Clinical, Cosmetic and Investigational Dermatology

Dovepress
Taylor & Francis Group

Open Access Full Text Article

CASE REPORT

# An Atypical Female Case of Ichthyosis Follicularis, Alopecia, and Photophobia (IFAP) Syndrome with Severe Lower Limb Contractures Requiring Orthopedic Surgery

Alireza Ghaznavi[1], Hoda Borooghani[2], Alireza Pahlevan Sabagh[1], Taghi Aghajanlou[1]

[1]Bone and Joint Reconstruction Research Center, Department of Orthopedics, School of Medicine, Iran University of Medical Sciences, Tehran, Iran; [2]School of Medicine, Iran University of Medical Sciences, Tehran, Iran

Correspondence: Taghi Aghajanlou, Bone and Joint Reconstruction Research Center, Department of Orthopedics, School of Medicine, Iran University of Medical Sciences, Tehran, Iran, Tel +989374768917, Email Aghajanloo.t@iums.ac.ir



**Background:** Ichthyosis follicularis, alopecia, and photophobia (IFAP) syndrome is a rare X-linked genodermatosis with follicular hyperkeratosis, non-scarring alopecia, and ocular abnormalities. Female cases are very uncommon and typically manifest with a milder phenotype, though severe presentations can occur. Orthopedic complications are not commonly described in IFAP.

**Case Presentation:** We present a 10-year-old girl with congenital alopecia and diffuse follicular hyperkeratosis who, despite lacking photophobia, progressed to develop flexion contractures of the knees and equinus deformities of the ankles, resulting in marked restriction of mobility. Ophthalmological examination demonstrated mild astigmatism and decreased visual acuity without corneal disease. Skin biopsy histopathology demonstrated orthokeratotic hyperkeratosis, acanthosis, and follicular plugging, which was in line with IFAP syndrome. The patient underwent posterior soft tissue release of the knees and Achilles tendon lengthening, which led to marked postoperative functional improvement in ambulation.

**Conclusion:** This case expands the phenotypic range of IFAP syndrome by describing a non-classical female presentation with no photophobia but with extreme musculoskeletal contractures requiring surgery. It emphasizes the need for early identification and multidisciplinary treatment, such as orthopedic intervention, to avert long-term disability and enhance the quality of life.

**Plain Language Summary:** Ichthyosis follicularis, alopecia, and photophobia syndrome (IFAP) is an uncommon genetic condition that affects the skin, hair, and eye tissues predominantly. It is usually seen in males, as the syndrome is linked with the presence of the X chromosome. In this report we describe a unique case of a 10-year-old girl. At birth, she had a complete baldness on the scalp, eyebrows, and eyelashes, and had coarse, thickened epidermic skin over her entire body. Differently from the rest of the IFAP patients, she never had intolerance to light (photophobia). With increasing age, she developed extensive stiffness and contractures in the legs, making it impossible for her to walk.

After several assessments, the diagnosis of IFAP syndrome was confirmed through skin biopsy. The patient was then treated with orthopedic surgery that relaxed tightened tissues in her legs and lengthened her Achilles tendons, followed by a physiotherapy protocol. These treatments led to better leg positioning as well as increased autonomy in her walking functions.

This case is useful as one that demonstrates that IFAP syndrome is possible in females and that the presentation can be unusual compared with the typical form. It further indicates the importance of a team, including dermatologists, orthopedic surgeons, and rehab specialists, working in unison. Prompt diagnosis and collaborative care can very much enhance the quality of life and functioning in patients with this rare disease.

