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NETHERTON'S DISEASE AND ICHTHYOSIS LINEARIS CIRCUMFLEXA

Report of a Case and Review of the Literature

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Abstract. A 6-year-old girl is reported with the association of ichthyosis linearis circumflexa and Netherton's disease. She had the typical clinical features of this syndrome with a serpiginous, migratory, scaling eruption on her skin, trichorrhexis invaginata and other defects on the hair shafts and an atopic diathesis. The relevant literature is briefly reviewed.

The first case reported with an association of hair shaft abnormalities and ichthyosiform skin changes was the case of Netherton in 1958 (9). His patient was a girl with congenital ichthyosiform erythroderma and unique nodular fragile deformities of the hair shafts, "bamboo hairs". In addition she later on developed an allergic asthma (18). After this original report of so-called Netherton's disease, 6 additional cases were published by 1967 (3, 7, 8, 15, 17, 18). In 1968 the association between Netherton's disease and ichthyosis linearis circumflexa (ILC) was stressed (14) and since then 13 additional cases with ILC and hair shaft abnormalities have been published (1, 5, 6, 12, 13, 14, 16).

In recent reports there has been discussion concerning the relationship between different forms of ichthyosis and structural hair shaft abnormalities (1, 5). To clarify the association there is still reason to publish new cases with hair shaft abnormalities and some kind of ichthyotic skin changes. This paper reports the case of a girl, the first published from Scandinavia, combining the features of ILC and Netherton's disease. The girl has derived a very good suppressive therapeutic effect on her skin changes from local treatment with betamethasone.

CASE REPORT

A 6-year-old girl was first seen in 1966 at the age of one year with a persistent, serpiginous, migratory, erythematous, scaling eruption present since soon after birth. Periodic exacerbations and remissions had been noted but the girl's skin had never been quite clear. Her face was often red and scaly and in the summer she was very irritated by the sun. Local treatment with betamethasone had a very good suppressive effect but the serpiginous skin lesions reappeared a week after the treatment had stopped. Her scalp hair was dry and lustreless but had appeared grossly normal until 1969. In 1969 she began to loose hair and the hairshafts were periodically very fragile. Intermittently there appeared clusters of darker hairs with fragile nodes on the shafts. Since 1968 she had suffered from attacks of asthma and from time to time urticaria and angio-oedema appeared after eating fish. There was no history of atopy or any skin disease in her family. She has two normal sisters.

Physical examination

An erythematous skin eruption with an arcuate serpiginous pattern and a scaly border was observed on the trunk and the upper arms (Figs. 1, 2). The primary lesions appeared to be small erythematous papules covered with a thin ostraceous scale. These papules enlarged by peripheral extension to form linear, annular and serpiginous lesions. A diffuse seborrhoeic-like scaling was present on the scalp and on the face. Her scalp hair appeared grossly normal with no definite areas of alopecia. The hair was lustreless and dry and at the vertex at some places the hairshafts were about 1–2 inches long, darker, and the shafts were very fragile. Macroscopically evident node formation was found in the hairs.

Laboratory findings

Routine laboratory findings (urine, blood counts, E.S.R.) were within the normal limits. Urinary amino acid analysis showed the amino acids to be excreted within the normal range. Multiple immediate reactions were obtained on standard intradermal tests with dog dandruff, house dust, fish and many other foods and inhalants.

Hair

Macroscopically node formation was found on many hairs. Microscopically the defects noted included pili torti-like hairs (Fig. 3), "bamboo nodes" (Fig. 4) and cup-like forms of trichorrhexis invaginata (Fig. 5).

