



Case Report

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A Rare Case report of Ichthyosis Follicularis, Alopecia and Photophobia (IFAP) Syndrome with developmental cataract

Niharika K Shetty¹, Chethan R Moogi²

¹ Professor, Department of Ophthalmology, Sri Siddhartha Medical College and Hospital, Tumakuru, Karnataka- 527107, India

² Post Graduate, Department of Ophthalmology, Sri Siddhartha Medical College and Hospital, Tumakuru, Karnataka- 527107, India

Abstract

Purpose: The IFAP syndrome is a rare X-linked genetic disorder with only 40 reported cases worldwide. We report a 23 year old, male patient with classical IFAP syndrome. **Method:** Descriptive single case report. **Case:** 23 years old male patient, presented with ocular findings of photophobia, corneal infiltrate, superior corneal vascularization and astigmatism along with dermatological manifestations. **Result:** Photophobia was pathognomonic in a patient presenting with Ichthyosis follicularis and alopecia. Associated ocular findings were corneal infiltrate, superior corneal vascularization, angio regression with pericytic infiltrate and Astigmatism. Our patient also presented with bilateral developmental cataract. **Conclusion:** Developmental cataract can be a primary manifestation with IFAP syndrome. Corneal infiltrates with photophobia as the only presenting symptom can be a rare finding associated with rare skin disorders like IFAP syndrome. They are also the most challenging symptoms to manage.

Keywords: Ichthyosis, Corneal neovascularisation, Alopecias.

INTRODUCTION

IFAP syndrome is an extremely rare genetic syndrome, with very few reported cases in the literature. This disease has been named according to its cutaneous and ocular manifestation. It is called as **Ichthyosis follicularis, alopecia, and photophobia syndrome [IFAP syndrome]**.^[1]

Superficial corneal vascularization, corneal scarring is known the ocular associations.

Atopic keratoconjunctival inflammation, chronic lacrimation, cataract, horizontal nystagmus, refractive errors like myopias, astigmatism are also seen ^[2].

Our patient presented with all the cutaneous features along with developmental cataract.

CASE REPORT

We report a case of a 23 years old male presenting to us with complaints dimness of vision and photophobia. There was photophobia since birth associated with redness and watering of eyes. He gave a history of undergoing cataract surgery in both his eyes at 17 years of age. Systemic examination showed dry rough skin with multiple brown macules on skin. There was history of diffuse hair loss involving facial and scalp hair since 8 years of age. Pedigree charting of patients family lineage showed that there was no history of a consanguineous marriage. The childhood history revealed normal growth and developmental milestones.

Similar complaints about dry rough skin was seen in the patient's mother and grandmother.

On Cutaneous Examination - Alopecia involving scalp was seen, however the eyebrows and facial hair was spared in the patient. The hairs on the face were easily pluckable (Fig 1). Also, there was reduction in the truncal and the axillary hairs. The skin on the hands showed extremely brownish hyperkeratotic plaques with dryness of the skin on the arms and the legs (Fig 2). The thumb nails and toe nails also showed dystrophy and pigmentation (Fig 2). Oral cavity showed whitish plaques on the soft palate (Fig 3).

*Corresponding author:

Dr. Niharika K Shetty

Professor, Department of Ophthalmology, Sri Siddhartha Medical College and Hospital, Tumakuru, Karnataka- 527107, India

Email:
niharika.shetty30@gmail.com



Figure 1: Alopecia predominantly in the scalp area



Figure 2: Hyperkeratosis and dystrophic Pigmentation



Figure 3: Oral Macular Paques

On Ophthalmic evaluation the best corrected vision was, OD showing 6/12 and OS showing 6/9. Both eyes Slit lamp examination revealed Superficial vascularisation of the cornea involving upper, 1/3rd of cornea spanning approximately 3 clock hours from 10' o clock periphery to 2' o clock periphery. We just encroaching the mid peripheral cornea in that area.

This vascularisation extended beyond the surgical section. The vascularisation also showed peripheral corneal punctate epitheliopathy extending beyond the vascularisation, almost up to mid periphery of the cornea (Fig 4).

