A rare case of adult-onset blepharophimosis, ptosis, and epicanthus inversus syndrome: Case report

Mahesha S[1], Shruthi Bhimalli[2], Manoj Y Bhat[2]

From [1]Chief Medical Officer, [2]Fellow in IOL, Department of Cataract and Trauma, Sankara Eye Hospital, Harakere, Shimoga, Karnataka, India

Correspondence to: Dr. Shruthi Bhimalli, Department of Cataract and Trauma, Sankara Eye Hospital, Harakere, Shimoga - 577202, Karnataka, India. E-mail: shruthibhimalli@gmail.com

Received - 02 June 2019 Initial Review - 24 June 2019 Accepted - 25 July 2019

ABSTRACT

Blepharophimosis, ptosis, and epicanthus inversus syndrome (BPES) is a rare genetic condition caused by a mutation in the FOXL2 gene and it is inherited in an autosomal dominant pattern. Identification and diagnosis of BPES syndrome by an ophthalmologist are relatively easy, based on the characteristic ocular manifestations. The most common age group at the time of diagnosis is 4 to 8 years. Here, we present an unusual case of BPES in a patient who presented with the syndrome at the age of 52 years. There is a need for increased awareness about this condition among ophthalmologists as early diagnosis is the key factor in preventing long term complications.

Keywords: *Blepharophimosis, Epicanthus inversus syndrome, Ptosis.*

Blepharophimosis, ptosis, and epicanthus inversus syndrome (BPES) is a genetic condition associated with mutations in the Fork head Box L2 (FOXL2) gene. The syndrome is inherited in an autosomal dominant pattern, with an estimated incidence of 1 in 50,000 births [1,2]. It is divided into two types depending upon the affected organs. The Type 1 BPES involves a defect in eyelids and ovaries, whereas, only eyelids are affected in the Type 2 BPES. The diagnosis is usually made at birth or during early childhood owing to its characteristic ocular deformities [3]. Primary presentation of BPES in older age is extremely uncommon and only scarcely been reported in the literature. We present a sporadic case of BPES Type 2which first presented and was diagnosed during the sixth decade.

CASE REPORT

A 52-year-old male patient presented to our hospital with gradually progressive diminution of vision in his left eye for the past two years. He had a history of vision loss in his right eye during his early childhood years. On detailed history, the patient revealed a past history of recurrent eye-related complaints of mild to moderate intensity. He was prescribed with corrective lenses two years earlier at another hospital. However, the patient was neither advised for corrective surgery nor for the screening of family members in any of his previous visits.

Systemic examination was normal and general physical examination revealed pre-auricular tag (Fig. 1) and high-arched palate (Fig. 2). On ocular examination, he had chin elevation with esotropia in his right eye. He also had bilateral blepharophimosis, bilateral severe ptosis with poor levator function, frontalis over-action, epicanthus inversus and telecanthus (Fig. 1). On acuity testing, his best vision was 'finger counting close to face' in his right eye and 'finger counting at one meter' in his left eye. He had corneal ectasia with scarring and vascularization (Fig. 3) in his right eye. On further examination, both eyes revealed decreased tear film height, and Schirmer's test score was low with reduced tear film break up time; thus suggestive of severe dry eyes.

Based on the characteristic examination findings, a diagnosis of BPES was made. Further, his only son, 16 years of age was evaluated in detail and no symptoms or signs of the syndrome were found. Additionally, no other family members were found to have similar signs or symptoms. The patient and family were counseled about the available treatment options, the prognosis

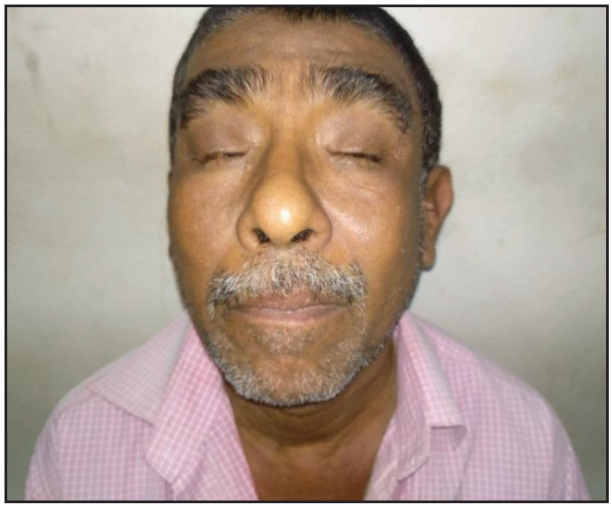

Figure 1 - Blepharophimosis, ptosis, epicanthus inversus and pre-auricular tag on the left side

