Two Cases of Anhidrotic Ectodermal Dysplasia with Atopic Dermatitis in Siblings

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Anhidrotic ectodermal dysplasia (AED) is characterized by a well-known tetrad of anhidrosis, hypotrichosis, hypodontia, and typical facies with a wide constellation of developmental defects of tissues derived from the ectoderm. Most of these patients have normal or borderline normal intelligence, but some present with mental retardation. A 15-year-old boy and his younger brother were evaluated for dry skin and intolerance to heat since their births. Their parents and other brother were normal. Both of them had atopic dermatitis. A skin biopsy was done on their left axilla, which showed a few immature eccrine glands in the dermis. We report herein two rare cases of AED in siblings with atopic dermatitis.

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Key Words : Anhidrotic ectodermal dysplasia

The term "hereditary ectodermal dysplasia" was first used by Weech[1]. He proposed hereditary ED to describe disorders in which the affected tissue was derived principally from the ectoderm. He suggested such defects were developmental, and hereditary transmission of the disorder was a constant feature. Clouston[2] distinguished two forms of hereditary ED, hidrotic and anhidrotic types. Hidrotic ectodermal dysplasia is present in eccrine sweat glands and normal facial features, without the typical saddle nose[2,3]. Hypotrichosis, nail dystrophy, and palmoplantar hyperkeratosis are the features of hidrotic ectodermal dysplasia[2,3]. An autosomal dominant gene is responsible in these cases[2,3]. Even though anhidrotic ectodermal dysplasia (AED) is characterized by partial or complete absence of sweat glands, hypotrichosis, hypodontia, and a typical appearance[4], most of these patients have normal or borderline normal intelligence, but some present with mental retardation[4]. The inheritance of this syndrome is determined by an X-linked recessive gene[5].

In Korean literature, several cases of AED[6-14] have been reported but there are only a few previous reports of AED associated with atopic dermatitis in Korean dermatologic literature[7,13]. We report herein two rare cases of AED in Korean siblings with atopic dermatitis.

CASE REPORTS

A 15-year-old boy(case 1) visited our clinic with dry skin and an intolerance to heat present since birth. His parents reported that the child had felt great discomfort in hot weather and had taken repeated cold baths.

On physical examination, his face had the typical appearance of anhidrotic ectodermal dysplasia with a large and square forehead, prominent supraorbital ridges, a saddle nose, wide nostrils and thick lips (Fig. 1A). Hair on the scalp was sparse (Fig. 1B). No hair could be seen on the rest of the body, including his eyebrows and pubic region (Fig. 2). The skin was dry, rough, pale, non-hairy and appeared prematurely senile. His nails, palms, and soles were normal (Fig. 3). Mucous membranes and genitalia were normal. He had severe atopic dermatitis, with involvement particularly in the

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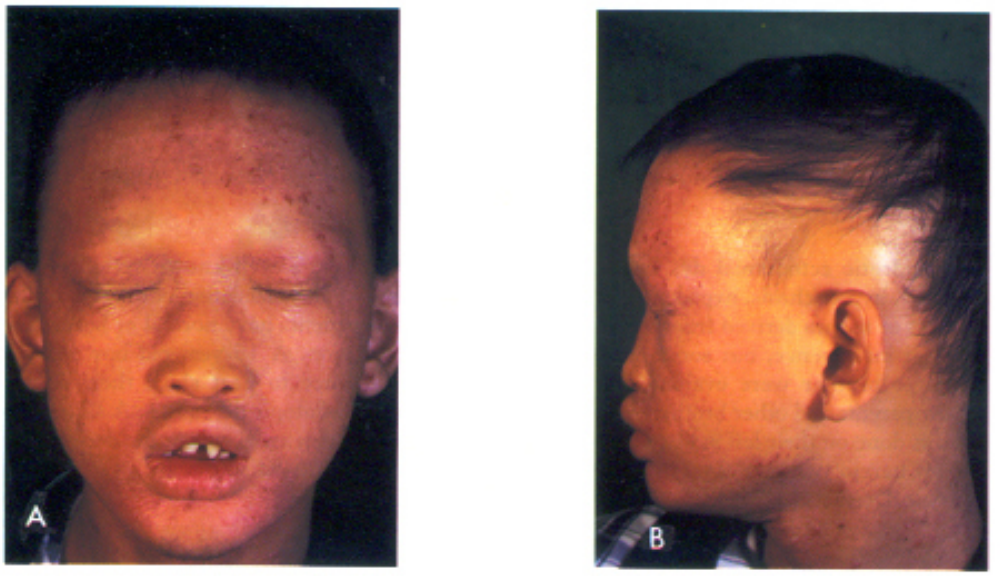

