IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 7 Ver. 2 (July. 2018), PP 15-18
www.iosrjournals.org

Hypohidrotic ectodermal dysplasia And keratoconus : A rare association.

Manasa Penumetcha[1], Reddy J K[2],Prabhakar G V[3], Derin Puthur[4]
1. Fellow in Department of Cataract surgery ,Sankara Eye Hospital,Coimbatore,Tamil Nadu,India
2. Consultant &Head ,Deapartment of Cornea, Sankara Eye Hospital,Coimbatore ,Tamil Nadu ,India
3. Fellow in Deapartment of Cornea, Sankara Eye Hospital,Coimbatore ,Tamil Nadu ,India
4.DNB student (post graduate), Sankara Eye Hospital,Coimbatore ,Tamil Nadu ,India
Corresponding author: Manasa Penumetcha

Abstract: *Ectodermal dysplasia is a hereditary disease characterized by dysplasia of tissues of ectodermal origin. Hypohidrotic ectodermal dysplasia(HED) is the most common type which presents with typical facial features. Ocular manifestations seen in this disease though rare are mainly ocular surface related. Keratoconus is a noninflammatory ectatic disorder of cornea, its association has been described with many systemic syndromes and hereditary diseases. However its association with HED is very rare. This case report discusses the systemic, ocular manifestations, and ocular treatment plan (tuck in lamellar keratoplasty for keratoconus) for HED and keratoconus. The treatment would provide functional boost to the patient in view of better visual outcome.*

Keywords: *Ectodermal dysplasia (ED), Hypohidrotic ectodermal dysplasia(HED), Keratoconus*

Date of Submission: 24-06-2018 Date Of Acceptance: 09-07-2018

I. Introduction

Ectodermal dysplasia (ED) is a disorder that results from abnormal formation of no less than two of the four major ectodermal derivatives in the developing embryo.

Hypohidrotic ectodermal dysplasia is a rare multisystem disorder affecting skin, teeth, hair and nails, sweat glands and part of the eyes.[1]

The clinical findings detected in patients with HED are as follows: hypotrichosis, hypohidrosis and cranial abnormalities. These patient's facies are smaller with respect to normal individuals because of frontal bossing, a depressed nasal bridge, absence of sweat glands resulting in smooth, dry skin and/or hyperkeratosis of hands and feet. Oral characteristics may present with anodontia, hypodontia and conical teeth. It is also known to affect mucous producing glands in the upper respiratory tract and in the endothelium in the lungs owing to recurrent upper and lower respiratory tract infections, feeding difficulties, vomiting and chronic diarrhoea in these patients.[2,3]

UgurKeklikci et al[4] described ocular manifestations in HED and EEC. 75 percent of these manifestations were ocular surface related. They described Periorbitalhyperpigmentation (88.9%) Eyebrows anomaly (88.9%) Lashes anomaly (83.3%) Dry eye symptoms (61.1%) Lacrimal duct anomaly (22.2%) Corneal Opacity (11.1%).

In 2012 M. Picconi et al[5] reported the first ever association between keratoconus and Hypohidrotic ectodermal dysplasia and also reported a missense mutation in the ED1 gene in the same patient.
We report a case with similar association of keratoconus and HED.

II. Case Report

A 17 year old male diagnosed case of Hypohidrotic ectodermal dysplasia was referred to our ophthalmology OPD in view of low vision in the right eye. History revealed the boy was born at term after an uneventful pregnancy and delivery. Family history was not relevant. The boy had suffered with repeated lower respiratory tract infections most of his life for which he was hospitalized.
Examination revealed distinctive facies: frontal bossing, brittle sparse scalp hair, saddle nose, prominent lips, dry dark pigmented skin with hypohidrosis and anodontia with atrophic alveolar ridge

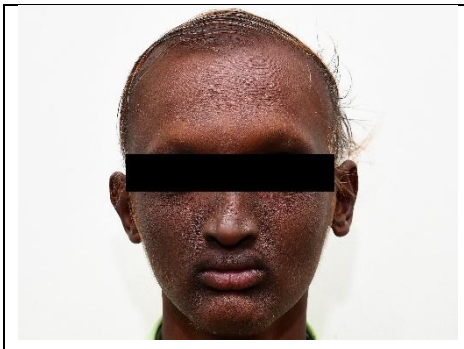

Fig 1a: Typical facies : frontal bossing, brittle sparse scalp hair, saddle nose, prominent lips, dry dark pigmented skin