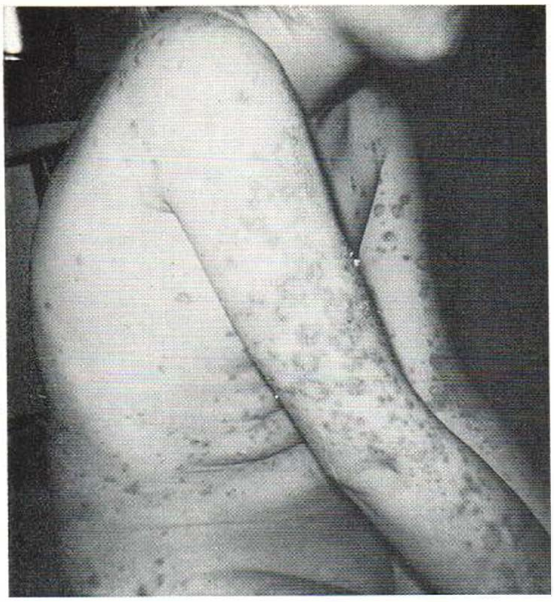

Fig. 1. The skin eruption on the trunk and upper arms had an arcuate serpiginous pattern. The primary lesions enlarged by peripheral extension to form annular, polycyclic and serpiginous scaling lesions.

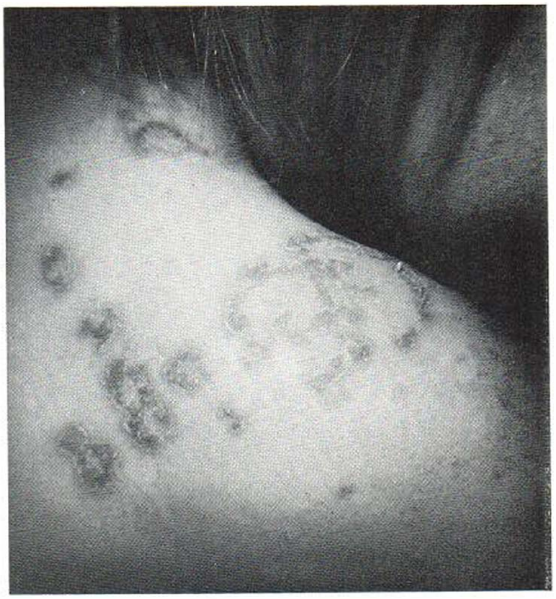

Fig. 2. Close view on right shoulder with red, annular, crusted lesions with scaly borders.

Histological examination of skin biopsies from the trunk revealed the following changes. The horny layer was parakeratotic and covered or lifted by a marked serepurulent crust. The Malpighian layer showed marked acanthosis with intracellular oedema and irregular spongiosis, which in one part beneath the horny layer changed into a spongiform vesiculopustule. Marked oedema in the papillae. Rather marked perivascular inflammatory infiltration, with lymphocytes, histiocytes and polymorpho-nuclear leucocytes, was present in upper corium (Fig. 6).

DISCUSSION

The present case is in all respects characteristic of Netherton's disease with ichthyosis linearis circumflexa as the skin manifestation. In Table I the symptoms and signs of the cases described in the literature are compared with those of the present case. There is a definite dominance of females and up to now there are only five reports concerning men (5, 8, 12, 13, 16).

The "bamboo hair" or trichorrhexis invaginata (18) is the typical hair shaft abnormality. That particular defect is found in all published cases except two (2, 7). As this defect is the key to the diagnosis, these two cases have not been considered in Table I. Microscopical observation of such hairs and hair follicles shows a distinctive type of invagination of hair shafts within themselves at the zone of incipient keratinization (18). The reason for this is a periodic disturbance in

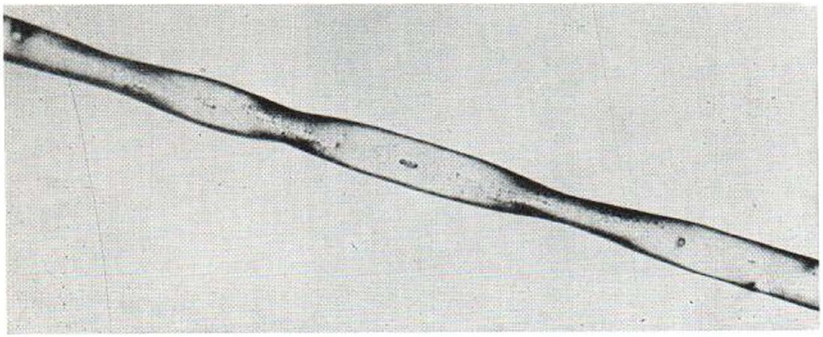

Fig. 3. Pili torti-like hairs.