Fig. 1. Face of case 1. (A) Anterior aspect: characteristic face consisting of prominent frontal head, lost eyebrows, saddle nose, thick everted lips, hypodontia and conical and pointed canines, thin wrinkles and erythematous scaly patches. (B) Lateral aspect: sparse hairs and prominent frontal bossing.

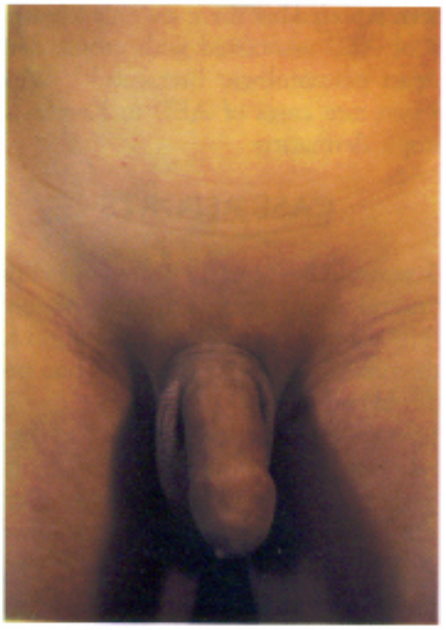

Fig. 2. Absence of pubic hairs of case 1.

popliteal and antecubital areas. According to his mother, his dermatitis flared when he ate eggs, wheat, and milk.

He was one of three siblings. The boy's 8-year-old

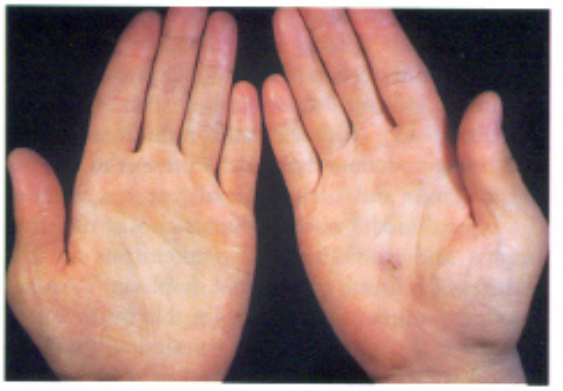

Fig. 3. Absence of palmar keratoderma of case 1.

brother(case 2) had similar complaints and clinical pictures, with mild atopic dermatitis (Fig. 4). They had normal developmental milestones and intelligence. His parents and other brother were normal (Fig. 5).

Results of the following laboratory tests were within normal limits or negative: complete blood count, liver function test, urinalysis, chest X-ray, electrocardiogram, and VDRL/TPHA. The test for sweating with starch-iodine and pilocarpine was negative(Fig. 6).

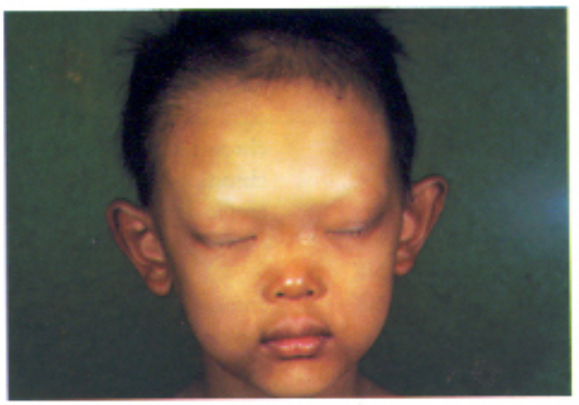

Fig. 4. Face of case 2. Prominent frontal head, loss of eyebrows, saddle nose, thick everted lips, large ears and hyperpigmentation on periorbital and perioral area were observed.

