Netherton's Syndrome*

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Netherton (1958) described the association in a young girl of congenital ichthyosiform erythroderma and an abnormality of the hair shafts. Four further cases have been reported and the atopic diathesis has been added to this syndrome (Marshall and Brede, 1961; Wilkinson, Curtis, and Hawk, 1964; Stankler and Cochrane, 1967). It is the purpose of this paper to describe an additional patient, the first male, and to comment on some other features of the disorder.

Case Report

The patient was born after a normal 38-week pregnancy and a normal delivery with a birthweight of 2.7 kg. (6 lb.). The neonatal period was uneventful except for the appearance of a red scaling rash within a few days of birth, and a refusal to feed. He was discharged from the hospital at 1 month of age, weighing 2.3 kg. (5 lb. 2 oz.). Subsequent growth and development were normal. Beginning at the age of 6 months the patient developed recurrent respiratory infections and he had a number of anaphylactoid reactions. These reactions were found to be caused by the ingestion of egg-yolk, and were characterized by flushing followed by pallor and respiratory distress. From an early age the patient had sparse scalp hair, and at 20 months the scalp had been shaved in an attempt to stimulate hair growth.

Examination at the age of 30 months showed a pleasant, well-developed boy with the following measurements: head circumference, 49 cm. (19½ in.); height, 82 cm. (32 in.); weight, 10.7 kg. (23 lb. 9 oz.). Physical examination was normal except for a generalized erythema and scaliness of the skin (Fig. 1) which had a peculiar 'musty' odour. The erythema and scales were most prominent over the extensor surfaces of the arms, legs, and neck, but the entire body was involved, including the face, scalp, palms, and soles. The nails and teeth were normal. There was no keratosis pilaris. Thick adherent yellow greasy scales were present on the scalp. The hairs of the scalp were short, none measuring more than 1 cm. Microscopical examination of these hairs showed a circumferential indentation of the shaft, with a swelling and concavity of the immediate

proximal portion which contained an enlarged distal hair shaft. The resultant abnormality resembled a ball-and-socket joint, similar to those in bamboo shoots (Fig. 2). Incomplete abnormalities consisting of only a circumferential indentation or of an empty proximal enlargement were also seen. These abnormalities occurred at frequent irregular intervals along the entire hair shaft. Irregular clumping of pigment granules in the central portion of the hair shaft with concentration near the proximal concavity was frequently seen (Fig. 2). There were no actively growing hairs among the 400 examined.

Laboratory studies showed a haemoglobin of 13.5 g./100 ml., white blood cell count 8400/cu.mm., with 40% neutrophils, 1% stab forms, 49% lymphocytes, 5%

FIG. 1.—Age 30 months: showing severe scaling of the face and scalp.

Received July 25, 1967.

* This investigation was supported by Grant GM10210 and a Post Doctoral Fellowship of the United States Public Health Service.

FIG. 2.—Scalp hairs: a bamboo abnormality in one hair and clumping of the pigment granules in another one.

monocytes, and 5% eosinophils. The urinalysis was normal. A radiograph of the wrist showed a bone age of 15 months. Urinary amino acids examined by two-dimensional paper chromatography were normal, as were serum protein electrophoresis and immunoelectrophoresis. The chromosomes of the patient were normal in cells from peripheral blood and in a fibroblast tissue culture from a skin biopsy. Punch biopsies were taken from the scalp and the back. Microscopical examination of the glabrous skin showed hyperkeratosis, hypergranulosis, and acanthosis in the epidermis. The upper corium contained scattered dilated small blood vessels which were surrounded by a mononuclear infiltrate. There were bamboo malformations within many of the hair follicles of the scalp.