**Keywords:** IFAP syndrome, ichthyosis follicularis, alopecia, orthopedic contractures, X-linked disorder



Received: 9 October 2025
Accepted: 16 December 2025
Published: 22 December 2025

## Introduction

Ichthyosis follicularis, alopecia, and photophobia (IFAP) syndrome is a rare genetic, oculocutaneous disorder.[1] A similar situation of ichthyosis follicularis and baldness was first described by MacLeod in 1909[2] but the first IFAP syndrome was reported by Eramo in 1985,[3] The syndrome has been characterized by a triad of clinical manifestations, which include follicular ichthyosis, non-scarring alopecia, and severe photophobia.[2,4] These are usually associated with other systemic features, such as developmental delays, intellectual disability, seizures, and recurrent infections of variable severity, which may confuse the diagnosis.[5,6] The condition is caused by mutations in the MBTPS2 gene on the X chromosome.[4,7] The dermatological hallmark of IFAP syndrome is generalized thorn-like follicular hyperkeratosis, giving the skin a rough, sandpapery texture.[3,7] These lesions are most prominent on the scalp, face, and extensor surfaces.[8–11] Alopecia may be present at birth or appear in early infancy and is typically limited to the scalp, eyebrows, and eyelashes, although it can progress over time to include all body hair.[6,12,13] Photophobia is the other cardinal feature, resulting from corneal abnormalities that include superficial erosions, vascularization, and scarring, which may lead to progressive visual impairment.[3,12,14] The other associated features are atopic dermatitis, psoriasiform plaques, dystrophic nails, and angular cheilitis, thus showing the systemic nature of the disorder.[4,9,11] IFAP syndrome has a genetic basis due to mutations in the MBTPS2 gene.[7,15] This gene encodes a membrane bound transcription factor protease that participates in cholesterol homeostasis and endoplasmic reticulum stress response.[4,7,11,12] Mutations in this gene impair these processes, resulting in failure of epidermal differentiation and the characteristic clinical features of the syndrome.[11] In most reported families, IFAP follows an X-linked recessive pattern; however, rare autosomal dominant presentations and possible autosomal recessive inheritance have been described. Therefore, family history, including consanguineous marriage, is an important consideration when evaluating patients with IFAP-like phenotypes.[4,7]

The incidence of IFAP syndrome is extremely rare, with fewer than 50 reported cases worldwide since its first description.[1,8] It follows an X-linked recessive inheritance pattern in most cases; hence it affects almost exclusively males; however, cases involving females are reported, usually with a milder phenotype due to X-chromosome inactivation (lyonization).[3,4,16] Although IFAP is classically X-linked, rare autosomal dominant and possible autosomal recessive cases have been reported, underscoring the importance of detailed family history, including consanguineous marriage, when assessing suspected IFAP.[3,4,16] The disorder is challenging because of overlapping clinical features with other genodermatoses, including keratosis follicularis spinulosa decalvans, keratitis-ichthyosis-deafness (KID) syndrome, and hereditary mucoepithelial dysplasia.[17]

Early recognition is important for the prevention of irreversible complications such as profound visual loss, growth failure, and neurological deterioration. Despite the clear clinical triad associated with IFAP syndrome, it is frequently misdiagnosed, particularly in atypical presentations.[7] We report a rare female case of IFAP syndrome, an entity that usually affects males because of its X-linked inheritance, thereby expanding the known phenotypic spectrum. Such cases not only expand the phenotypic spectrum of the condition but also emphasize the need for increased clinical alertness among female patients with similar features. The present case adds to the literature on IFAP syndrome, from which several key points have been documented concerning its diagnosis, management, and genetic basis.

This report tries to raise awareness and recognition of IFAP syndrome by outlining its clinical features, diagnostic challenges, and management strategies. It also emphasizes the importance of specialized care and points out the need for further research on this rare disease in order to improve the situation of affected individuals.

## Case Presentation

A 10-year-old girl was presented to our orthopedic clinic with severe progressive limb deformities and functional restriction that caused impairment in ambulation. She was the third child of healthy, non-consanguineous parents, and there were no such similar conditions among her siblings. The patient was born at 36 weeks of gestation by normal vaginal delivery, with a birth weight of 2.9 kg, length 49 cm, and head circumference 33 cm. The mother needed an injection of Rho(D) immune globulin (RhoGAM) at 24 weeks of gestation because of the risk of Rh incompatibility between the mother and the fetus. However, due to unavailability, it was administered at 28 weeks. The father's blood

group was O positive; the mother's blood group was A negative, and the child's blood group was A negative. There were no reported neonatal complications, and she had no other systemic disease history or prior hospitalization.