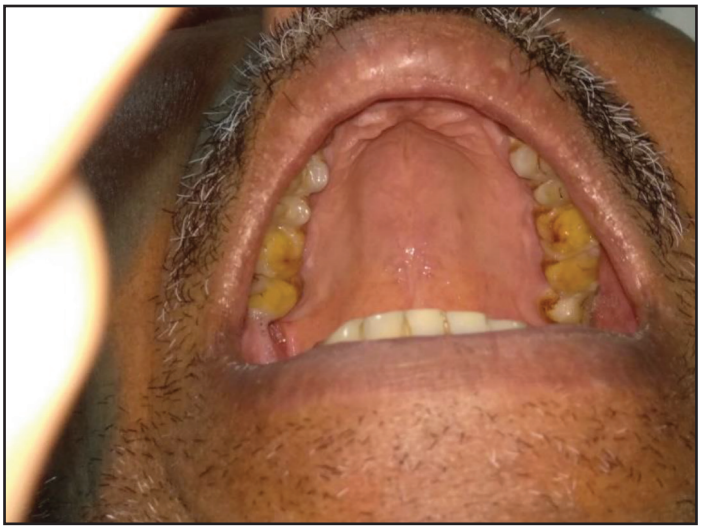

Figure 2: High arched palate

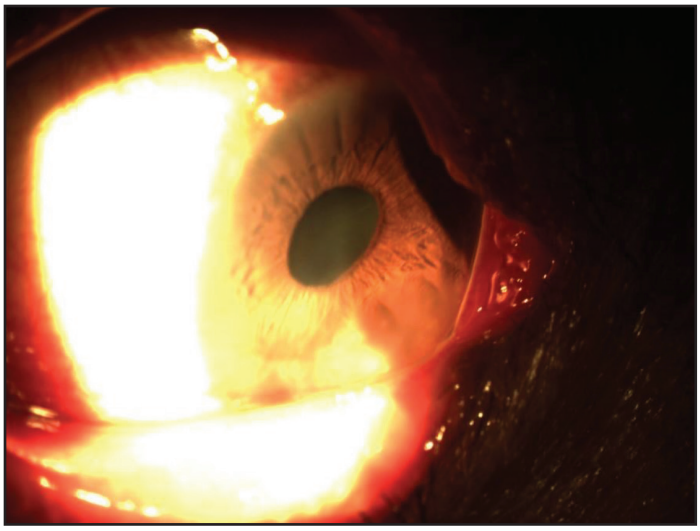

Figure 3: Corneal Ectasia

of the disease and the patient was advised to undergo cataract surgery followed by staged correction for BPES for cosmetic purpose with ptosis and squint correction. But the patient refused for further treatment after right eye cataract surgery. On follow up, after one month his right eye best-corrected distance visual acuity (BCVA) was 6/9.

DISCUSSION

Blepharophimosis, ptosis, and epicanthus inversus syndrome (BPES) is a developmental disorder and its diagnosis isbased on four major features: blepharophimosis, ptosis, epicanthus inversus, and telecanthus [4,5]. All these characteristic features were present in our patient. The patients with BPES have a high incidence of bilateral strabismus and amblyopia [2]. There is also a high incidence of refractive errors in patients suffering from BPES. Our patient had esotropia in his right eye; however, refractive errors could not be assessed in him because of the presence of cataract in both eyes. Rare ocular findings which have been reported by some authors include microphthalmos, anophthalmos, microcornea, hypermetropia, and nystagmus. None of these rare features were detected in our patient. In addition to the above-mentioned findings, our patient was also found to have a high arched palate. The patients with BPES have also been reported to present with congenital cardiac deformities along with the high risk of acquired cardiac conditions due to the lack of estrogen.

There have been several case reports reporting isolated cases of BPES. Most of these case reports had reported 4 and 8 years as the most common age group at the time of diagnosis [2–5]. In contrast, our patient was primarily diagnosed at an age of 52 years which is an unusual age of presentation. Few of the several reasons for the delay in diagnosis may include birth at home rather than a hospital, rural background, low socioeconomic status, male sex, lack of involvement of other organs, and unfamiliarity of the syndrome among the medical professionals. Several reports indicate that the diagnosis for the syndrome was made in otherwise asymptomatic female patients during evaluation for infertility [3].

BPES has its genetic basis in a mutation of the FOXL2gene,which is located on the long arm of chromosome 3 (3q23).Four types of deletions in chromosome 3q have been described in BPES (viz. 46XY, del 3qter; 46XY, del 3q26.3; 46XX, del 3q24-25 and 46XY, del 3q26-qter). Patients who are cytogenetically normal should be further evaluated for FOXL2 sequence variations. Complete or partial loss of FOXL2 protein function leads to the development of BPES Type I and II, respectively. The FOXL2 gene instructs the proteins involved in the eyelid muscles and ovarian development. More than 100 FOXL2gene mutations have been identified in BPES, which include, but are not limited to, frameshift insertions, nonsense mutations and missense mutations [2]. In our case, we did not study genetic anomaly of the patient as a diagnosis of typical genetic anomaly is not a diagnostic criterion of BPES, which is largely a clinical diagnosis. Further, genetic studies do not help in differentiating between the types of the syndrome. Additionally, it provides no useful information required for planning the management for the patient.

