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NETHERTON'S SYNDROME AND NEONATAL HYPERNATREMIA*

A Case Report

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Netherton's syndrome is characterized by ichthyosiform desquamation, bamboo hair and often atopic diathesis. It is transmitted as an autosomal-recessive trait. In this paper we report a baby with Netherton's syndrome who developed hypernatremia during the neonatal period. This complication should be remembered in erythrodermic infants as a preventable cause of neonatal morbidity. *Key words: Netherton's syndrome, newborn, hypernatremia.*

In 1958, Netherton's syndrome was first described as a hair shaft defect (bamboo hair), pruritis and congenital ichthyosiform erythroderma (CIE)[1,2]. Since then, Netherton's syndrome has come to indicate the triad of the hair shaft defect, an atopic diathesis and either ichthyosis linearis circumflexa (ILC) or CIE. It is transmitted as an autosomal-recessive trait[3-5]. In addition to these diagnostic criteria, some patients have been noted to have hypernatremia in the newborn period, aminoaciduria, mental deficiency, neurologic defects, delayed growth, recurrent infections, and hyper-or hypoglobulinemia[2].

In this report, we present a newborn with a rare combination of Netherton's syndrome, CIE and hypernatremia.

Case Report

A seven-day-old girl was admitted to our hospital with erythematous, peeling skin. Her parents were first-degree relatives who were both healthy. She was born by normal vaginal delivery at term (39 weeks) following an uneventful pregnancy. At birth she weighed 2550 g (10^{th}-25^{th} percentile) and had an Apgar score of seven at five minutes. It was learned that the patient's three-year-old brother had died of degenerative brain disease (unknown origin). The patient's

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other brother, who had had similar skin lesions, had also died in the newborn period. She had one healthy sister. Her three nephews, whose parents had first-degree consanguinity, had ichthyosis. One of them was a stillbirth, and the others had died with similar skin lesions at 1.5 and two months of age. Until our patient was admitted to our hospital she was breastfed. She had no history of vomiting or diarrhea.

Physical examination revealed a small, hypoactive and spactic infant with a generalized erythroderma and lamellar scaling. She did not have eyelashes (Fig. 1). She had purulent discharge from the umbilicus, and her subcutaneous fat tissue was diminished. We could not evaluate the skin turgor of the patient because of the presence of the skin lesions and the loss of subcutaneous fat tissue. Her anterior fontanel was depressed, and her eyes were sunken. We accepted the patient as having a moderate degree of dehydration.

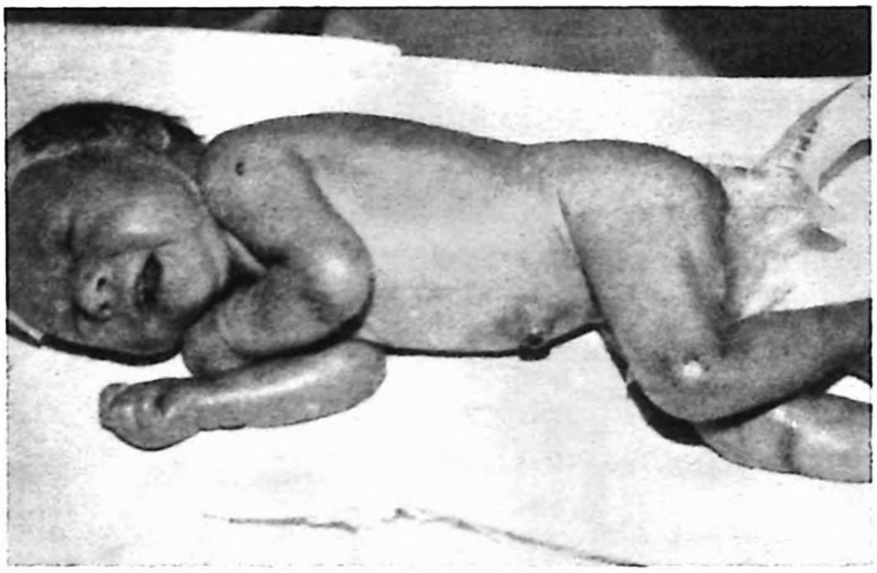

Fig. 1: The infant with generalized erythroderma and lamellar scaling.

Microscopically, the patient's, her parents' and her healthy sister's hair was normal. Her hemoglobin was 14.2 g/dl, hematocrit 47 percent, and the white blood cell count was 7,500/mm^3 with 60 percent neutrophils, 36 percent lymphocytes, and four percent band forms. Red blood cells were normochromic and macrocytic. Urine analysis was normal excluding mild proteinuria. The urinary specific gravity was 1025. Other studies indicated serum sodium 174 mEq/L, potassium 5.8 mEq/L, chloride 98 mEq/L, total protein 6.6 g/dl, albumin 4.4 g/dl, BUN 50 mg/dl, uric acid 8.6 mg/dl, creatinine 1.2 mg/dl, calcium 8.7 mg/dl and phosphorus 7 mg/dl. Abdominal and cranial ultrasonic examination,

plasma and urinary amino acid analyses, and scalp hair on light microscopic examination were normal. Staphylococcus aureus was isolated from the umbilical culture.