## Early History and Development

The patient had congenital alopecia of the scalp, eyebrows, and eyelashes, which was first observed at birth. She also had diffuse follicular hyperkeratosis that thickened with age and involved the trunk and limbs (mostly extensors) but not the palms and soles. There were no contractures at birth, but there was progressive joint stiffness and flexor contracture over the years, both in upper and lower limbs and lumbar area, resulting in marked restriction of mobility. During childhood, she could not sit independently and required external support. Parents reported episodes of stomach pain upon trying to straighten her back.

## Neurological and Growth Evaluation

The physical growth parameters were normal (current height 128 cm, weight 24.5 kg). There was no hearing problem, but, speech development was delayed; vocabulary and sentence structure were like those of a 5 years old child, and speech was intelligible only to the family members. She had never attended school. There was no history of vision difficulty, photophobia, or symptoms of dry eye.

## Clinical Examination

Examination showed generalized rough, spiny follicular hyperkeratosis with thick plaques and scales, especially over extensor surfaces of knees and elbows, with lichenification and fissuring. She required frequent use of emollients to the skin; otherwise, in one to two months, the entire surface of her skin peels off in large sheets. There was a generalized burning sensation of the skin that worsens with an increase in ambient temperature. Scalp alopecia was total, and eyebrows and eyelashes were sparse. There was no erythema or vesiculation. Musculoskeletal examination demonstrated severe flexion contractures of the knees and equinus deformities of the ankles, with resultant fixed flexed posture and inability to walk independently (Figure 1). The elbows also had mild contractures. Muscle atrophy was noted in both lower limbs, but neurovascular examination was normal (Figure 2).

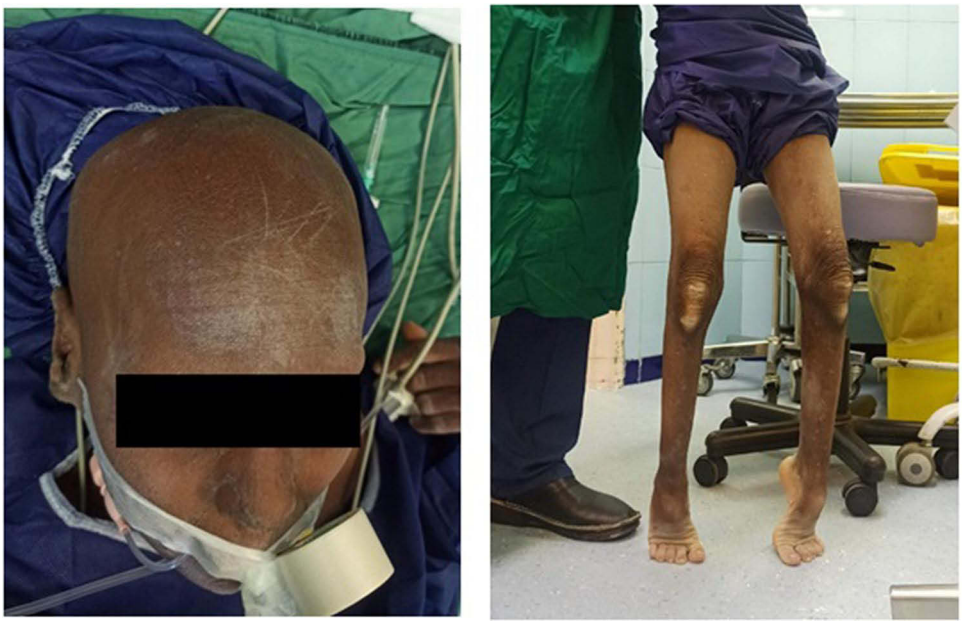

**Figure 1** Clinical photograph showing generalized follicular hyperkeratosis with rough skin texture and complete alopecia of the scalp, eyebrows, and eyelashes. Note the severe flexion contractures of the knees and equinus deformities of the ankles. (Ocular region covered for patient privacy).