The patient was the younger of two children. At the time of his birth the father and mother were 29 and 27 years old, respectively; they were in good health and not related by blood. The mother's first pregnancy resulted, after 38 weeks, in a stillborn male. The patient's older brother was examined at 6 years of age and was in good health except for flexural atopic eczema. Several members of the mother's family were reported to have a skin disorder resembling ichthyosis, with only males affected. Clinical examination and biopsies were possible in three maternal great uncles of the patient. The clinical disorder and microscopical examination of the skin in these three subjects was uniform. In each, dry skin and scanty hair had been noted within a few months of birth. At puberty the dry skin and hair growth showed marked improvement, and dry scaly skin was present only during the winter. Examination of the skin showed large (greater than 1 mm.) grey-black loosely adherent scales, mostly on the extensor surfaces of

the arms, legs, and neck. The hair was normal grossly and microscopically. Punch biopsies from the extensor surface of the arm showed hyperkeratosis, scattered areas of parakeratosis, a normal granular and prickle layer, and numerous downward projections of the rete ridges, with moderate hyperpigmentation in the basal layer (Fig. 3).

The incidence of allergic disease was high in the kindred. Twenty-two descendants of the maternal great grandmother (10 males and 12 females) were evaluated. Allergic disease was present in 7 males and 3 females; in each, the allergic reactions to various injected biologicals were of the immediate type, and characterized by generalized urticaria and angio-oedema, followed by fever, malaise, and swollen tender joints. The exact number of miscarriages in this kindred could not be established; but there were at least five stillborn males.

Discussion

This patient had allergic reactions, skin disease, and in addition the bamboo hair abnormality. Congenital ichthyosiform erythroderma is usually inherited as an autosomal recessive; it is possibly related to ichthyosis vulgaris (Wells and Kerr, 1966a). The histological appearance of the glabrous skin in the present patient shows similarity to the one observed in the sex-linked recessive form of ichthyosis vulgaris (Wells and Kerr, 1966b).

Several suggestions have been made to explain the formation of the bamboo hair abnormality.

FIG. 3.—Photomicrograph of skin biopsy from extensor surface of arm of maternal great uncle of patient. (H. and E. $\times 250$.)

Van Scott (1964) has suggested that the abnormality of the hair arises secondary to plugging of hair follicles. Pinkus (1964) has proposed that a transient defect in keratinization occurs, producing a decrease in the rigidity of the splinting tube of the innermost hair sheath so that the hair is intussuscepted at a time it is still soft. Many factors can alter the keratinization of hair; among these are fever, infection, hormonal imbalance, haemorrhage, allergic reactions, and various drugs. In the present patient the development of bamboo abnormalities probably dated from birth; the precipitating events which caused the abnormality to appear at irregular intervals along the hair shaft remain unknown. The bamboo abnormality disappears at puberty, but the clinical features of this syndrome in the adult are as yet unknown. The absence of aminoaciduria in the child is of interest because, of the 5 cases hitherto reported, 2 have shown an aminoaciduria. Recently the occurrence of aminoaciduria in another abnormality of the hair, trichorrhexis nodosa, has been reported (Rauschkolb *et al.*, 1967), but these findings have to be considered tentative at present. The variability in aminoaciduria in the 5½-year-old girl reported by Stankler and Cochrane (1967) suggests a relation to diet.

Of a total of 5 cases reported to date, all have been female. The only familial occurrence has been described in 2 sisters (Stankler and Cochrane, 1967). The finding in the present family of what

could possibly be a sex-linked recessive form of ichthyosis vulgaris, with a high incidence of anaphylactoid reaction, may provide some additional evidence for a genetic factor.

Summary

A young boy with Netherton's syndrome has been described; other patients with this syndrome, hitherto reported, have been girls. The salient features of the syndrome are congenital ichthyosiform erythroderma, an abnormality of the hair shaft (bamboo hair), and frequent allergic reactions. There was a high incidence of allergic disorders and skin disease in the child's family.

We are indebted to Dr. K. Benirschke for cytogenetic studies, to Dr. Katherine Merritt for evaluation of the immunoproteins, and to Dr. Mary L. Efron for urinary amino acid studies.

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