Netherton syndrome: a case report and review of the literature.

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ABSTACT:

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Netherton syndrome is a rare autosomal recessive condition characterized by ichthyosiform erythroderma, trichorrhexis invaginata and atopic manifestations. This disease is caused by mutations in the SPINK5 gene on chromosome 5q32, which encodes for the serine protease inhibitor LEKTI. Treatment with a variety of agents has not show any consistent improvement and no cure. Newly treatment with tacrolimus and pimecrolimus is useful in the treatment of skin lesions in Netherton syndrome. We report a case of possible Netherton syndrome in a 2 year-old girl.

Key words: Netherton syndrome, congenital ichthyosiform erythroderma, ichthyosis linearis circumflexa, trichorrhexis invaginata

บทคัดย่อ:

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สถาบันโรคผิวหนัง

Netherton syndrome เป็นโรค ถ่ายทอดทางพันธุกรรมแบบ autosomal recessive ที่พบน้อยมีลักษณะทางคลินิกที่จำเพาะประกอบด้วย ผื่นผิวหนังที่เป็น ichthyosiform erythroderma,เส้นผมเปราะ และมีลักษณะเหมือนปล้องไม้ไผ่ที่เรียกว่า trichorrhexis invaginata ร่วมกับมีประวัติเกี่ยวกับภูมิแพ้ โรคนี้เกิดจากความผิดปกติของ SPINK5 gene บน chromosome 5q32 ซึ่งควบคุมการสร้างโปรตีนชื่อ serine protease inhibitor LEKTI การรักษามีหลายวิธี แต่ยังไม่มียาชนิดใดที่มีประสิทธิภาพในการควบคุมโรค และทำให้โรคหายขาด ล่าสุดมีรายงานว่าการทายา tacrolimus และ pimecrolimus ช่วยทำให้ผื่นดีขึ้น แต่อย่างไรก็ตามการทายาในปริมาณมากอาจทำให้เกิดผลข้างเคียงได้โดยเฉพาะในเด็ก ซึ่งในรายงานนี้ได้นำเสนอผู้ป่วยเด็กเพศหญิงอายุ 2 ขวบ ที่มีผื่นผิวหนังและลักษณะเส้นผมเหมือน Netherton syndrome

คำสำคัญ: กลุ่มอาการนิเธอทัน กลุ่มอาการผิวแดงลอกเป็นขุยตั้งแต่กำเนิด ผมรูปร่างผิดปกติเป็นปล้องคล้ายไม้ไผ่

Introduction

Netherton syndrome is identified as entry 256500 in the Online Mendelian Inheritance of Man database**.** It has been observed almost only in females. This disease is uncommon autosomal recessive condition.

Case report

A 2-year-old Thai girl born to nonconsanguineous parents came to our outpatient department for the evaluation of a non-bullous congenital erythroderma accompanied by scaling that had been present since birth. The lesions were accentuated on the face and scalp. Her mother noted the lesions were pruritic. At the age of 4 months, she developed hair loss. No appearance of the hair shaft abnormality on first hair examination with light microscopy. Initial diagnosis was congenital ichthyosiform erythroderma with a differential diagnosis of Netherton syndrome. During the follow up period, she still had scaly erythematous skin and a history of skin infection.

She was the product of normal pregnancy and delivery with normal growth and development. She had no history of food allergy, asthma or allergic rhinitis. Other family members were healthy.

Physical examination:

The skin examination showed generalized erythroderma covered by fine, translucent scales on extremities, scalp, face predominantly on the lower eyelid (Figure 1, 2). Both palms and soles were spared. Well-circumscribed erythematous papules and plaques on limbs. Non-scarring alopecia on scalp with dry, lusterless and brittle hair (Figure 3). Hair pull test was negative. No mucosal or nail involvement.