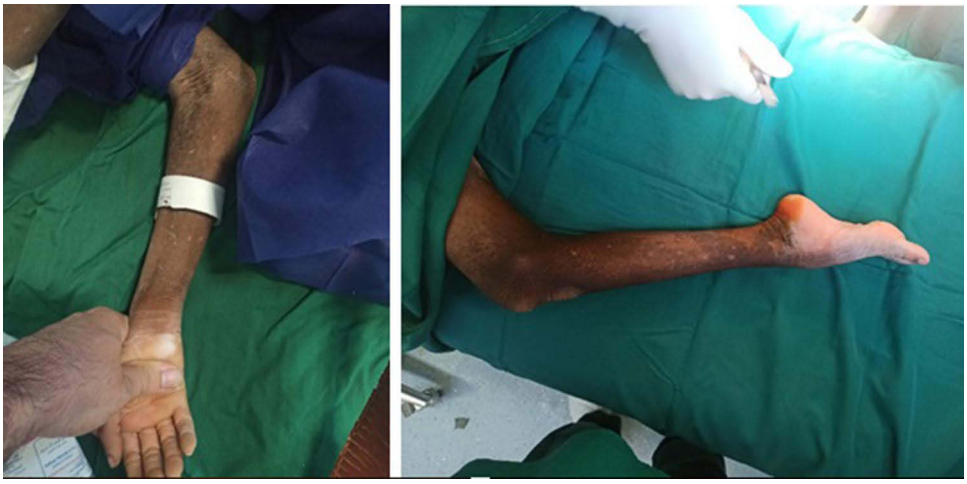

**Figure 2** Preoperative lateral view of the lower limb demonstrating fixed flexed posture and contractures before orthopedic release surgery.

## Ophthalmologic Assessment

An ophthalmologic evaluation was conducted to assess for the pathognomonic photophobia of IFAP syndrome. Uncorrected visual acuity was 9/10 in the right eye and 7/10 in the left eye, which improved to 10/10 with correction. The refractive error in the left eye was −0.75 D myopia. Ocular motility was normal, and no deviation was observed in primary gaze. On anterior segment examination, superficial corneal erosions consistent with dry eye were noted. In the posterior segment, the optic nerves in both eyes appeared pink and sharp, with no evidence of edema. The only positive finding was reduced foveal reflex in both retinas. These results confirmed that the patient's ocular condition was unusual for classical IFAP, as she did not have photophobia and keratopathy, but the visual loss can partially be explained by neurological or developmental delay.

## Radiographic Findings

Plain radiographs of the lower extremities revealed normal bony structures and joint spaces, with no skeletal dysplasia or fractures. Contractures were explained by soft tissue fibrosis secondary to chronic skin changes.

## Histopathology

During the orthopedic surgery, a skin biopsy was also taken from the hyperkeratotic areas of the extensor surface of the knees for pathological examination which demonstrated orthokeratotic hyperkeratosis, acanthosis, and papillomatosis, with follicular plugging. There was no epidermolysis or perinuclear keratin shells (as observed in Curth-Macklin Ichthyosis Hystrix). These were consistent with a diagnosis of Ichthyosis Follicularis, Alopecia (atypical, without photophobia) (Figure 3).

Diagnosis of Ichthyosis Follicularis, Alopecia, Photophobia was made on the basis of clinical and histopathological findings. Treatment was given with emollients, keratolytics, and counseling about the chronic nature of the disease. The family was referred for genetic counseling.

## Orthopedic Management

Because of the severity of the contractures, she underwent surgical release of the hamstring flexors, and after 30 sessions of physiotherapy she showed significant improvement in walking. Intraoperatively, there were dense fibrotic adhesions that were released with resultant improved extension and neutral position of the feet. She was immobilized post-operatively in above-knee casts and initiated on physiotherapy and skin care with emollients. On follow-up, she experiences abdominal pain when extending her back but there was improved walking ability with the patient recovering partial independent ambulation. (Figure 4) Notably, psychomotor development showed significant improvement following surgical intervention.

