

Dear Editor

Atopic Dermatitis with Ichthyosis Follicularis, Atrichia, and Photophobia Syndrome: A Case Report

IFAP syndrome (OMIM 308205) is a rare X-linked genetic disorder.¹ It is characterized by the triad of ichthyosis follicularis, atrichia, and photophobia.¹ We report the first case of IFAP syndrome concurrent with atopic dermatitis in Korea. This case was diagnosed by a mutation in the MBTPS2 (300294) gene

on chromosome Xp22.²

A 9-year-old boy presented with persistent eczema and alopecia from birth. At birth, alopecia including the eyebrows was noted. By the first year of age, he suffered from xerosis, ichthyosis, and skin desquamation (Fig. 1). Nail dystrophy and oligodontia were also noticed. RAST (radioallergosorbent test) was done and egg was sensitized strongly (>100 kUA/L) while buckwheat, peanut and soybean were sensitized weakly. Total IgE was 475 IU/ml. He underwent conservative treatment for atopic dermatitis with moisturizers and topical steroids. By the age of 3, skin biopsy of his scalp and sole was performed.



Fig. 1 Clinical appearance and dermatologic findings of the patients. Note the alopecia with an absence of scalp hair, eyebrows, and lashes (**a**). The skin was dry and scaly, and itch erythema was observed over the lower extremities (**b**, **c**). The patient had normal-sized but deformed and thickened nails (**d**).

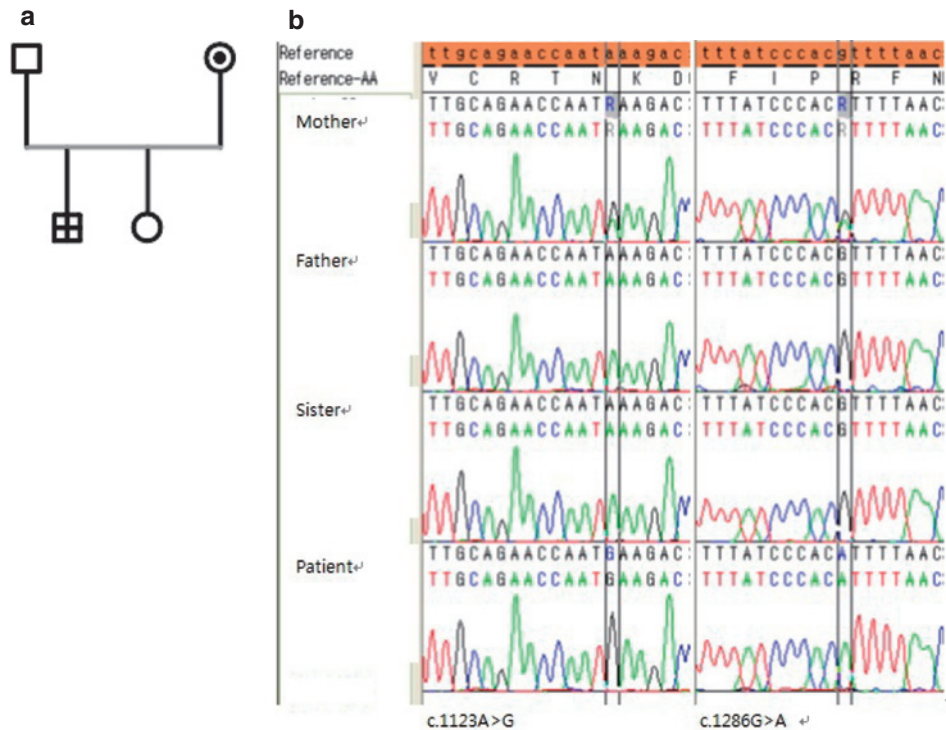


Fig. 2 Family pedigree and mutation analysis. (a) Family pedigree (b) The sequence analyses of the patient showed a c.1286G>A and c.1123A>G variant in MBTPS2, which predicts p.Arg429His and p.Lys375Glu. The mother was heterozygous for the mutation.

There was marked hyperkeratosis and hypoplasia of the hair and sebaceous glands with mononuclear cell infiltration in the perifollicular area. At the age of 4, ichthyosis follicularis, and alopecia persisted. Iodine starch test was done for sweating, and anhidrotic ectodermal dysplasia was diagnosed. His mother noticed that he would not open his eyes in a brightly lit room and photophobia was suspected. At the age of 9, direct sequencing, MBTPS2 (membrane-bound transcription factor protease site 2) all coding sequence (11 exons) (Fig. 2) was performed. c.1286G>A (p.Arg429His) and c.1123A>G (p.Lys375Glu) mutations were detected. C.1286G>A mutation has previously been detected in Japan. Functional analysis has revealed that this mutation causes severe phenotype while C.1123A>G is a novel mutation.

IFAP syndrome is an X-linked congenital anomaly disorder with variable severity.¹

It was reported by McLeod in 1909 and since then 37 cases have been announced in the world.³ The classic triad consists of ichthyosis follicularis, atrichia, and photophobia.¹ Some patients have brain anomalies, intellectual disability, ectodermal dysplasia, skeletal deformities, ear or eye anomalies, renal anomalies with or without Hirschsprung disease and cleft palate or cryptorchidism.⁴

Dermatologic findings are variable. Follicular Ichthyosis is a distinctive form of ichthyosis and occurs

mainly in hair follicles. Onset is at birth or in early childhood. Congenital alopecia involving the scalp and eyebrows is another essential cutaneous manifestation. A collodion membrane may be present in the neonate. Ectodermal dysplasia can also be seen. This is a group of syndromes all deriving from abnormalities of the ectodermal structures. It is characterized by sparse hair (atrachosis or hypotrichosis), abnormal or missing teeth (anodontia or hypodontia) and inability to sweat due to lack of sweat glands (anhidrosis or hypohidrosis).⁵

Keratosis follicularis spinulosa decalvans (KFSD) is another rare follicular syndrome associated with widespread keratosis pilaris and progressive scarring alopecia due to mutations in the MBTP2 gene. This genetic mutation features atopy, deafness, mental retardation, acne keloidalis nuchae and tufted hair folliculitis, aminoaciduria and woolly hair.^{6,7} There have been no reports of IFAP syndrome with atopic dermatitis and the incidence of KFSD with atopy is less common. Skin histopathology is non-specific. The number of hair follicles are not decreased suggesting that the pilosebaceous hypoplasia might arise from impaired maturation.⁸

Photophobia can be present early in life or later in childhood.⁸

MBTPS2 mutation causes IFAP syndrome. MBTPS2 encodes a membrane-embedded zinc metal-

loprotease for cholesterol homeostasis and endoplasmic reticulum stress response. A missense mutation (c.1286G>A, [p.Arg429His]) in MBTPS2 could lead to failed differentiation of epidermal structures, resulting in IFAP syndrome.⁹⁻¹¹ It is thought to lead to a decline in the barrier function of the skin barrier which may be the cause for atopic dermatitis.

Yoon Ha Hwang¹², Jin Uck Choi¹,

Seung Hwan Oh³ and Sung Won Kim¹

¹Department of Pediatrics, Busan St. Mary's Medical Center, ³Department of Laboratory Medicine, Inje University Busan Paik Hospital, Busan, Korea and

²Department of Pediatrics, National Hospital Organization Fukuoka National Hospital, Fukuoka, Japan

Email: hyh190@naver.com

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