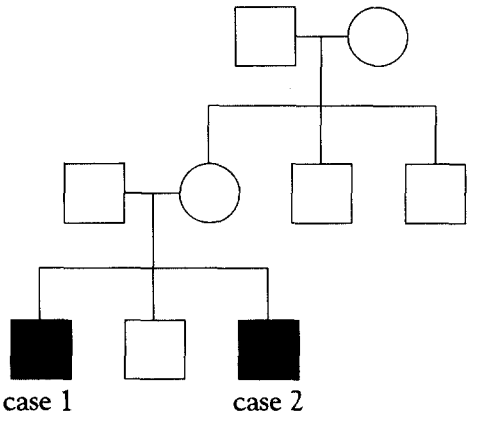

Fig. 5. Pedigree of the patients.

Fig. 6. The test for sweating with starch-iodine and pilocarpine was negative.

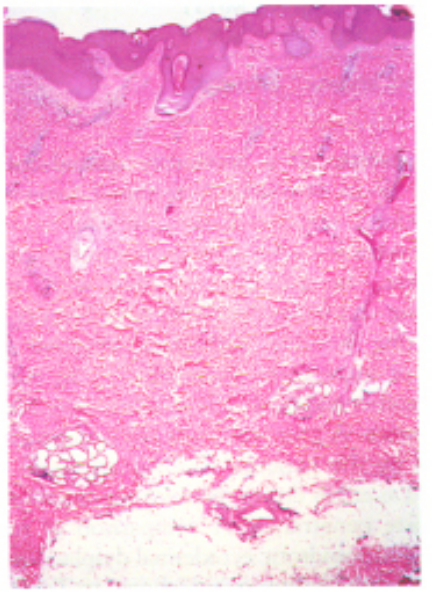

Fig. 7. A histopathological specimen from the left axilla revealed a few immature eccrine glands in the dermis. No sebaceous or any skin adnexal glands were seen (H&E, ×20).

A biopsy specimen was taken from the left axilla which revealed a few immature eccrine glands in the dermis. No sebaceous or any skin adnexal glands were seen(Fig. 7).

DISCUSSION

Anhidrotic ectodermal dysplasia (AED) is a rare entity characterized by faulty development of ectodermal structures, resulting most notably in anhidrosis, hypotrichosis, and abnormal dentition. The first report of this disease was by Thurman[15]. Weech[1] first coined the term "anhidrotic ectodermal dysplasia" for patients with absence of sweating. AED is a heredofamilial disorder, although the genetic basis is debatable. The condition has been thought to be an X-linked recessive disorder affecting males only, characterized clinically by anhidrosis, sparse blond hair, and dental abnormalities with distinctive facies[16,17]. Linkage studies have mapped this disorder to Xq12-q13.1[18,19]. Recently, Kere at el.[20] reported that AED is caused by a mutation in a novel transmembrane protein (a seemingly complete cDNA consists of two exons that are separated by a 200-kb intron in genomic DNA and the product is likely to be a small transmem-

Table 1. A comparison of reported cases of hypohidrotic ectodermal dysplasia in Korean dermatologic literature

Case No.	Authors	Sex/Age	Family Hx.	Inheritance	Nail change	Mental Retardation	Associated diseases
1	Lee et al[6]	M/15Y	+	XR(?)	-	-	chronic atrophic rhinitis
		M/10Y	+	XR(?)	-	-	chronic atrophic rhinitis
2	Lee et al[7]	M/16M	-	NK	-	-	atopic dermatitis
3	Chun et al[8]	F/23Y	-	AR(?)	NK	NK	NK
4	Kim et al[9]	M/20Y	-	NK	-	NK	-
5	Cho et al[10]	M/7Y	+	NK	NK	NK	corneal opacity
6	Cho et al[11]	M/19Y	-	NK	+	-	cataract, chronic otitis media
7	Lee et al[12]	M/18Y	-	NK	NK	NK	-
8	Choi et al[13]	M/18Y	-	NK	-	-	atopic dermatitis
9	Kim et al[14]	M/16M	-	XR(?)	-	-	-
10	Our cases	M/15Y*	+	XR(?)	-	-	atopic dermatitis
		M/8Y*	+	XR(?)	-	-	atopic dermatitis

NK : not known, * : siblings.

brane protein of a previously unanalyzed class, with a 39- or 44-residue N-terminal domain and a 74-residue C-terminal domain with slight homology to collagens but no regular helix-forming pattern). However, heterozygous females with reduced sweating and faulty dentition have been reported, suggesting possible autosomal recessive inheritance or incomplete dominance[21,22]. In our cases, their mother and her family members were normal in appearance. A gene study was not performed due to refusal by the patients. The former could be explained as either due to spontaneous mutation or incomplete penetrance. A comparison of reported cases of hypohidrotic ectodermal dysplasia in Korean dermatologic literature is shown in Table 1.