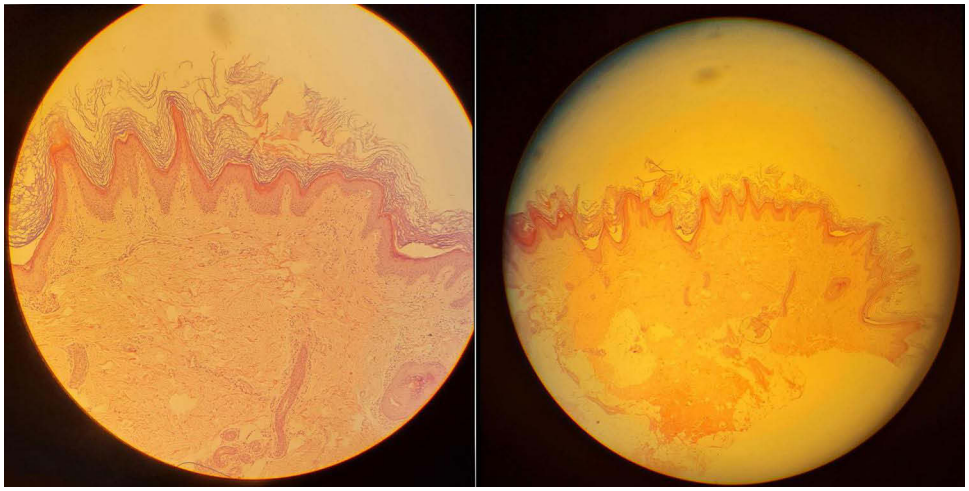

**Figure 3** Histopathology of skin biopsy (low power view, H&E stain) showing marked orthokeratotic hyperkeratosis, acanthosis, and papillomatosis.

