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Dermoscopic and reflectance confocal microscopy features of Netherton syndrome

Netherton syndrome (NS) is a recessive autosomal ichthyosis arising from germline mutations in the serine protease inhibitor of the Kazal type 5 (SPINK5) gene, located on chromosome 5q31-32 [1]. NS, first described by Comel in 1949 and by Netherton in 1958 [2], has an estimated incidence of 1/200,000. It is characterized by the triad of congenital ichthyosiform erythroderma (CIE)/ichthyosis linearis circumflexa (ILC), hair shaft defects, and atopic diathesis [3]. We present a patient with NS including a dermoscopic and reflectance confocal microscopy (RCM) study, and correlate this data with histopathological findings.

A 25-year-old woman was referred to our dermatology clinic with an undiagnosed skin eruption that had developed shortly after birth. She had pruritic erythroderma and desquamation involving most of her body. She was the first child of non-consanguineous parents, born after an uneventful pregnancy. Her height was 140 cm and her weight was 56 kg. She had normal intelligence but poor social ability. Physical examination revealed widespread serpiginous and polycyclic erythematous plaques with double-edged peripheral scaling on the trunk, abdomen, folds and extremities (*figure 1A*). Some small blisters were present, which thereafter ruptured. Her scalp hair was curly and eyebrows were sparse. Laboratory investigations revealed an elevated serum IgE level

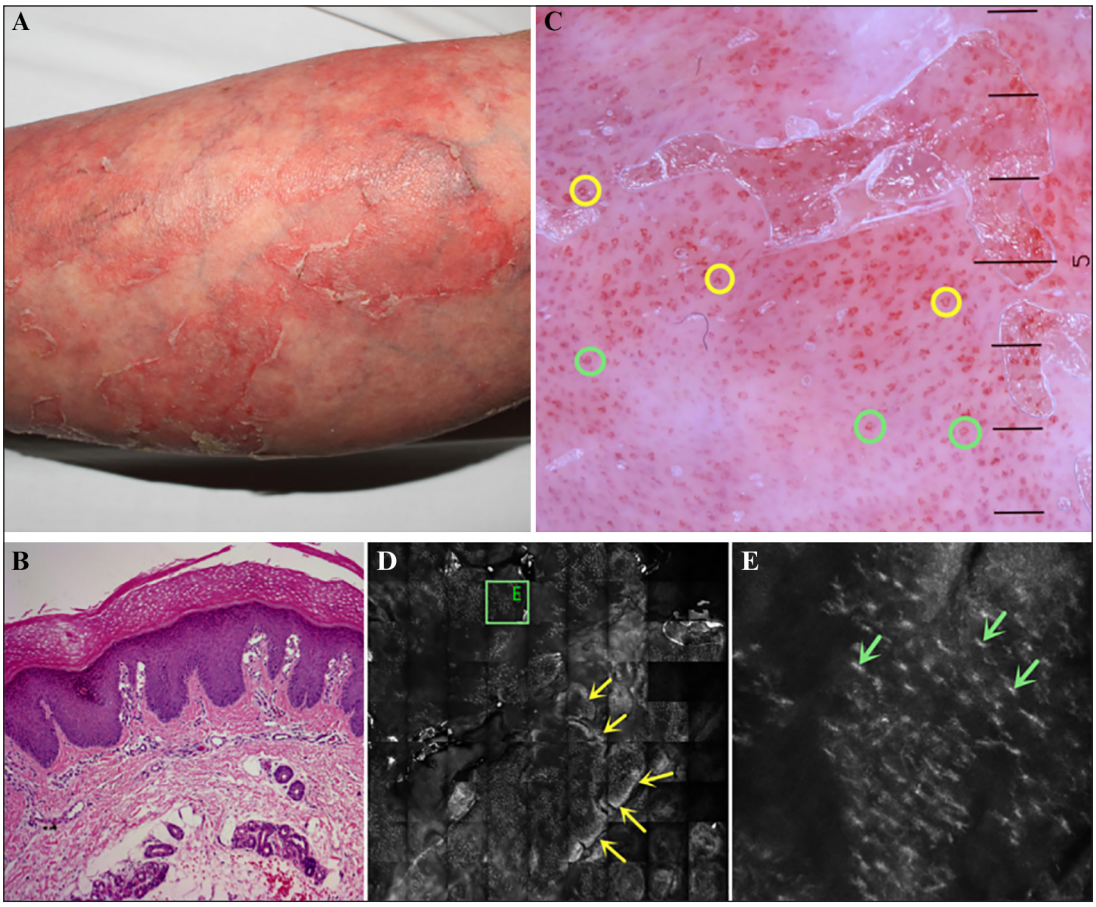

Figure 1. A) Serpiginous and polycyclic erythematous plaques with double-edged peripheral scaling on the lower limbs. **B**) Histological examination of the lesions shows basket-weave hyperkeratosis, mild acanthosis, and psoriasiform epidermal hyperplasia, associated with a mild perivascular inflammatory cell infiltration and dilated blood vessels in the dermis (H&E stain; ×200). **C**) Dermoscopic findings include shiny white serpiginous scales and a milky-red background with diffuse red dotted, globular (green circles) or hairpin-like vessels (yellow circles). **D**) RCM mosaic of 1.5x1.5 mm at the stratum corneum shows continuous tortuous high-diopter stripes (yellow arrows), indicative of double-edged peripheral scaling of the lesion. **E**) Numerous medium or highly refractile parallel granules or streaks (green arrows) are visible, corresponding to a thick layer of basket-weave hyperkeratosis seen histologically.