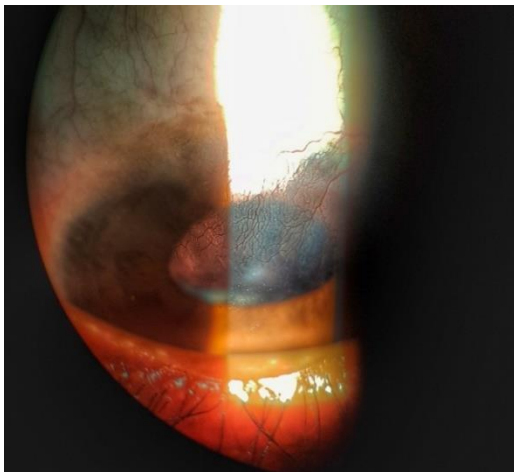


Figure 4: Corneal infiltrates extending till mid periphery



Figure 5: Corneal infiltrate extending for 3' Clock hours

The corneal epitheliopathy ranged from 0.5 mm to 1 mm in size.

The Anterior chamber, iris and pupil were normal. The patient had pseudophakia with IOL placement inside the bag (Fig 5).

Both corneas showed similar vascularisation in the upper quadrants. There was no evidence of deep vascularisation in the cornea.

Posterior segment examination on 20 Diopter and 90 Diopter did not reveal any abnormality.

The best correction for the right eye was 6/6 on Snellens visual acuity chart with - 2.50 Dcyl at 90°.

And in left eye 6/6 with -0.5 Dsph / -0.5 Dsph at 50°.

The patient was treated with photochromatic bifocal spectacles with Topical lubricants. The patient was briefed regarding his condition and the ocular affections of the disease. We also started topical steroids in form of Fluomethalone eyedrops (0.1%) eyedrops. One week follow up showed some improvement in his symptoms, however we expected a relapse of epiphora and photophobia, and hence he was advised for a regular follow up for monitoring the corneal scarring. Since corneal

neovascularisation and photophobia remain the challenging aspects of IFAP syndrome, and hence the patient was kept on a regular follow up for the same every 6 monthly. The Corneal scarring following the vascularisation can lead to blindness in these patients.

The astigmatism seen in our patient was contributed by both cataract surgery incision and corneal neovascularization infiltrates.

DISCUSSION

Ichthyosis follicular, alopecia, and photophobia as a syndrome was first time described by MacLeod in 1909 [3].

The prominent cutaneous manifestation of ichthyosis in this syndrome is characterized by non-inflammatory thorn like projections all over the body. Hyperkeratotic papules with pigmentation are most pronounced over the extensor extremities of these patients. Females are carriers and they generally show milder keratosis which are predominantly distributed along lines of Blaschko [4].

Apart from follicular pattern of ichthyosis, psoriaform plaques and even lamellar pattern of ichthyosis have been described with these diseases [5,6].

The follicular ichthyosis has been best treated with keratolytic, emollients, also urea preparations. Systemic retinoids have also shown promising results, however topical though preferable are not being used as it acts as an irritant to skin [7].

The Ichthyosis further needs proper hydration of the skin to avoid excessive dyskeratosis. The hydrating agents available as urea formations are Glycerol, urea, and propylene glycol [8,9]. Mixing hydrating and keratolytic agents can be effective for such refractory keratosis as seen in this syndrome [9-11]. But, the risk of systemic absorption of the ingredient is a fear when used in infants.

Oral acitretin and isotretinoin also are used [12]. Neonates might present with more severe cutaneous manifestation, in form of collodion membrane, dystrophic nails, psoriasiform plaques, atopic eczema, angular cheilitis, hypohidrosis, and Peringuineal inflammation [13].

The second important finding is alopecia. The hair follicles in the cutaneous area are surrounded by inflammatory infiltrate [14]. This is a non-cicatrizing type of alopecia.

The manifestation of photophobia is as early as in infancy, however sometimes it can get manifested in early childhood.

Photophobia is said to be a pathognomonic feature of this syndrome. [13]

The ichthyoses are basically a heterogeneous group of diseases linked by abnormal barrier function, which leads to increased transepidermal water loss and compensatory hyperproliferation. They are generally associated with manifestations like erythroderma, palmoplantar keratoderma, hypohidrosis, and recurrent infections [15].

