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CASE REPORT
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A Rare Case of Blepharophimosis, Ptosis, Epicanthus Inversus Syndrome with Antimongloid Slant: Case Report

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Abstract

Blepharophimosis, ptosis, 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 a case of BPES in a patient who presented to our OPD side with the syndrome at the age of 20 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.

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Introduction

Blepharophimosis, ptosis, and epicanthus inversus syndrome (BPES) is a genetic condition associated with mutations in the Forkhead 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 on the affected organs. Type 1 BPES involves a defect in eyelids and ovaries, whereas only eyelids are affected in type 2 BPES. The diagnosis is usually made at birth or during early childhood owing to its characteristic ocular deformities.[3]

Case Report

A 20-year-old male patient presented to our hospital with a complaint of small bilateral eyes with bilateral drooping of upper eyelids. According to the patient, he has had these symptoms since birth, as told by his parents to him. On detailed history, the patient revealed that his father also had the same facial features with no visual impairment. The patient also had no visual complaints since childhood and he never visited any hospital for these complaints.

Systemic examination was normal and general physical examination revealed an antimongloid slant, which was more prominent in his childhood as depicted by his old photos (Figure. 1) . On ocular examination, he had chin elevation

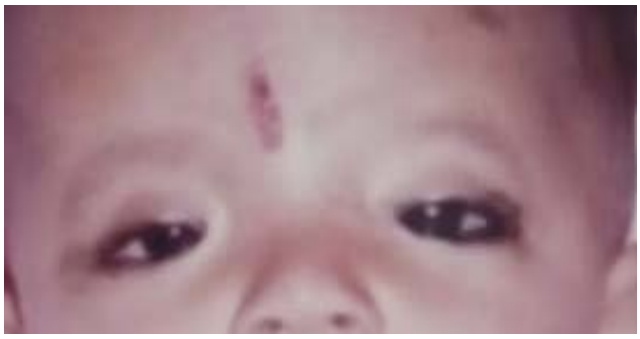

Figure 1: Childhood picture of a patient with BPES

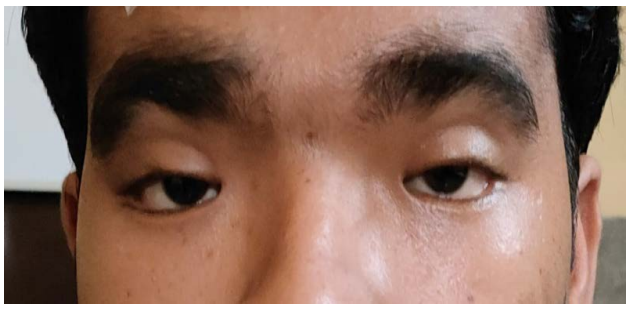

Figure 2: Preoperative picture of a patient

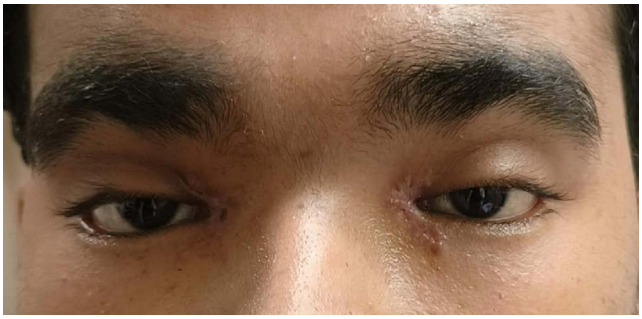

Figure 2: Post operative (Day 1) picture

with pseudoesotropia in both his eye. He also had bilateral blepharophimosis, severe bilateral ptosis with fair levator function, epicanthus inversus and telecanthus (Figure. 2). On acuity testing, his best vision was 20/20 in his both eyes.

Based on the characteristic examination findings, a diagnosis of BPES was made. Further, his family history was taken and as earlier mentioned father had similar facial features but his brother did not have any such symptoms. The patient was counseled about the available treatment options and the prognosis of the disease and the patient was advised two staged corrections for BPES for blepharophimosis, telecanthus and epicanthus inversus in the first setting and ptosis in the second stage. The patient underwent stage 1 correction for BPES and followed up was done at day 1, and day 10 with satisfactory results, as stated by the patient himself regarding a cosmetic point of view (Figure 3).

Discussion

Blepharophimosis, ptosis, and epicanthus inversus syndrome (BPES) is a developmental disorder and its diagnosis is based on four major features: blepharophimosis, ptosis, epicanthus inversus, and telecanthus.[4,5] All these characteristic features were present in our patient. 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. Some authors have reported rare ocular findings including 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 antimongloid slant which was more significant in his childhood (Fig. 3). 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]

BPES has its genetic basis in a mutation of the FOXL2 gene, 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). Cytogenetically normal patients should be further evaluated for FOXL2 sequence variations. Complete or partial loss of FOXL2 protein function leads to BPES Type I and II development, respectively. The FOXL2 gene instructs the proteins involved in the eyelid muscles and ovarian development. More than 100 FOXL2 gene 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 the 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 differentiate between the syndrome types. Additionally, it needs to provide more useful information 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. The 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 a hypoestrogenic state.[3] These patients require long term follow-up and treatment by a multidisciplinary team, including an ophthalmologist, gynecologist, endocrinologist, and cardiologist.[4] Furthermore, genetic counseling for the patient's family is required once someone in the family is identified to have BPES.

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 abnormal lower eyelid positioning allow more 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 ophthalmologists and gynecologists about this condition. Early diagnosis is the key factor in improving the patients' long-term outcomes and overall prognosis.

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