A case of a Comél-Netherton syndrome patient treated with UVA1 phototherapy

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Abstract

Comél-Netherton syndrome is a rare autosomal recessive genodermatosis characterized by a triad of manifestations, such as ichthyosis linearis circumflexa, characteristic hair shaft deformities and atopic diathesis. Conservative treatment consists of emollients, keratolytics and antibiotics. Here we present a case of 16-year-old female patient, hospitalized at the Department of Dermatology of Poznan University of Medical Sciences and diagnosed as Netherton syndrome. The patient was treated with medium doses of UVA1 radiation (40-60 J/cm^2) generated by GP-24H (Cosmedico, Germany). The expositions were performed tree times weekly, 20 exposures, up to the total dose of 970 J/cm^2 have been proposed in the treatment. Clinical improvement of both types of skin lesions i.e. ichthyotic and eczematous was observed. But after cessation of phototherapy they gradually relapsed after approximately 4 months. Later as the patient was treated with small doses of systemic corticosteroids without any clinical effect. Thereafter systemic retinoids were introduced but although they caused satisfactory clinical improvement severe hair loss developed leading to the withdrawn of the medication. The above results underlined that due to the complexity of etiopathogenesis as well as clinical diversity treatment of Netherton Syndrome remains to be a great challenge for the physicians.

Key words: Comél-Netherton syndrome, treatment, UVA1 phototherapy.

Introduction

Comél-Netherton syndrome is a rare autosomal recessive genodermatosis characterized by a triad of manifestations, such as ichthyosis linearis circumflexa, characteristic hair shaft deformities and atopic diathesis [1]. This disorder of keratinisation is caused by the mutation of a gene, localized to chromosome 5q31 near the interleukin-4 cytokine cluster, which has been identified as SPINK5 (serine protease inhibitor, Kazal type-5). The SPINK5 gene encodes a 15-domain serine protease inhibitor LEKTI (lympho-epithelial Kazal-type-related inhibitor), which is expressed in thymus but also in outer layers of the skin and may play a protective role against allergens [2, 3]. The actual incidence is not known, but approximately less than 200 cases have been reported in the literature. The clinical manifestation is varied [4, 5]. Neonates usually present congenital ichthyosiform erythrodermia which evolves into typical migratory ichthyosis linearis circumflexa. The pathognomonic hair shaft abnormalities for this syndrome are trichorrhexis invaginata, known as bamboo-hair, but other deformities may also occur such as pili torti or trichorrhexis nodosa. The skin histopathology of Netherton syndrome shows non-specific or psoriasiform changes, acanthosis, hyperkeratosis, parakeratosis and elongation of rete ridges. Upper stratum malpighi shows inter- and intracellular oedema and sometimes multilocular vesicles and pustules within the horny layer. This is not typical for ichthyosis linearis circumflexa, but resembles spongiotic dermatitis [6, 7]. Atopy diathesis may present itself mainly as atopic dermatitis (AD), asthma and elevated IgE levels. Major complications, particularly in children, are hypernatraemia, infections, immunological deficiencies and growth retardation. The course is chronic with exacerbations of one of the ichthyotic or eczematoid components. Currently there is no specific therapy. Only future gene therapy might offer a solution [8]. The classic treatment consists of emollients, keratolytics and antibiotics, while other forms of treat-

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ment are usually not effective. Treatment with corticosteroids or calcineurin inhibitors such as pimecrolimus and tacrolimus may lead to their absorption and increased levels in the blood, particularly in children [9-12]. Also systemic retinoids used with success in other disorders of keratinization in this syndrome may exacerbate the atopic component of this syndrome [13].

Case report

A 16-year-old female patient who was a collodion baby was diagnosed by paediatricians as having erythrodermia desquamativa Leiner. At the age of one, AD was diagnosed. The classic treatment for AD was administered with topical emollients, steroids, antibiotics, antihistamines, and finally even immunotherapy. Broadband UVA/UVB and also narrowband 311 nm UVB phototherapy were also introduced, with mixed results. In 2009 she was admitted to the Department of Dermatology of Poznan University of Medical Sciences due to exacerbations of skin lesions. The patient presented disseminated polycyclic hyperkeratotic plaques with migratory double-edged scaling at the margins. Her hair was very dry and brittle. Laboratory findings revealed certain abnormalities such as mild leukopenia, lymphocytosis and highly elevated levels of serum immunoglobulin IgE (tIgE) 2313 kU/l as well as specific IgE (asIgE) against rye, velvet grass, grey alder, silver birch and hazel pollen allergens. Skin prick tests were positive to tree pollen allergens and house dust mites.