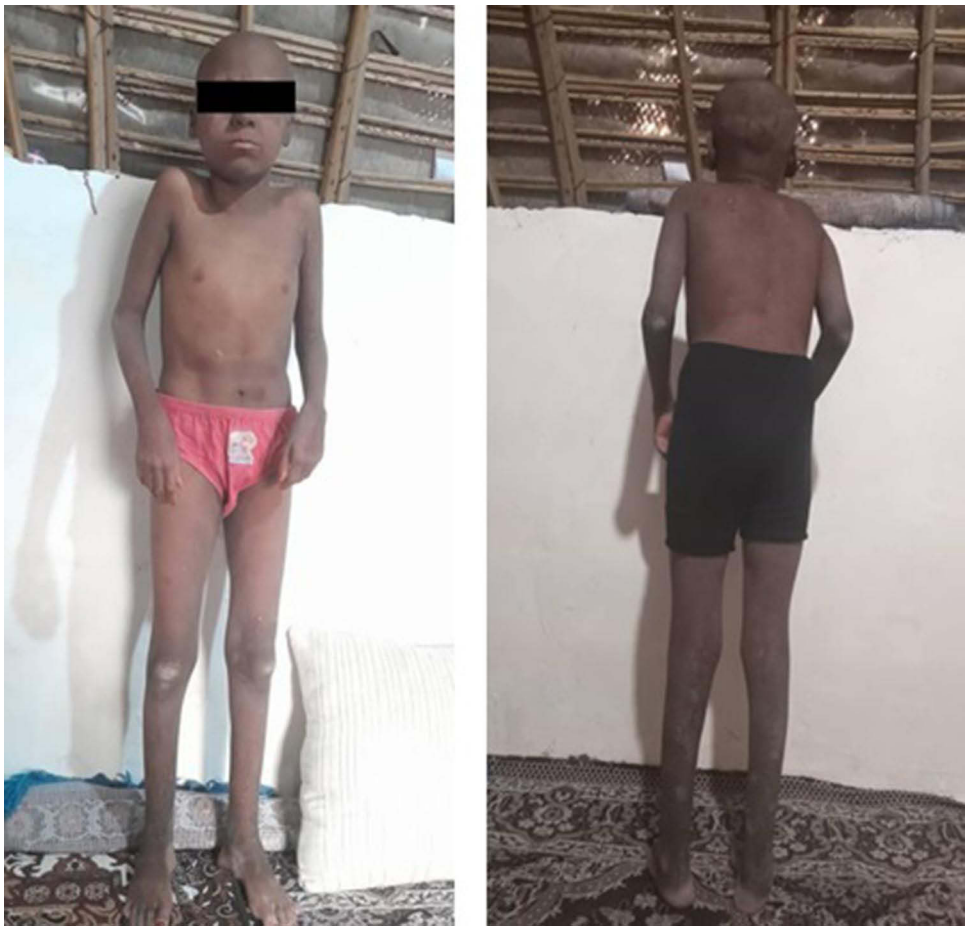

**Figure 4** Postoperative photograph showing improved limb alignment after posterior soft tissue release and Achilles tendon lengthening.

## Discussion

This case expands the phenotypic spectrum of IFAP syndrome in three key aspects: its occurrence in a female patient, the absence of photophobia despite typical cutaneous features, and the development of severe lower limb contractures

requiring orthopedic surgical intervention. Female cases are rare and usually reported with milder manifestations, making the severe musculoskeletal involvement in our patient particularly noteworthy.

IFAP syndrome is a rare X-linked genetic disorder, which is defined by the triad of ichthyosis follicularis, atrichia, and photophobia.[4,8] Since the first case reported, fewer than 50 patients were diagnosed with this disease which led to the importance of this case report.[8,12] Female cases, as in our patient, are uncommon and often attributed to X-chromosome lyonization, leading to variable phenotypic expression.[18–20] This case report highlights the clinical complexity of IFAP syndrome and highlight the need for heightened awareness among clinicians.

One of the main challenges about this disease is the broad phenotypic spectrum of the syndrome.[21] Although the main features usually start in infancy, additional findings like intellectual disability, nail and dental abnormalities, and ocular complications including keratitis and corneal vascularization may not appear until later in life.[3,6,8,14] A significant challenge about this syndrome is that there is not a curative treatment.[7,22] Current therapies are usually supportive, just targeting the symptoms like emollients, keratolytic, and systemic retinoids for the skin problems with varying degrees of success especially for retinoids due to their potential ocular side effects.[7,10,22] Genetic counseling is crucial for affected families due to its hereditary nature.[19] Orthopedic monitoring should be considered in patients with progressive contractures, as timely intervention can significantly improve functional outcomes.[8] Regular orthopedic assessments from an early age are recommended to identify and manage emerging contractures before they become severe, to prevent long term disability and improving quality of life in these patients.

Her delayed speech and limited cognitive functioning are consistent with previous reports describing neurodevelopmental delay and intellectual disability in IFAP syndrome, further supporting its multisystem nature and the need for early neurodevelopmental assessment and support.

Another unique feature of this case was the progressive musculoskeletal involvement. The patient also developed profound flexion contractures of the knees and ankles with equinus deformities, which severely compromised ambulation. The profound flexion contractures and equinus deformities likely reflect a combination of chronic skin hyperkeratosis, pain, and reduced joint mobility leading to periarticular soft tissue fibrosis, as supported by the dense fibrotic adhesions observed intraoperatively. Early dermatologic management together with physiotherapy may help preserve range of motion and potentially prevent such severe deformities, but in this instance, established deformities necessitated surgical correction. Posterior soft tissue release and lengthening of the Achilles tendons were successful in restoring limb alignment and mobility, highlighting the contribution of multidisciplinary care, including orthopedic surgery, in carefully selected patients with IFAP.

The absence of photophobia and corneal pathology in our patient shows that ocular involvement in IFAP is important and may be influenced by the specific underlying MBTPS2 variant or modifying factors. Although genetic testing was not available in our setting, the atypical ocular findings underline the importance of not excluding IFAP only on the basis of preserved corneal integrity and the lack of light intolerance, and clinical suspicion must be strong in the presence of other characteristic findings like diffuse follicular ichthyosis and congenital alopecia.