The Alopecia which is seen in this syndrome is essentially congenital. The typical involvement of facial hair like scalp area, eyebrows and eyelashes is seen in this syndrome.

In cicatricial alopecia, the hair follicle is irreversibly destroyed and replaced by fibrous tissue.

Some causes of non-cicatricial alopecia are androgenetic alopecia, telogen effluvium, post chemotherapy alopecia, tinea infection of scalp, etc. but these can eventually progress to cicatricial alopecia if the treatment is not effective. The conditions which have shown such a progressive include tinea which has superadded bacterial infection like trichotillonia [16].

Superficial corneal infiltration is known to cause vascularization which may lead to progressive corneal scarring and photophobia in this syndrome. Generally male members with IFAP manifests with more aggressive progression of corneal vascularization and loss of vision [17,18].

Apart from photophobia other features include, Atopic keratoconjunctival inflammation, chronic epiphora, nystagmus, cataract, astigmatism, and myopia [18].

Our patients manifested with a developmental cataract, which was operated at a younger age and hence patient had a good visual rehabilitation. However, the morphological prototype and the type of cataract has not been described in literature.

The cornea may show severe punctuate keratopathy, with pain. There are cases reported with progressive vascularization and corneal opacity [17].

Female carriers are known to present with photophobia and sometimes with retinal vascular tortuosity.

Topical steroids are usually first-line of treatment in corneal vascularization as it is assumed to be secondary to some degree of inflammation. Since steroids do not act on the mediators of angiogenesis and also raise the intraocular pressure, there always exists a risk with long term treatment as in case of IFAP [19].

Vascular endothelial growth factor, have been proven as a major cause of Corneal neovascularization, especially in inflamed and vascularized corneas [20]. Topical and/or subconjunctival administration of VEGF has been shown to be effective in refractory cases [21].

The efficacy of anti- VEGF is predominantly against the actively growing vasculature in the cornea. It has been proven that established vasculature do not need VEGF for proliferation. It has been said that pericytic cuff around the vasculature terminates the sensitivity of the vasculature towards the Circulating VEGF and actually leads to regression and apoptosis of these vessels. This period is believed to be lasting for 3 months from the inception of the neo -vessels till the first few weeks. In this particular lesion since the neovessels are believed to start in the early childhood, we desire a anti regressive therapy as against anti-angiogenesis. Hence the role of Anti VEGF may be questionable [22].

Considering this theory, probably fine needle diathermy or laser photocoagulation may be more effective in IFAP cases [23].

For recalcitrant cases these approaches can be tried.

Some patients may show neurological findings, such as delayed neuropsychomotor development. There are also cases of mental retardation, epilepsy and other neurological findings [24].

IFAP syndrome is due to a missense mutation in the membrane-bound transcription factor protease site 2 which is called *MBTPS2* gene [25]. *MBTPS2* gene is known to be a membrane-embedded zinc metalloprotease that activates signaling proteins which is needed in control of transcription and stress response of endoplasmic reticulum [26,27]. It reduces the efficacy of cholesterol homeostasis and cellular ability to endure endoplasmic reticulum stress. Studies have proven this mutation with worst phenotype [25].

Hence to consider for a comprehensive treatment of IFAP, acitretin therapy at a dose of 0.3 to 1 mg/kg/day can be used for cutaneous features and corneal erosions but alopecia and photophobia remain refractory as noted in some patients [24,28].

Hence the newer methods of treatment of corneal neovascularization may be tried under strict supervision and titrated according to patient's response so as to prevent corneal scarring.

CONCLUSION

Bilateral developmental cataract was a rare association and was seen in our case. Photophobia and corneal infiltrates remain a challenge for management in Ichthyoses, Follicularis Alopecia Photophobia Syndrome. Newer methods for the management of photophobia needs to be explored. Also, the cataract needs to be evaluated on a regular basis for these patients as it is preventable blindness.

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Conflict of Interest

We confirm and deny any conflicts of interest existing.

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