The diagnostic skin biopsy showed skin lesions localised within the trunk and revealed slight acanthosis, granulosis and hyperkeratosis as well as mild perivascular inflammatory infiltrate (H + E, original objective magnification 20×, Fig. 1). A scalp hair light microscopy examination revealed pili torti (original objective magnification 20×, Fig. 2).

After obtaining consent from her parents, the patient started treatment with medium doses of UVA1 radiation (40-60 J/cm^2) generated by GP-24H (Cosmedico, Germany). The procedures were performed tree times a week over 20 cycles, adding up to a total dose of 970 J/cm^2, which was well tolerated. Standard photography documentation was collected before and after therapy.

Clinical improvement of both types of skin lesions, i.e. ichthyotic and eczematous, was observed (Fig. 3). But after cessation of phototherapy they gradually relapsed after approximately four months. Later the patient was treated with small doses of systemic corticosteroids but there was no clinical effect. Thereafter systemic retinoids were introduced. Although they caused satisfactory clinical improvement, severe hair loss developed, leading to the withdrawal of medication.

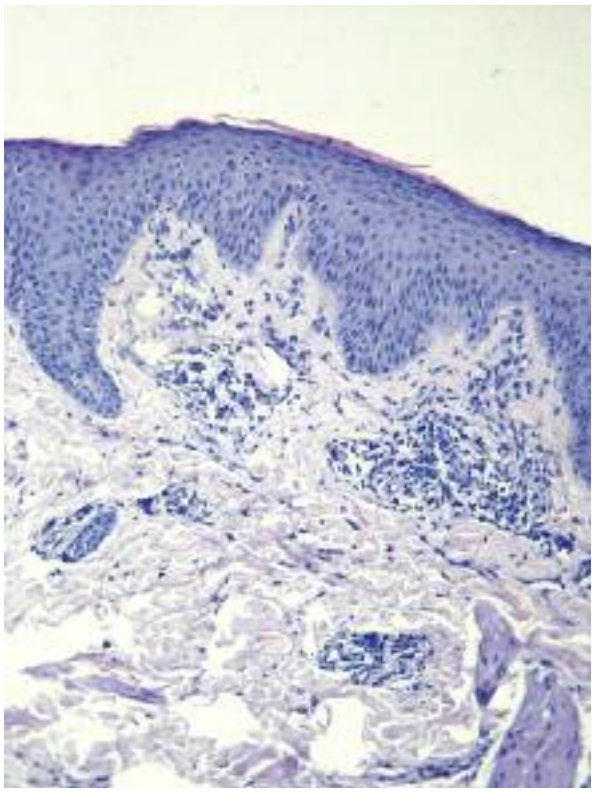

Fig. 1. Diagnostic skin biopsy – skin lesions localized within the trunk revealed slight acanthosis, granulosis and hyperkeratosis as well as mild perivascular inflammatory infiltrate (H + E, original objective magnification 20×)

Fig. 2. Scalp hair light microscopy examination showed: *Pili torti* (original objective magnification 20×)