Although IFAP is typically X-linked, rare autosomal dominant and recessive patterns have been proposed.[4,9] In our patient, the absence of a family history of similar manifestations and the non-consanguineous parents are against a straightforward autosomal recessive form, but without genetic testing, an underlying MBTPS2 or another pathogenic variant cannot be excluded.

This report is limited by its single-patient design and the lack of molecular confirmation of an MBTPS2 variant, which prevents definitive genotype–phenotype correlation. Nonetheless, the detailed clinical, histopathological, and surgical findings provide useful insights into the broader phenotypic spectrum and musculoskeletal manifestations of IFAP syndrome.

Histopathology supported the diagnosis, revealing orthokeratotic hyperkeratosis, acanthosis, papillomatosis, and follicular plugging, in line with IFAP and ruling out other ichthyotic conditions like Curth-Macklin Ichthyosis Hystrix, where perinuclear keratin shells are seen. This also emphasizes the role of clinicopathological correlation in distinguishing IFAP from phenotypically allied conditions like keratitis-ichthyosis-deafness (KID) syndrome and keratosis follicularis spinulosa decalvans.

## Conclusion

This case is about an atypical presentation of IFAP syndrome in a female patient, which is distinguished by the absence of photophobia and the presence of progressive limb contractures requiring orthopedic surgical intervention. It highlights the importance of considering IFAP even in incomplete phenotypes and emphasizes the role of a multidisciplinary approach combining dermatologic, orthopedic, and genetic care to optimize outcomes. Early recognition and intervention are very important for preventing long term disability and improving quality of life in these patients.

## Declaration of Generative AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work, the authors used ChatGPT-4o (OpenAI) to improve the readability and clarity of the manuscript. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

## Abbreviations

IFAP, ichthyosis follicularis, alopecia, and photophobia; KID, keratitis-ichthyosis-deafness syndrome.

## Ethics Approval Statement

According to the policies of our local institutional review board, ethics approval was not required for a single-patient case report.

## Patient Consent Statement

Written informed consent was obtained from the patient and the legal guardian for publication of this case report and any accompanying images.

## Disclosure

The authors declare that they have no conflicts of interest relevant to this manuscript. No external funding was received for the preparation of this case report.

## References

1. Nagakeerthana S, Rangaraj M, Karthikeyan K. Ichthyosis Follicularis,Alopecia, and Photophobia Syndrome. *Int J Trichol*. 2017;9(2):67–69. doi:10.4103/ijt.ijt_69_16
2. MacLeod J. Three cases of'ichthyosis follicularis' associated with baldness. *Br J Dermatol*. 1909;21:165–189.
3. Eramo LR, Esterly NB, Zieserl EJ, Stock EL, Herrmann J. Ichthyosis Follicularis With Alopecia and Photophobia. *Arch Dermatol*. 1985;121 (9):1167–1174. doi:10.1001/archderm.1985.01660090081019
4. Mégarbané H, Zablit C, Waked N, Lefranc G, Tomb R, Mégarbané A. Ichthyosis follicularis, alopecia, and photophobia (IFAP) syndrome: report of a new family with additional features and review. *Am J Med Genet A*. 2004;124A(3):323–327. doi:10.1002/ajmg.a.20352
5. Keyvani K, Paulus W, Traupe H, et al. Ichthyosis follicularis, alopecia, and photophobia (IFAP) syndrome: clinical and neuropathological observations in a 33-year-old man. *Am J Med Genet*. 1998;78(4):371–377. doi:10.1002/(SICI)1096-8628(19980724)78:4<371::AID-AJMG13>3.0.CO;2-F
6. Dumić M, Cvitanovic M, Ille J, Potocki K. Syndrome of short stature, mental deficiency, microcephaly, ectodermal dysplasia, and multiple skeletal anomalies. *Am J Med Genet*. 2000;93(1):47–51. doi:10.1002/1096-8628(20000703)93:1<47::AID-AJMG8>3.0.CO;2-A
7. Bin Rubaian NF, Al-Awam BS, Alluhaybi AH, Alsaati AA. Ichthyosis Follicularis, Alopecia, and Photophobia Syndrome in a Saudi Child: a Case Report. *Clin Cosmet Invest Dermatol*. 2023;Volume 16:3527–3533. doi:10.2147/CCID.S439288
8. Mégarbané H, Mégarbané A. Ichthyosis follicularis, alopecia, and photophobia (IFAP) syndrome. *Orphanet J Rare Diseases*. 2011;6(1):29. doi:10.1186/1750-1172-6-29
9. van Gelderen HH, Opitz JM. Syndrome of total alopecia, multiple skeletal anomalies, shortness of stature, and mental deficiency. *Am J Med Genet*. 1982;13(4):383–387. doi:10.1002/ajmg.1320130406
10. Cursiefen C, Schlötzer-Schrehardt U, Holbach LM, Pfeiffer RA, Naumann GOH. Ocular Findings in Ichthyosis Follicularis, Atrichia, and Photophobia Syndrome. *Archives of Ophthalmology*. 1999;117(5):681–684. doi:10.1001/archopht.117.5.681
11. Cambiaghi S, Barbareschi M, Tadini G. Ichthyosis follicularis with atrichia and photophobia (IFAP) syndrome in two unrelated female patients. *J Am Acad Dermatol*. 2002;46(5):S156–S158. doi:10.1067/mjd.2002.112930
12. Khandpur S, Bhat R, Ramam M. Ichthyosis follicularis, alopecia and photophobia (IFAP) syndrome treated with Acitretin. *J Eur Acad Dermatol Venereol*. 2005;19(6):759–762. doi:10.1111/j.1468-3083.2005.01318.x