Deficiency of eccrine sweat glands causes thermoregulatory problems. Despite appropriate heat stress, either environmental or fever-induced sweating is absent or slight, and febrile seizures may occur. Hyperthermia can affect mental development. Most of these patients possess normal intelligence[4]. Repeated febrile episodes can produce mental retardation. For this reason, it is important to entertain the diagnosis of AED when evaluating an infant with unexplained pyrexia[22]. In our cases, the children felt great discomfort in hot weather, but fortunately had normal intelligence.

Eyelashes, eyebrows, and scalp hairs are characteristically sparse and fine. When present, the hair is short and is usually blond. Body hair is likewise scanty[23]. The beard, pubic, and axillary hair are often sparse and other terminal hair on trunk and limbs may be absent. In our cases, their scalp hairs and eyebrows were sparse and fine. Case 1 had no pubic hairs.

Dentition is usually delayed. Dental abnormalities varying from anodontia to hypodontia may involve deciduous and permanent teeth, resulting presumably from a lack of the dental lamina, an ectodermally derived structure[24]. The canines and/or incisors are characteristically conical and pointed. In our cases, they showed hypodontia and conical and pointed canines.

The typical appearance of AED is a square forehead with prominent frontal bossing, prominent supraorbital ridges overhanging a depressed saddle nose, a narrow palpebral fissure, thick protruding lips, low large protruding ears, a small pointed chin, sparse thin blond hair, total or partial anodontia, and midfacial hypoplasia with smooth, thin, wrinkled skin giving a prematurely old look[22]. In our cases, they showed all these findings.

The skin is shiny, wrinkled, dry, soft and thin. Subcutaneous vessels are readily visible. The nail involvement is rare, and the palms and soles are normal on gross examination. Palmoplantar keratoderma is a feature of hidrotic ectodermal dysplasia but not usually of AED.

Atopic dermatitis is commonly present[25]. Moreover, because of reduced or absent secretion of

mucus from the respiratory tract, these patients are predisposed to development of atopic symptoms, such as asthma and allergic rhinitis[24]. In our cases, they have suffered since childhood because of atopic dermatitis.

The typical facies are pathognomonic but may not be recognized in infancy. Assessment of the dental status of the child and siblings may establish the diagnosis. In the older child with the full syndrome the diagnosis is unmistakable[26]. Stimulation of sweating can be induced by heat or by the injection of cholinergic drugs. The presence of sweat can be detected by inspection or by the starch-iodine method. The starch-iodine reaction produces blue black dots[27]. In our cases, starch-iodine and pilocarpine tests were negative. Diagnosis is confirmed by histopathological examination. Microscopic findings known to occur in AED include absent or premature eccrine glands and hypoplasia of the hair follicles and sebaceous glands[28]. In our cases, a few immature eccrine glands and no sebaceous or any skin adnexal glands were revealed in the dermis.

Treatment of the individuals suffering from ectodermal dysplasia is difficult. Rest with temperature control is important. Parents should be instructed to keep the child's clothing to a minimum and to avoid exposure to hot environments. Cold baths may be used if fever is suspected. Prosthodontic techniques can modify or improve existing dentition, so that chewing is improved and a better cosmetic result achieved[27]. The abnormal ears may be helped by otoplasty[26]. Psychiatric care may be required to help the individual adjusting to his appearance and to limitations imposed on his lifestyle by the disease.

Our patients exhibited typical facies and the characteristic abnormalities of skin, hair, and teeth seen in AED. In our patients, atopic dermatitis was slightly improved in 2 months after Gamma-linolenic acid (Epogam®) medication and topical steroid application. AED in Korean siblings is rare. We report herein two rare cases of AED in siblings with atopic dermatitis.

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