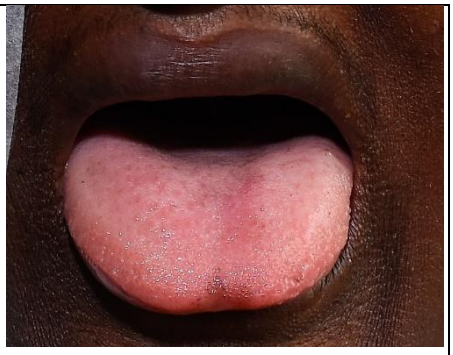

Fig 1b: Anodontia

Ophthalmological evaluation showed loss of eyebrows and scanty eyelashes, apart from skin changes rest of the lids and adnexa and lacrimal apparatus was essentially normal. Right eye had UCVA of 3/60 and BCVA of 6/60 with -7DS/-6DCy@130 in the right eye. Left eye has UCVA of 6/36 and BCVA of 6/6 with -1DS/-DCy @140. Diffuse and slit examination of the left eye was within normal limits.

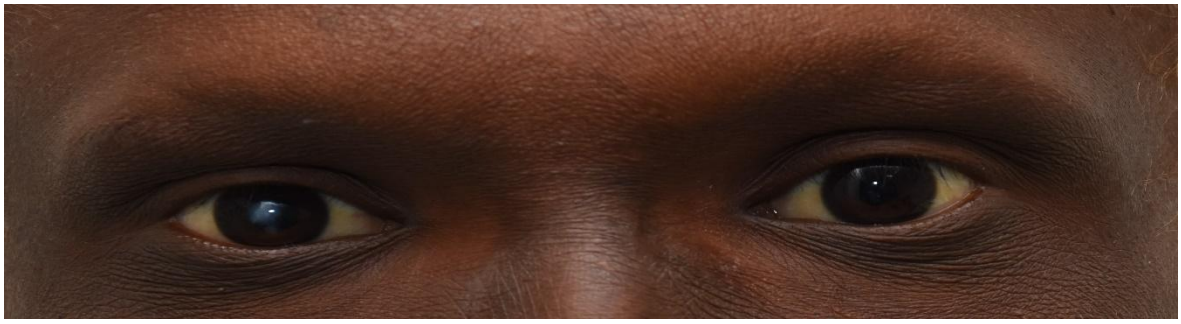

Fig 2: loss of eyebrows

Examination of the right eye on diffuse illumination revealed the cornea was normal in size with conical shape apex of which is central. A 5 * 3 mm area of paracentral macular to leucomatous opacity lies at the apex of the cone. On slit examination the scarring involves all layers of the cornea. Retinoscopy revealed scissoring reflex and oil droplet sign. Rest of the ocular examination was within normal limits. The above findings are suggestive of Right eye severe keratoconus with central scarring secondary to acute hydrops. Corneal topography was done which showed classical signs of keratoconus.

Fig 3a:Right eye- keratoconus (side profile)

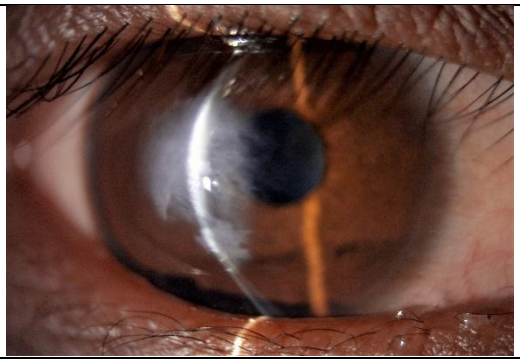

Fig 3b: Right eye severe keratoconus with paracentral scarring secondary to acute hydrops.

III. Treatment

Tuck in lamellar keratoplasty was done for the right eye. Patient was on regular follow up during the immediate post operative period. At 6 weeks follow up patient is doing well with UCVA of 6/18 and BCVA of 6/6 with-2Cy @180.