Diagnosis of BPES by an ophthalmologist is relatively easier owing to the characteristic ocular manifestations. Early identification and establishing a family pedigree help in starting the specific treatment in the early phases of the disease; thus, avoiding the risk of any irreversible damage such as amblyopia [4]. Another important non-ophthalmic complication to keep a close watch for is infertility in females. Females with infertility are often found to undergo several expensive investigations for the evaluation of the problem, which can be avoided in patients with BPES related infertility by diagnosing this syndrome through its typical facial features.

Goals of treatment include fertility preservation by cryopreservation of ovarian tissue, prevention of long-term side effects of hypoestrogenic state and prevention of amblyopia by early corrective surgery of eyelid and strabismus. Hormone replacement therapy in higher doses should be continued until

menopause to prevent hypoestrogenic state [3]. These patients require long term follow-up and treatment by a multidisciplinary team including ophthalmologist, gynecologist, endocrinologist and cardiologist [4]. Furthermore, once someone in the family is identified to have BPES, genetic counseling for the patient's family is required.

Selecting the timing for eyelid surgery is controversial. It involves weighing the risk-benefit ratio. While early surgery would prevent deprivation amblyopia, late surgery would allow for more reliable ptosis measurements, which will further provide a better surgical outcome. Further, ptosis surgery is hampered by the dysplastic structure of the eyelids [6]. The surgical management is traditionally performed in two stages and involves a medial canthoplasty for the correction of blepharophimosis, epicanthus inversus, and telecanthus between the age of three to five years, followed about a year later by ptosis correction, which usually requires a brow suspension procedure [6,7]. Alternatively, a one-stage procedure in which medial canthoplasty and ptosis correction are performed simultaneously has been described [8]. Recent insights into the causes of the abnormal lower eyelid positioning allow amore targeted surgical reconstruction that produces a more natural appearance [9].

CONCLUSION

Blepharophimosis, ptosis, epicanthus, inversus syndrome (BPES) is a rare disease that is not difficult to diagnose as it has typical clinical features. However, awareness needs to be raised among both the ophthalmologists and gynecologists about this condition. Early diagnosis is the key factor in improving long-term outcome and overall prognosis of the patients.

REFERENCES

1. Zlotogora J, Sagi M, Cohen T. The blepharophimosis, ptosis, and epicanthus inversus syndrome: delineation of two types. Am J Hum Genet. 1983;35:1020-7.
2. Chawla B, Bhadange Y, Dada R, Kumar M, Sharma S, Bajaj MS, *et al*. Clinical, radiologic, and genetic features in blepharophimosis, ptosis, and epicanthus inversussyndrome in the Indian population. Invest Ophthalmol Vis Sci. 2013;54:2985-91.
3. Niharika D, Sandipan C, Vinita G, Jaya C, Rajlaxmi M. Blepharophimosis ptosis epicanthus inversus syndrome (BPES): A rare cause of primary ovarian insufficiency. J Case Rep Images Gynecol Obstet. 2016;2:20-4.
4. Verdin H, De Baere E. Blepharophimosis, Ptosis, and Epicanthus Inversus. 2004 Jul 8 [Updated 2015 Feb 5]. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, *et al*., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle. 1993-2019.
5. Gupta AK, Gupta DC, Khan SA, Razi SM. Blepharophimosis Ptosis Epicanthus Inversus Syndrome (BPES) Type 1 in an Indian Family. J ASEAN Federation Endo Soc. 2017;32:68.
6. Beckingsale PS, Sullivan TJ, Wong VA, Oley C. Blepharophimosis: a recommendation for early surgery in patients with severe ptosis. Clin Exp Ophthalmol. 2003;31:138-42.
7. Sa HS, Lee JH, Woo KI, Kim YD. A new method of medial epicanthoplasty for patients with blepharophimosis-ptosis-epicanthus inversus syndrome. Ophthalmology. 2012;119:2402-7.
8. Wu SY, Ma L, Tsai YJ, Kuo JZ. One-stage correction for blepharophimosis syndrome. Eye (Lond). 2008;22:380-8.
9. Decock CE, Claerhout I, Leroy BP, Kesteleyn P, Shah AD, De Baere E. Correction of the lower eyelid malpositioning in the blepharophimosis-ptosis-epicanthus inversus syndrome. Ophthalmic Plast Reconstr Surg. 2011;27:368-70.

Funding: None; Conflict of Interest: None Stated.

How to cite this article: Mahesha S, Bhimalli S, Bhat MY. A rare case of adult-onset blepharophimosis, ptosis, and epicanthus inversus syndrome: Case report. Indian J Case Reports. 2019;5(4):363-365.

Doi: 10.32677/IJCR.2019.v05.i04.023