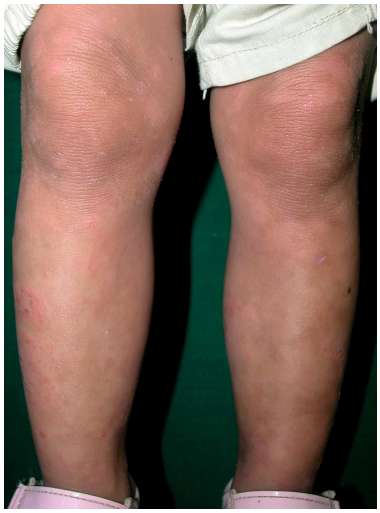


Figure 1



Figure 2



Figure 3

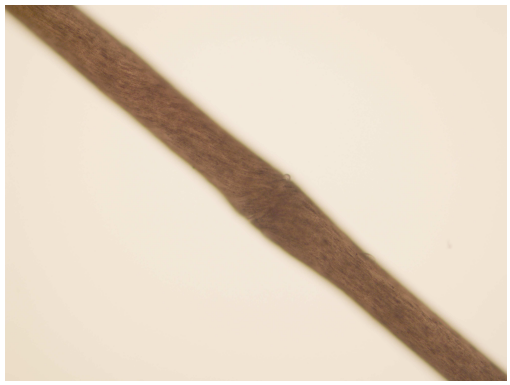


Figure 4

Investigation:

- Light microscopy of the hair: Trichorrhexis invaginata (bamboo hair) (Figure 4)
- Chromosome analysis can not be assessed.

Discussion:

Netherton syndrome (NS) is a rare autosomal recessive disease consisting of ichthyosiform dermatosis, hair shaft abnormalities (trichorrhexis invaginata), and an atopic diathesis.[1] Most patients develop generalized erythroderma and scaling, which is evident at birth or during the first weeks of life or continuous peeling of the skin. Collodial membrane has

not been reported. Ectropion and taut facial skin can develop in older patients with severe disease. Pruritus is universal.[2] Ichthyosis linearis circumflexa (ILC) is a characteristic serpiginous migratory annular/polycyclic rash with double-edged scale. It is pathognomonic and usually occurs after 2 years[3] of age**.**

Hair shaft defects usually develop during infancy and early childhood. The scalp hair is sparse short spiky lusterless and brittle. The eyebrows also have sparse broken hair. Light microscopy of the hair usually appear as bamboo nodes or a ball and socket (trichorrhexis invaginata) [4,5] or nodular thickening of the distal end of broken hair shafts (golf tree). [6] Individual hairs are lusterless spiky and brittle. Typically, diagnosis is delayed until the appearance of the pathognomonic hair shaft anomaly.

All patients at some stage in their disease develop allergy to foodstuffs especially nuts, eosinophilia, or serum IgE are markedly elevated. Most have an atopic predisposition, with a strong family history of asthma, atopic dermatitis.[7]

Patients with NS have been found to have a mutation on chromosome 5q32 in a gene named SPINK5 (serine protease inhibitor, Kazal type-5), which encodes an inhibitor of serine proteases called LEKTI. This serine protease inhibitor have critical role in barrier function.[8,9]

Emollients, keratolytics, and antibiotics remain the mainstays of treatment. Topical steroids are helpful, but complications such as aminoaciduria and pituitary adrenal axis suppression were reported. In one case, split body treatment with 12% lactic acid lotion surprisingly cleared the eruption on the treated side (control side emollient).[10] One Japanese patient respond to psoralen plus ultraviolet light A (PUVA). Retinoids are not helpful, though 1 report of improvement with a low dose has been published.[11] Although topical tacrolimus and pimecrolimus is useful in the treatment of atopic dermatitis and skin lesions in NS[7], but systemic absorption may occurs.

Complications consisting of cutaneous and systemic infections, inability to regulate body temperature.[13] Some infants with Netherton syndrome develop progressive hypernatremic dehydration, failure to thrive and enteropathy. These complications can be fatal. Erythroderma and hair abnormality persist. The disease tends to improve with age, but the course can be fluctuated by intermittent exacerbations.[14]

Our patient presented with congenital ichthyosiform erythroderma, trichorrhexis invaginata, while no history of atopy was obtained. These findings suggested the diagnosis of NS. She had been treated with chlorphe niramine, cream base, Dermo shampoo and 3%vioform, without improvement.

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