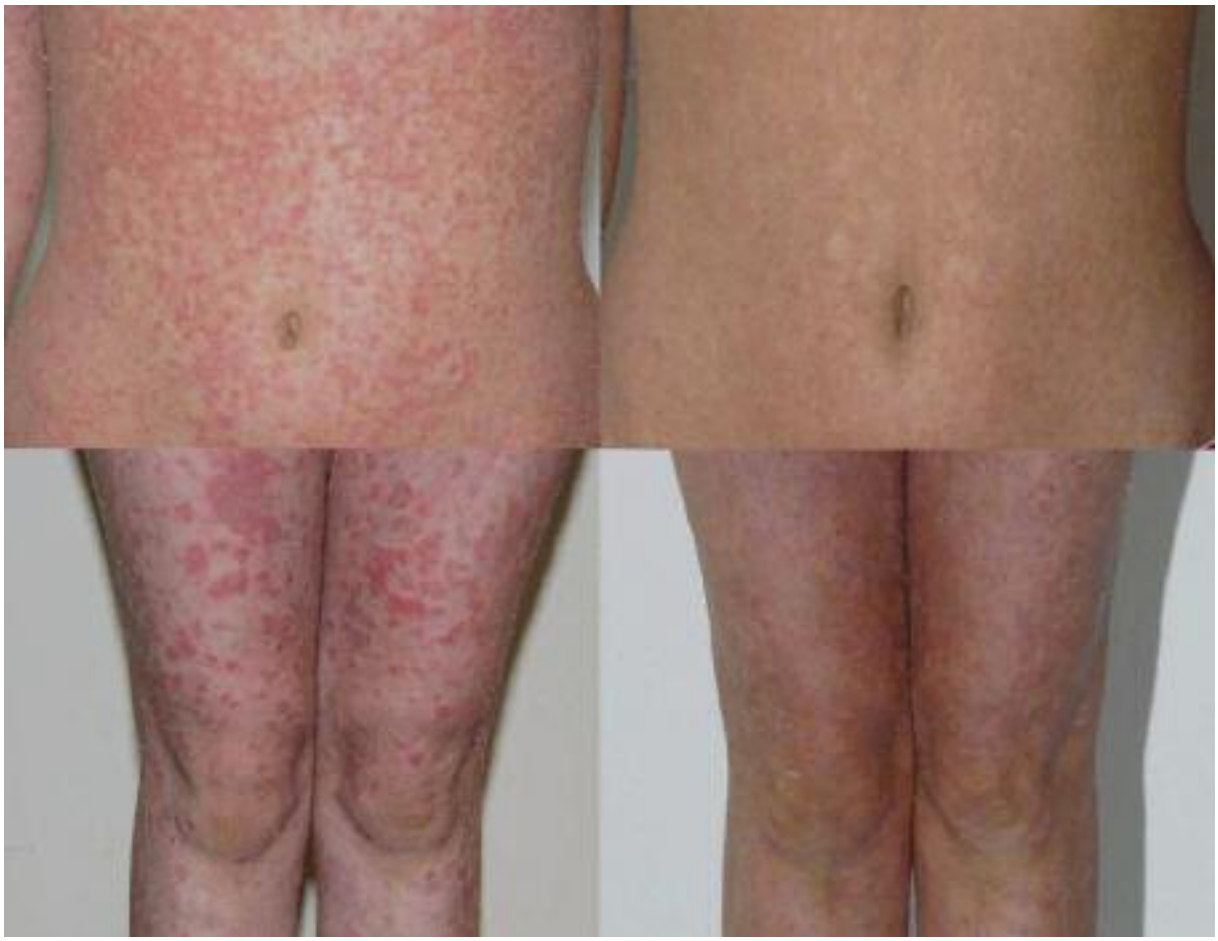

Fig. 3. Clinical improvement of both types of skin lesions: ichthyotic and eczematous

Discussion

Different forms of phototherapy and photochemotherapy broadband UVB/UVA and psoralen plus UVA (PUVA) have been tried in the treatment of patients with ichthyosis linearis circumscripta, with mixed effects [14-16]. The successful administration of a novel form of phototherapy, i.e. long-wave UVA (UVA1), in patients suffering from AD, as well as good results from the treatment mentioned above in immunodeficient patients with psoriasis, lead to the application also in a Netherton syndrome patient [17-20]. Italian authors reported a case of a 36-year-old female patient treated with medium doses of UVA1 (40 J/cm^2), three times a week, (a total of 24 doses), with complete remission in two months. They repeated this form of phototherapy again after eleven months. The treatment was well tolerated [17]. The proposed mechanism of action of UVA1 in this complex condition is bilateral. The UVA1 could enhance the synthesis of deficient serine protease inhibitor in skin but not in the hair due to the deeper localization of hair bulbs. On the other hand, known immunomodulatory effect through the early T lymphocytes and mastocytes apoptosis could influence the atopy component [17]. The advantages of UVA 1 phototherapy in comparison to PUVA therapy are the avoidance of systemic side effects of psoralens and lower risk of phototoxic reactions, combined with deeper penetration of radiation. In the not too distant future, further modifications of this phototherapy are expected, for example the combination of UVA1 phototherapy and small doses of retinoids. Obviously the side effects of phototherapy should always be considered and the possibility of secondary malignancies has to be emphasized. The results of UVA1 phototherapy are not really consistent and clinical improvement reported by some of the authors mentioned above is unfortunately transient in nature. The above results underline that due to the complexity of aetiopathogenesis as well as clinical diversity, treatment of Netherton syndrome remains a great challenge for physicians.

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