Frydman-Cohen-Karmon syndrome: a rare syndromic association of blepharophimosis

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DESCRIPTION

Blepharophimosis refers to the reduced horizontal length of the palpebral aperture. It is found to be associated with multiple syndromes.¹ Frydman-Cohen-Karmon syndrome (FCKS) is an autosomal recessively inherited syndrome characterised by the presence of features, including blepharophimosis, blepharoptosis, prognathism, camptodactyly and syndactyly.² Its inheritance pattern being autosomal recessive marks it as a separate entity from blepharophimosis ptosis epicanthus inversus syndrome (BPES), which usually follows an autosomal dominant pattern of inheritance but can also occur from spontaneous mutation. It is an extremely rare syndrome with unknown incidence with no specific molecular genetic data background.

A 13-year-old girl was presented to our outpatient department with drooping of both of her eyelids since birth (figure 1A,B). She was the first born in a family of healthy non-consanguineous married couple with three siblings, none of the others being affected. However, her parents gave the history of her great grandmother having similar facial features. She had a full-term birth with a birth weight of 2.7 kg. There was no history of any developmental delay. Parents gave a history of her having webbed fingers in both of her hands and feet for which she had undergone surgery when she was 6 years old. She had

Figure 2 Clinical picture showing surgically corrected syndactyly of (A) hands and (B) legs.

Figure 1 (A) Clinical picture of the patient showing bilateral ptosis, absent lid crease, frontalis overaction and blepharophimosis. (B) Clinical picture of the patient wearing glasses showing arched eyebrows indicating frontalis overaction to compensate for ptosis.

Figure 3 Clinical picture of the patient showing flat nasal bridge, malar hypoplasia and mandibular prognathism.

recurrent episodes of diarrhoea and was evaluated for the same and was diagnosed to have coeliac disease, with antiendomysial antibody positive. On general examination, it was found that she was 134 cm tall, which was grossly short for her age, being below 3rd percentile for her respective age group. She had broad hands and feet, short bent camptodactyly fingers. There were scars

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Figure 4 Postoperative clinical picture of the patient wearing glasses showing no frontalis overaction and formation of new lid crease indicating successful surgical outcome.

from previous surgery in second and third web spaces of both the hands (figure 2A). Similar scars were also noted in the first web space of both feet (figure 2B).

On systemic examination, no systemic disease was noted. On examining her face, she was noted to have a broad nasal bridge, with a prominent large nose, bilateral maxillary hypoplasia, mandibular prognathism and thick lower lid vermilion (figure 3). On examination of her eyes she was seen to have bilateral blepharophimosis with horizontal palpebral fissure length of 23 mm, blepharoptosis with margin reflex distance 1 of -2 mm, bilateral levator palpebralis superioris excursion of 2 mm along with telecanthus, inner canthal distance of 42 mm, inter pupillary distance of 60 mm and outer canthal distance 88 mm. Extraocular movements were normal and indirect ophthalmoscopy showed a healthy disc and macula with no peripheral treatable lesion. There was also evident lid lag, Bell's phenomenon in both eyes being fair. Her unaided vision was 4/60 and her best corrected visual acuity (BCVA) was 6/12 in both eyes and her cycloplegic refraction was $+5.00$ DS $/+0.50$ DC at 90 and $+5.00$ DS $/+0.50$ DC at 90 in the right and left eye, respectively.

A two-dimensional echocardiogram was done to rule out cardiac anomalies. Echocardiogram was obtained which also revealed no abnormalities. A genetic analysis was done to

exclude BPES and no mutation was found in the FOXL2 gene or any other gene.

She was diagnosed to be a case of FCKS with both eye hypermetropia, blepharoptosis and blepharophimosis with telecanthus with coeliac disease. She started on a gluten-free diet and was prescribed spectacle correction for hypermetropia. A frontalis sling surgery was planned for the correction of her ptosis keeping in mind that her hyperopic glasses which by magnification will reduce the amount of apparent blepharophimosis. Her postoperative outcome was satisfactory (figure 4).

FCKS is an extremely rare inherited syndrome, which was first documented by Frydman *et al* in Egypt.² They had reported it in six individuals in three related families of Yemenite with Jewish background with features of prognathism, synophrys and thick eyebrows, along with additional features of short stature, borderline head circumference and toe syndactyly. The disease Online Mendelian Inheritance in Man entry number is 210745. There is no known genetic defect for this condition and at present the diagnosis is made based on a phenotype pattern. It differs from the typical BPES described by Kohn and Romano,³ with its inheritance pattern being autosomal recessive. Our case was a 13-year-old girl with a history of small palpebral apertures along with a history of syndactyly surgically repaired at a younger age. On examination, the patient had features similar to that described by Frydman *et al*, that is, female sex, short stature, history of syndactyly, camptodactyly, mandibular prognathism, facial features being blepharophimosis and ptosis with telecanthus. However, our patient did not have a V-pattern esotropia. There was also a history of her great grandmother having similar facial features, which indicates an autosomal recessive condition. In 2002, there has been a report of two brothers having congenital ptosis with esotropia with a pedigree similar to that reported by Frydman *et al*; however, unlike FCKS both had undescended testis and one had polythelia.⁴ To our knowledge, this is the first reported case of FCKS in Asia.

The management of autosomal dominant BPES involves a two-staged procedure. The first stage involving correction of the horizontal shortening, followed by the correction of ptosis.⁵ In our case, the child being a hypermetropic, wearing high power hypermetropia glasses had a magnifying effect, thereby the patient did not require the correction of horizontal palpebral shortening.

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Patient's perspective

My daughter was not looking well from her time of birth. We knew that she has many problems. I hope everything can be treated.

Learning points

- Blepharophimosis can be associated with rare syndrome like Frydman-Cohen-Karmon syndrome, other than the more widely described blepharophimosis ptosis epicanthus inversus syndrome.
- Since there are no known genetic associations to date, a thorough paediatric examination is critical in making a diagnosis.
- A careful ophthalmological examination and proper visual assessment are essential to detect strabismus, refractive error, amblyopia and ptosis, thus, ensuring a proper visual development.
- Ptosis correction surgery can be performed either alone or as a staged procedure after medial canthoplasty.

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