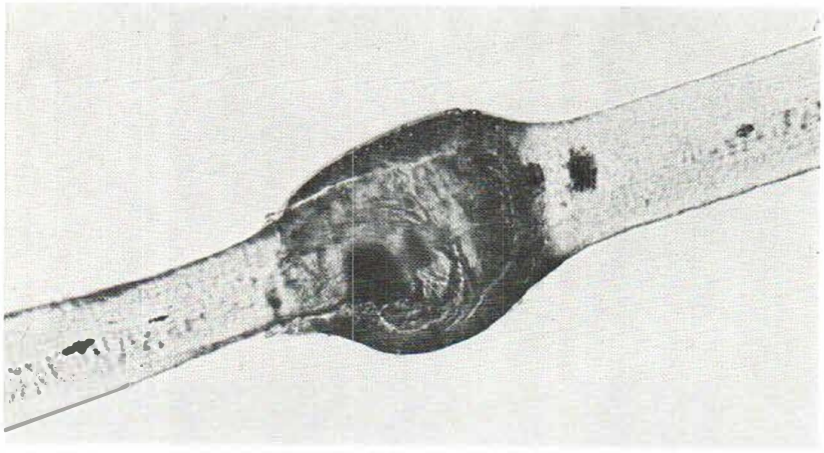

Fig. 4. Bamboo-like node on a hairshaft.

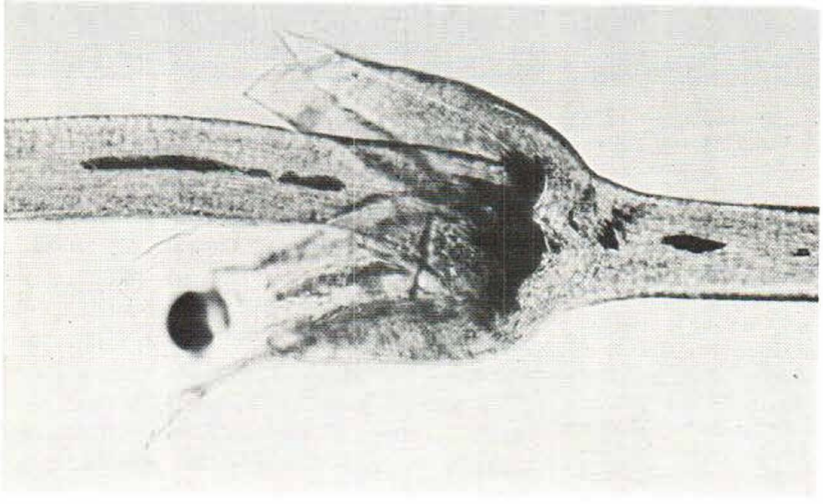

Fig. 5. Cup-like form of trichorrhexis invaginata.

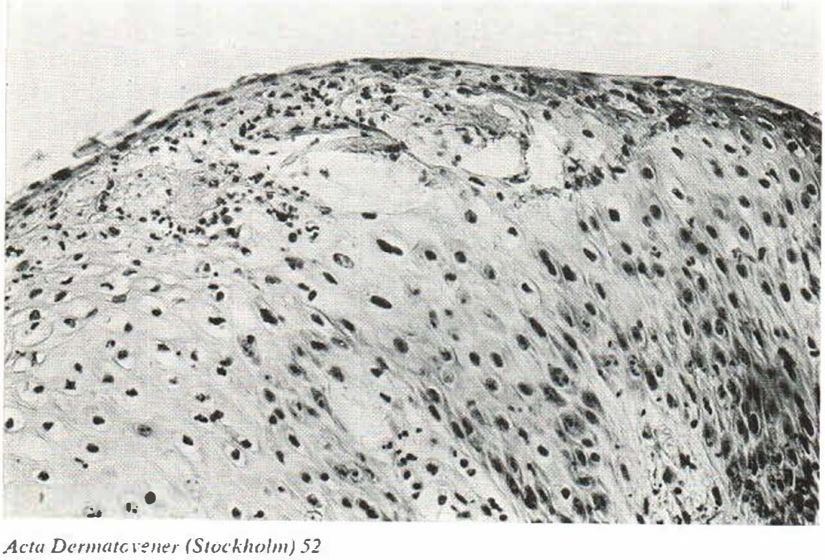

Fig. 6. Section of skin from the trunk.