In order to correct the fluid and electrolyte imbalance, we began administering intravenous fluids to the patient (160 ml/kg/day, 1/5 isotonic saline in five percent dextrose solution). We treated the omphalitis with penicillin (100,000 U/kg/day) and netilmycin (5 mg/kg/day). We administered phenobarbital for spasticity and five percent lactic acid in vaseline for the skin lesions. After the fluid and electrolyte imbalance was corrected, her mild proteinuria resolved the spasticity was corrected and the biochemical values became normal. Lamellar scaling cleared up and the erythema diminished after treatment with five percent lactic acid in vaseline. After one week of treatment in the hospital, the patient was discharged. It was learned that she died at home at the age of 40 days. The cause of death was not detected.

Discussion

Netherton's syndrome has a clinical spectrum ranging from congenital ichthyosiform erythroderma (CIE) to ichthyosis linearis circumflexa (ILC). The skin lesions in the newborn period are characterized by lamellar ichthyosis; in adults these lesions change to ichthyosis linearis circumflexa[6]. Our patient with diffuse erythroderma and lamellar ichthyosis can be defined as having CIE. Beginning with a collodion baby appearance is a very rare condition, was not seen in a series of 69 patients with Netherton's syndrome[7]. We also did not detect a collodion baby appearance in our patient. Hair shaft anomalies in Netherton's syndrome are different manifestations of the same keratinization defect. These hair anomalies represent a large spectrum such as trichorrhexis nodosa, pili torti, monilethrix, angle-bent hair, and trichorrhexis invaginata, which is the latest stage[8]. Different hair shaft defects can be detected in the same family or in different regions of the same patient[9]. Hair shaft dysplasia is very rare in the newborn period, and can be due to the absence of dysplasia and a later presentation or to insufficient examination. In a series of 90 newborns with Netherton's syndrome, a hair shaft defect was noted in four patients[8]. Bamboo hair and other hair shaft defects were not detected in either the parents or our patient. We think that further investigations for hair dysplasia, would be beneficial.

In the literature, severe hypernatremia in the newborn period was reported in 13 of 99 patients without gastrointestinal and renal diseases[2,8,10]. It has been reported that the CIE phenotype of Netherton's syndrome is associated with severe hypernatremia[8]. Hypernatremia, rarely seen in the neonatal period, was also found in our patient. The causes of hypernatremia, including diarrhea, high

fever, polyuria, insufficient water intake due to poor sucking, and treatment with $NaHCO_3$, were not detected in our case. The urinary specific gravity showed a concentrating ability, making a diagnosis of diabetes insipidus unlikely. A diagnosis of hypernatremia, which has been recognized in premature infants born between 24 and 30 weeks of gestation, was not considered because our patient was a term baby. The mechanism of hypernatremia in Netherton's syndrome is not clear. Abnormal renal sodium handling, which is thought to be one etiology of hypernatremia, has not been found in patients with Netherton's syndrome. The most probable cause of hypernatremia in patients with Netherton's syndrome is the loss of transepidermal water. On electron microscopic examinations, the finding of basal membrane thickness supports this hypothesis[11]. However, if this hypothesis is correct, the question arises as to why hypernatremia is not reported more often in neonates who are erythrodermic for another reason, not just as a result of Netherton's syndrome.

In the neonatal period, in the lamellar ichthyosis form of Netherton's syndrome, the skin loses its ability to form an effective barrier. Both skin water homeostasis and temperature regulatory function are defective. Garty et al.[10] reported hypothermia in four of five patients with hypernatremic dehydration and congenital lamellar ichthyosis. We did not detect hypothermia in our patient during her hospitalization.

In the follow-up of patients with Netherton's syndrome, 26 percent of cases have been found to have staturo-ponderal retardation, 16 percent mental retardation, and 13 percent atopic diathesis. Intestinal malabsorption also has a role in staturo-ponderal retardation[8]. We observed our patient only in the newborn period, so her mental development, atopic status and staturo-ponderal state could not be evaluated.

Oral vitamin A, zinc, topical tretinoin, topical steroids, propylene glycol and five percent lactic acid lotions have been used and found ineffective in the treatment of Netherton's syndrome[12]. In other studies, five percent[13] and 12 percent lactic acid solutions[12] were reported as effective. Photochemotherapy and chemotherapy (cyclophosphamide) have also been used in therapy[9,14]. We treated our patient's skin lesions with five percent lactic acid in vaseline.

The possible diagnoses of Netherton's syndrome and hypernatremia should be remembered in newborns with lamellar ichthyosis. Early recognition of hypernatremia and prompt institution of corrective fluid and electrolytes may prevent avoidable neonatal morbidity in these erythrodermic neonates.

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