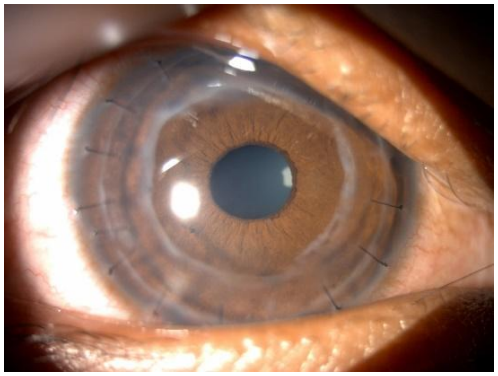

Fig 4: Post tuck in lamellar keratoplasty (6 weeks)

IV. Discussion

The ectoderm of the embryo forms the skin, teeth, hair and nails, sweat glands and part of the eyes. Surface ectoderm in the eye gives rise to Corneal epithelium, Conjunctival epithelium, Epithelium of eyelids and cilia, meibomian glands, and glands of Zeis and Moll and Epithelium lining nasolacrimal system. Over 200 different types of ectodermal dysplasias have been described. The classification of which is according to clinical findings , molecular genetic data and corresponding clinical features or according to the function of the protein encoded by the mutated gene.[6,7,8] However the most commonly seen among these are Hypohidrotic ectodermal dysplasia (HED), ectrodactyly-ectodermal dysplasia-clefting (EEC) syndrome ankyloblepharonectodermal dysplasia-clefting (AEC) syndrome and hidrotic ectodermal dysplasia.

X linked hypohidrotic ectodermal dysplasia was first described by thurnam in 1848.[9]In 1996, the EDA gene was first identified and a mutant form was found to be responsible for X-linked hypohidrotic ectodermal dysplasia (XLHED), the most common genetic disorder of ectodermal development in human beings.[10]Several studies determined the function of EDA expression on development of ectodermal structures such as teeth, hair, and several exocrine glands including sweat glands and meibomian glands.[11] The above association explains the distinctive facies of the disease.

Subsequently in 2017 Sanming Li et al [12]described the role of EDA gene in ocular structures, they described its role in:

1. Meibomian gland development, which instead secretes EDA protein
2. Corneal epithelial proliferation and would healing via the EGF-EGFR signalling pathway, with no role in cell migration.

The above explains the well known ocular features known to be associated with HED as described by UgurKeklikciet al.[4]

KC is a non-inflammatory corneal ectatic disorder characterized by progressive corneal steepening and stromal thinning leading to progressive decrease in BCVA and severe astigmatism.[13] Its association with HEDs in a case was first described in 2012.[5] Its onset is usually at puberty and the estimated prevalence ranges from 50 to 230/100 000 in the general population. The etiology of keratoconus is multifactorial with its association with multiple syndromes. The management of this condition in early stages includes spectacles, rigid contact lenses and scleral lenses. In more severe cases treatment options include penetrating keratoplasty.

Patients intolerant to contact lenses can be advised the use of INTACS. In Progressive keratoconus the progression can be controlled with collagen cross linking .[13]

In corneal ectatic disorders routine penetrating keratoplasty is technically difficult and is associated with poor visual results. This is due to the discrepancy between host and donor corneal thickness, and progressive thinning of the diseased corneal periphery after the surgery. To avoid the problem of progressive thinning in the diseased cornea larger size grafts were used but they are associated with high rates of rejection. Lamellar grafts are associated with loss of limbal stem cells. In order to provide adequate tectonic support to central as well as peripheral cornea while avoiding damage to limbal stem cells, the technique of Tuck in lamellar keratoplasty (TILK)was devised. In this technique, the donor lenticule has a full-thickness central part and a peripheral flange of partial thickness posterior stromal tissue. The central 8.5 mm part of the full thickness graft provides tectonic support to the central ectatic cornea while the thin peripheral flange tucked into the

intrastromal pocket integrates into the host and provides tectonic support to the peripheral cornea. Since dissection of the superficial limbal region is avoided, there is no damage to the recipient's limbal stem cells.[14]

V. Conclusion

The etiology of KC is still unknown, but the association with genetic syndromes (such as Leber's congenital amaurosis, trisomy 21, and Turner's syndrome) and genetic epidemiologic studies indicate that genetic factors may play an important role. Several attempts have been made to identify susceptibility gene loci for KC, but the lack of consistent chromosomal loci among different studies indicate genetic heterogeneity and illustrates the complex nature of the genetic contribution to the disease. Hence the need to report the above association between keratoconus and hypohidrotic ectodermal dysplasia and help in early referral of these patients to the ophthalmology department.

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