Table I. *Clinical features in 22 cases of Netherton's disease from the literature and the present case*

	Positive/Investig.	Case
Trichorrhexis invaginata, "bamboo hair"	22/22	+
Other hair shaft abnormalities	16/17	+
Ichthyosis linearis circumflexa (ILC)	19/22	+
Cong. ichthyosiform erythroderma	3/22	−
Atopic diathesis	14/19	+
Aminoaciduria	7/16	−

the normal keratinization of the anagen hairs (13, 14) dependent on a lack of certain amino acids (10). In some patients (1, 5, 7, 16), as in the present case, multiple defects, mostly pili torti, of the hair shafts have been reported. Recently Orfanos et al. (11) have published a thorough study with the scanning- and the transmittance electron microscope on "bamboo hairs" and found a pathologically changed keratin in the nodes—a dystrophic keratin of the cortex.

Ichthyosis linearis circumflexa (ILC) has been reported in 19/22 cases in the literature. The skin changes of the present case are consistent with the description of ILC both clinically and microscopically. Histologically, as in other cases, there are psoriasiform features and the name psoriasiform ichthyosis has been proposed for this group of atypical ichthyosis (1). The association of ILC and Netherton's syndrome proposed by Schnyder & Wiegand (14) has been confirmed in later reports. Since their article in 1968 13 more cases have been published, including the present case, with hair shaft abnormalities and typical ILC (1, 4, 5, 13, 16).

An additional interesting finding in Netherton's syndrome is *aminoaciduria* reported in 7 of 16 examined cases. In many patients the abnormalities were inconstant (16) suggesting that the aminoaciduria may be intermittent. No definite conclusions have been drawn in the literature concerning the association of aminoaciduria with hair shaft defects (15, 16).

There are very few reports in the literature about treatment experiences. A transient effect of local steroid treatment has been noted (13, 14). Topically administrated vitamin A resulted in irritation and betamethasone orally had no effect (5). Local treatment with betamethasone in the present case cleared the skin almost completely (Fig. 7). The treatment must, however, be repeated once or twice a week. Psychologically

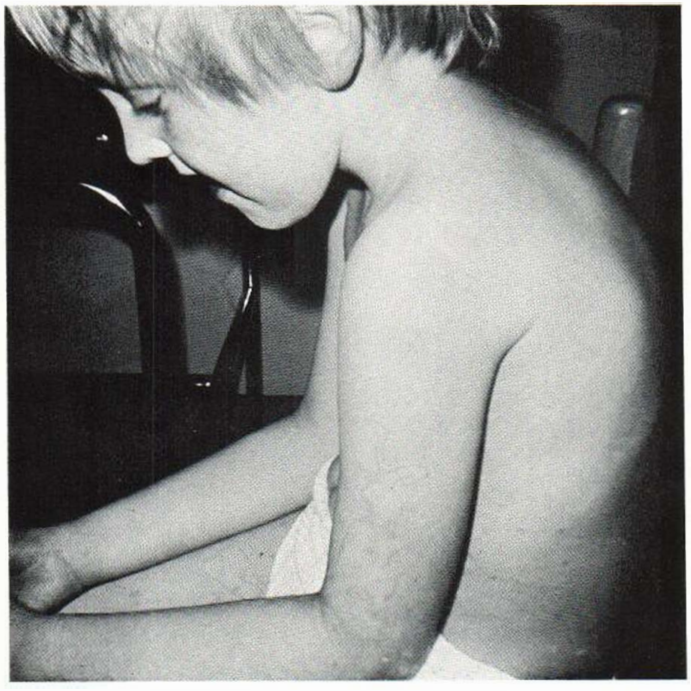

Fig. 7. Local treatment with betamethasone cleared the skin almost completely.

this treatment effect, though transient, is of great importance. ILC with its psoriasiform histological appearance thus seems to be influenced by locally administered potent steroids. This is another sign differentiating this ichthyosiform dermatosis from the more distinct forms of ichthyosis.

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