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CASE REPORT

FRASER SYNDROME: A CASE REPORT

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ABSTRACT

Fraser syndrome (cryptophthalmos syndrome) is a congenital anomaly in which cryptophthalmos is the main feature. Other malformations can include syndactyly, craniofacial and urogenital anomalies. It is a rare autosomal recessive condition with FRAS1, FREM2 and GRIP1 genes mutation. We report a case of 2 months old male child born to consanguineous parents. He presented with unilateral cryptophthalmos and some features that were compatible with diagnostic criteria of Fraser syndrome such as syndactyly, high arched palate with ankyloglossia, cryptorchidism and hypospadias. It can be diagnosed by antenatal ultrasound and clinical examination. We also present the criteria for diagnosing Fraser syndrome, its prenatal findings and ocular management.

KEY WORDS: Cryptophthalmos (MeSH); Fraser syndrome (MeSH), Urogenital Abnormalities (MeSH); Syndactyly (MeSH).

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INTRODUCTION

Fraser syndrome (cryptophthalmos syndrome) also known as Cryptophthalmos Syndactyly syndrome, Ulrich Feichtiger syndrome, Fraser Francois syndrome or Meyer Schwickerath's syndromeis characterized by cryptophthalmos, genitalia anomaly, syndactyly, orofacial clefting, renal agenesis, skeletal defects, mental retardation, umbilical hernia and malformations of ears, nose and larynx.[1] It is an autosomal recessive disease affecting 0.04 in 10,000 live births.[2] Cryptophthalmos is a condition in which eyelids are replaced by skin. In complete cryptophthalmos, skin covers the microphthalmic eye with no separation between eyelids. Rudimentary lids are present in incomplete cryptophthalmos.[3] It maybe unilateral or bilateral.[4] Mutations in FRAS1, FREM2 and GRIP1 genes are present that disrupt epidermal adhesion.[5]

CASE REPORT

A 2 months old child was brought to us with complaint of skin covering his right eye. He was born to consanguineous parents and had no siblings. He was delivered by normal vaginal delivery at full term and weighed 3 kg. Prenatal record was unavailable. There was no family history of congenital malformations. Parents belonged to low socioeconomic background.

On clinical examination, there was complete cryptophthalmos in the right eye with partially formed eyebrow and absence of eyelids and eyelashes (Figure 1). A small globe was felt on palpation on the right side. He had conjunctivitis in the left eye, however it was morphologically normal. Hypertelorism was also present (Figure 1).

Other findings noted on systemic examination include cutaneous syndactyly of hands (Figure 2), low set ears (Figure 1), high arched palate (Figure 3) with ankyloglossia (Figure 4), cryptorchidism and hypospadias (Figure 5). Fraser syndrome was diagnosed on the basis of clinical features. Genetic tests couldnot be done due to financial constraints. Ocular surgical management was not possible as the patient expired due to multiple systemic complications.

DISCUSSION

FRAS1 gene mutation on chromosome 4q21 is identified in Pakistani population.[6] Other gene mutations loci are FREM2 on chromosome 13 and GRIP1 on chromosome 12.[7] In our case, the patient had complete cryptophthalmos in the right eye, cutaneous syndactyly of hands, low set ears, hypertelorism, high arched palate with ankyloglossia, cryptorchidism and hypospadias. Diagnosis is made if 2 major and 1 minor criteria or 1 major and 4 minor criterion are present. We have 3 major and 2 minor features that confirm the diagnosis of Fraser syndrome according to Thomas diagnostic criteria as shown in Table I.[8] The primary feature of Fraser syndrome is cryptophthalmos which is present in 84-93% of the patients[4]. In our case, the patient had right eye complete cryptophthalmos.

Cutaneous syndactyly occurs in 60% of cases, malformed ears in 60%, renal agenesis in 40% and abnormal genitalia in 20% cases.[6] In a study done by Gauttuso et al syndactyly was seen in 54% and cryptophthalmos in 93% cases.[9] Hypospadias, phimosis or cryptorchidism may present in males and clitoromegaly with uterine and vaginal agenesis in females.[4] In this case, cutaneous syndactyly of hands was noted along with low set ears, high arched palate, ankyloglossia, cryptorchidism and hypospadias, 15% cases have consanguinity in families and autosomal recessive inheritance. 25% recurrence rate is seen among siblings.[10] Kinship was also observed in our case.

Prenatal ultrasound is suggested, and high serum alphafetoprotein levels may also be present.[9] Surgical intervention may be done if there is visual potential on electrodiagnostic tests; however, visual prognosis is limited. It also depends on the degree of eyelid involvement and integrity of underlying structures. Mucous membrane or eyelid sharing grafts (pedicle rotation flaps or mustarde flaps) are used for eyelid reconstruction.[11]

CONCLUSION

Fraser syndrome carries poor prognosis. Prenatal diagnosis and genetic counseling is the best approach to prevent this lethal disease.

TABLE I: DIAGNOSTIC CRITERIA FOR FRASER SYNDROME[8]

MAJOR CRITERIA	MINOR CRITERIA
1. Cryptophthalmos	1. Congenital malformation of Nose, Ears, Larynx
2. Syndactyly	2. Skeletal defects
3. Ambiguous genitalia	3. Cleft lip and/or palate
	4. Renal agenesis
	5. Umbilical hernia
	6. Mental retardation

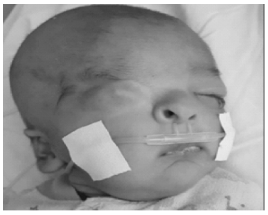

Figure 1: Cryptophthalmos, low set ears, hypertelorism

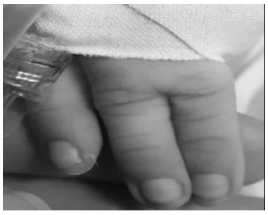

Figure 2: Syndactyly

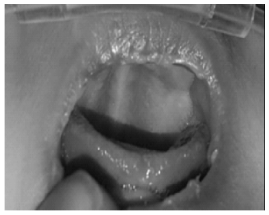

Figure 3: High Arched palate

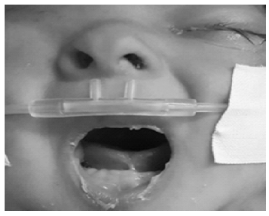

Figure 4: Ankyloglossia

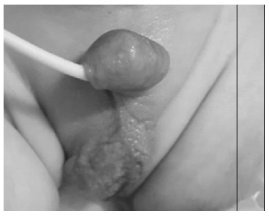

Figure 5: Hypospadias and Cryptorchidism

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

MW: Identification, diagnosis & management of the case, drafting the manuscript, critical review, approval of the final version to be published

HW & MNK: Diagnosis & management of the case, critical review, approval of the final version to be published

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

Authors declared no conflict of interest

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.