(2,500 IU/mL; normal<100 IU/mL). Routine blood, hepatic and renal function tests, IgA, IgG, IgM, IgG, complement (C3, C4), tumour markers, and antinuclear antibodies were negative or within normal range. Trichorrhexis invaginata was not detected by trichoscopy. A biopsy from the arm revealed basket-weave hyperkeratosis, mild acanthosis and psoriasiform epidermal hyperplasia. Mild perivascular inflammatory cell infiltration and dilated blood vessels were present in the dermis (*figure 1B*). DNA sequencing analysis of the SPINK5 gene (NM_001127698.1) showed a heterozygous mutation c.2468dupA in exon 26 and c.2211-2214del in exon 23, respectively, confirming the diagnosis of NS. Considering the rarity of the disease, dermoscopy and RCM were performed. Dermoscopy (Dermlite hybrid, X10; 3 Gen, San Juan Capistrano, California, USA) revealed shiny white serpiginous scales and a milky-red background, studded with diffuse red-dotted, globular or hairpin-like vessels (*figure 1C*). RCM (VivaScope1500®, Caliber: imaging and diagnostics, Rochester, NY, USA) mosaic of 1.5x1.5 mm at the subcuticular layer exhibiting continuous tortuous high-diopter stripes (*figure 1D*). In addition, we observed a parallel distribution of medium or highly refractile granules or streaks (*figure 1E*).

The histological features of NS are diverse and non-specific. A study of 80 skin biopsies from 67 patients with NS revealed that the most frequent histological findings were psoriasiform hyperplasia with a hyperplastic epidermis and a mild, dermal inflammatory infiltrate [4]. The histopathological features of our case are consistent with these findings. Dermoscopy demonstrated shiny white serpiginous scales. The lesions were studded with red dotted, globular or hairpin-like vessels, which is consistent with the histopathological presence of dilated vessels in the dermis. When skin lesions were examined dermoscopically perpendicular to the dilated dermal papillary vessels, dotted or globular vessels were seen. When slanted at an angle to the dermal papillary vessels, hairpin-like patterns were observed.

RCM showed a parallel distribution of medium or highly refractile parallel granules or streaks at the subcuticular level, which clearly correlated with the thick layer of basket-weave hyperkeratosis seen microscopically. In a previous study, the classic histological criteria of NS were compared with dermoscopic and RCM findings [5]. RCM showed pronounced basket-weave parakeratosis with densely packed, bright keratinocytes. In our case, we visualized the characteristic basket-weave hyperkeratosis by RCM. This can be seen in some dermatoses with abnormal keratinization, but few articles have reported this. Moreover, we observed continuous high-diopter and tortuous stripes corresponding to double-edged peripheral scaling of the lesion. RCM indeed complements vertical histopathological sections by providing sections in horizontal plane.

To summarize, dermoscopy and RCM can be applied as non-invasive ancillary diagnostic techniques for NS. Data on further patients is required in order to better delineate the dermoscopic and RCM features of NS. ■

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A new frameshift mutation in a patient with neurofibromatosis type I

A 22-year-old, unmarried and childless woman had been experiencing scattered coffee-coloured spots, papules, and nodules with intermittent mild pain throughout her body for 22 years. Additionally, she had noticed a gradual increase in a lumbosacral mass over the past 19 years, as well as a painful subcutaneous nodule behind her left ear over the past two years. At birth, the patient had light brown spots scattered all over her body, which varied in shape, including circular, spindle-shaped, oval-shaped, or irregular in size. Over time, the number of spots and skin-coloured papules increased, and the papules and nodules developed a soft texture similar to that of hernias. There were also slightly noticeable soft lumps in the lumbosacral region. Over the past two years, the patient had experienced intermittent mild burning pain associated with the papules, nodules, and masses. The patient is a postgraduate student with normal intelligence and no significant past medical history, personal history, or family history of similar symptoms. Her parents are not close relatives. During physical examination, no obvious systemic abnormalities were found. In terms of dermatological findings, multiple coffee-coloured spots, ranging from 0.2 to 8 cm in diameter, were scattered on the face, trunk, and limbs. Freckle-like pigmentation was observed in the armpits and groin. Skin-coloured papules and nodules, with a diameter ranging from 0.3 to 2 cm, were frequently seen on the trunk and limbs. Additionally, there was a soft-textured exogenous mass, measuring 8.7 cm in diameter, in the