13. Bains A, Vedant D, Verma A, Bhardwaj A, Nalwa A. Ichthyosis Follicularis, Alopecia, and Photophobia (IFAP) Syndrome: a Case Report and Review of Cases Reported from India. *Indian Dermatol Online J*. 2019;10(6):686–691. doi:10.4103/idoj.IDOJ_19_19
14. Araújo C, Gonçalves-Rocha M, Resende C, Vieira AP, Brito C. A Case of IFAP Syndrome with Severe Atopic Dermatitis. *Case Report Med*. 2015;2015(1):450937. doi:10.1155/2015/450937
15. Rothe MJ, Weiss DS, Dubner BH, Weitzner JM, Lucky AW, Schachner L. Ichthyosis Follicularis in Two Girls: an Autosomal Dominant Disorder. *Pediatric Dermatol*. 1990;7(4):287–292. doi:10.1111/j.1525-1470.1990.tb01027.x
16. Binić I, Janković A, Ljubenović M. Ichthyosis follicularis with alopecia and photophobia (IFAP): late diagnosis in 18-year-old man. *Int J Dermatol*. 2011;50(4):450–453. doi:10.1111/j.1365-4632.2010.04501.x
17. Bhattacharjee H, Yadav A. A rare case of ichthyosis follicularis, alopecia & photophobia syndrome. *Indian J Med Res*. 2013;138(6):1033.
18. Happle R. What is IFAP syndrome? *Am J Med Genet A*. 2004;124(3):328. doi:10.1002/ajmg.a.20353
19. König A, Happle R. Linear lesions reflecting lyonization in women heterozygous for IFAP syndrome (ichthyosis follicularis with atrichia and photophobia). *Am J Med Genet*. 1999;85(4):365–368.
20. Happle R. X-chromosome inactivation: role in skin disease expression. *Acta Paediatrica*. 2006;95(451):16–23. doi:10.1111/j.1651-2227.2006.tb02384.x
21. Tang L, Liang J, Wang W, Yu L, Yao Z. A novel mutation in MBTPS2 causes a broad phenotypic spectrum of ichthyosis follicularis, atrichia, and photophobia syndrome in a large Chinese family. *J Am Acad Dermatol*. 2011;64(4):716–722. doi:10.1016/j.jaad.2010.02.045
22. Alfadley A, Al Hawsawi K, Al Aboud K. Ichthyosis Follicularis: a Case Report and Review of the Literature. *Pediatric Dermatol*. 2003;20(1):48–51. doi:10.1046/j.1525-1470.2003.03011.x