustules. Atopy is usually manifested with different symptoms and signs, including the elevated IgE. Patients with NS usually have normal values of serum immunoglobulin levels. Histologically, characteristics of both psoriasis and atopic dermatitis are present. Ultrastructural analyses of skin in patients with NS show premature secretion of lamellar bodies and foci of electron dense material in the intercellular spaces of stratum corneum which appear to be relatively specific markers for NS. Patients with NS may suffer from severe bacterial infections and selective antibody deficiency to bacterial polysaccharide antigens. The therapy with topical steroids, tars, emollients, PUVA, and oral vitamin A derivatives is not satisfactory, and offers temporary effects. Even the strict hypoallergenic diet does not improve skin condition and dystrophy characterized by a poor weight gain can be present in patients with NS.

We propose ultrastructural analysis of skin, evaluation of functional antibody response to bacterial antigens, and a light microscopic hair examination as standard diagnostic procedures, when NS is suspected, and/or when the origin of erythroderma in early childhood remains unknown.

REFERENCES

1. Krafchik BR. What syndrome is this? Netherton syndrome. Pediatr Dermatol 1992; 9: 157-60.

2. Schwayder T, Bernarjee S. Netherton syndrome presenting as congenital psoriasis. Pediatr Dermatol 1997; 14: 473-6.

3. Judge MR, Green SL, Müller SA. Netherton syndrome. Report of a case and review of the literature. J Am Acad Dermatol 1985; 13: 329-37.

4. Plautin P, Delaire P, Guillet MH, Labouche F, Guillet G. Netherton syndrome, current aspects. A propose of 9 cases. Ann Dermat et Venereol 1991; 118: 525-30.

5. Blaschke S, Möller R, Hauser I, Lamprecht IA, Paul E. Comel-Netherton-Syndrom. Hautartzt 1998; 49: 499-504.

6. Hurwitz S, Hereditary skin disorders: the genodermatoses, "In" Hurwitz, Clinical pediatric dermatology, Philadelphia, WB Saunders, 1993, 173.

7. Griffiths WAD, Judge MR, Leigh IM, Disorders of Keratinization, "In" Rook, Textbook of Dermatology, Oxford, Blackwell, 1998, 1511-4.

8. Judge MR, Pradeaux L, Olives JP et al. Digestive and nutritional manifestation of Netherton syndrome. Arch Pediatr 1991; 48: 95-8.

9. Caputo R, Vanutti P, Bertani E. Intermittent aminoaciduria have been observed in some patients. Arch Dermatol 1984; 120: 220-2.

10. Stryk S, Siegfried EC, Knutsen AP. Selective antibody deficiency to bacterial polysaccharide antigens in patients with Netherton syndrome. Pediatr Dermatol 1999; 16: 19-22.

11. Judge MR, Morgan G, Harper JI. A clinical and immunological study of Netherton syndrome. Br J Dermatol 1994; 131: 615-21.

12. Williams ML. Ichthyosis and Disorders of Cornification. In: Schachner LA, Hansen RC eds. Pediatric Dermatology. New York: Churchill Livingstone, 1988: 412.

13. 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 implication. Arch Dermatol 1999; 135: 823-32.

14. Kansky A, Podrumac B, Prelog I. Hereditary ichthyosis. Pathogenesis and possibilities of treatment. ACTA Dermatoven APA 1997; 6: 47-54.

AUTHORS' ADDRESSES

Vlasta Dragoš MD, dermatovenereologist. Dpt. Dermatovenereology, University Medical Centre, Zaloška 2, 1525 Ljubljana, Slovenia.
Aleksander Godič MD, MSc, resident, same address.