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ENT manifestations of Fraser syndrome

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Abstract
Fraser Syndrome is a rare autosomal recessive disorder (Gupta and Saxena, 1962; Smith, 1982). The most consistent feature is cryptophthalmos (hidden eye), but frequently abnormalities of the ears (meatal stenosis, dysplastic pinna), nose (hypoplastic notched nares, choanal stenosis or atresia), and larynx (glottic web, subglottic stenosis), as well as numerous other anomalies are encountered. We present four cases that have been treated at the Hospital for Sick Children in the last ten years, and describe the various ENT anomalies characteristic of this syndrome.

Introduction

The first description of cryptophthalmos was by Zehender (1872), as an isolated abnormality in which there is a failure of development of the eyelid folds. The epithelium which is normally differentiated into cornea and conjunctiva becomes part of the skin that passes from the forehead to the cheek.

Fraser (1962) described a syndrome with cryptophthalmos and multiple abnormalities in two sets of siblings, and Francois (1965) described four characteristics of the syndrome: (1) Cryptophthalmia; (2) Dyscephaly (including ear and nasal abnormalities, cleft lip and palate and meningocoele); (3) Syndactyly; (4) Malformed genitalia.

TABLE I
REPORTED ABNORMALITIES IN FRASER SYNDROME

Otological	Stenosis or atresia of the external auditory canal; microtia; low set ears; absent pinna; skin of upper helix continuous with scalp.
Nasal	Narrowed hypoplastic nares; notching of the nostrils; coloboma of the alae nasae; broad nasal bridge; beak-like nose; choanal atresia.
Laryngeal	Laryngeal atresia or stenosis.
Ophthalmological	Cryptophthalmos (complete or partial); congenital symblepharon; hypertelorism; microphthalmia; coloboma of upper eyelid; supernumerary eyebrow.
Urogenital	Renal agenesis; hypospadias; cryptorchidism; enlarged clitoris; fused labia; bicornuate uterus; malformed fallopian tubes.
Miscellaneous	Cleft lip and palate; tongue tie; syndactyly; umbilical hernia; meningo- encephalocele; mental retardation; anal stenosis or atresia; widely separated symphysis pubis; widely spaced nipples; hair growth on lateral forehead extending to lateral eyebrow.

A large number of characteristic abnormalities in Fraser Syndrome have now been reported (Gupta and Saxena, 1962; Sugar, 1968; Ide and Wollschlaeger, 1969; Dinno *et al*, 1974; Waring and Shields, 1975; Varneck, 1978; Smith, 1982), and these are listed in Table I.

Case reports

Case 1

A 7-year-old girl presented at birth with left cryptophthalmos (Fig. 1), bilateral meatal stenosis with right microtia, a notched left nostril (Fig. 2), syndactyly, anal stenosis and tongue-tie. Soon after delivery she was noted to have mild inspiratory stridor. At the age of one month, she underwent microlaryngoscopy and bron-

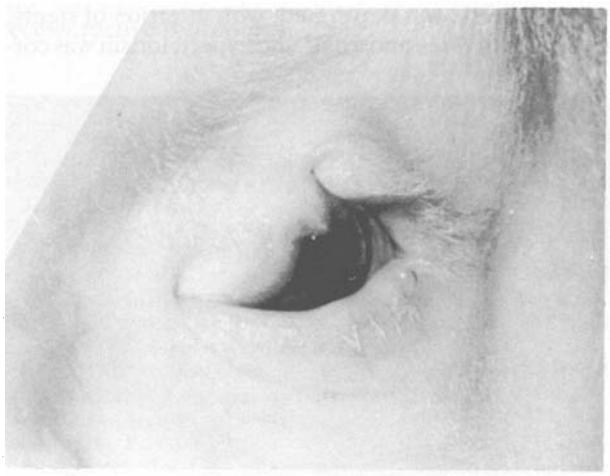

Fig. 1
Left cryptophthalmos.

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TABLE II
ABNORMALITIES IN INDIVIDUAL CASES

Abnormality	Case 1	Case 2	Case 3	Case 4
Otological	Bilateral meatal stenosis Right microtia	Bilateral meatal stenosis Bilateral microtia Low set ears	Bilateral meatal stenosis Low set ear	Bilateral meatal stenosis
Nasal	Notched left nostril	Small nostrils Broad nasal bridge Bilateral choanal atresia	Widely set nostrils Left choanal stenosis	Small Nostrils Broad nasal bridge
Laryngeal	Subglottic stenosis	Subglottic stenosis	Subglottic stenosis	Subglottic stenosis (Tracheostomy)
Ophthalmological	Left cryptophthalmos	Bilateral cryptophthalmos Hypertelorism	Bilateral cryptophthalmos Hypertelorism	Left cryptophthalmos
Urogenital		Absent left kidney Enlarged clitoris	Absent right kidney Ambiguous genitalia	Absent left kidney Hypospadias
Miscellaneous	Syndactyly Anal stenosis Tongue tie		Syndactyly Anal stenosis Hiatus hernia Widely separated symphysis pubis	

choscopy. The arytenoids were fixed together with a narrow glottic chink. A repeat microlaryngoscopy and bronchoscopy three months later showed normal arytenoid mobility and mild subglottic stenosis. At present she has mild stridor on exertion. A hearing assessment at the age of four showed a threshold of 60–80 dB on both sides and therefore a bone conduction hearing aid was fitted. At the age of six she developed a chronic right-sided ear discharge. A CT scan showed a normal middle and inner ear on the left, but on the right there was a soft tissue mass in the middle ear with bony erosion in the region of the attic. A mastoid exploration on the right revealed a large cholesteatoma and she underwent a modified radical mastoidectomy and a meatoplasty.

Case 2

A 4-year-old girl was found at birth to have bilateral cryptophthalmos, hypertelorism, bilateral meatal stenosis and microtia with low set ears, small nostrils with a broad nasal bridge, bilateral choanal atresia (confirmed by CT scan), and an enlarged clitoris. Further investigation revealed an absent left kidney.

At the age of two years, surgery for correction of the choanal atresia was performed, with insertion of stents. At the age of three and a half, the hypertelorism was corrected and at intubation she was found to have subglottic stenosis. At present she has mild stridor on exertion. A hearing assessment has shown a threshold of 60–70 dB on both sides and a bone conduction hearing aid has been fitted.

Case 3

A 2-year-old girl presented at birth with bilateral cryptophthalmos, hypertelorism, bilateral meatal stenosis with low set ears (Fig. 3), widely set nostrils, ambiguous genitalia, syndactyly, and anal stenosis with a fistula

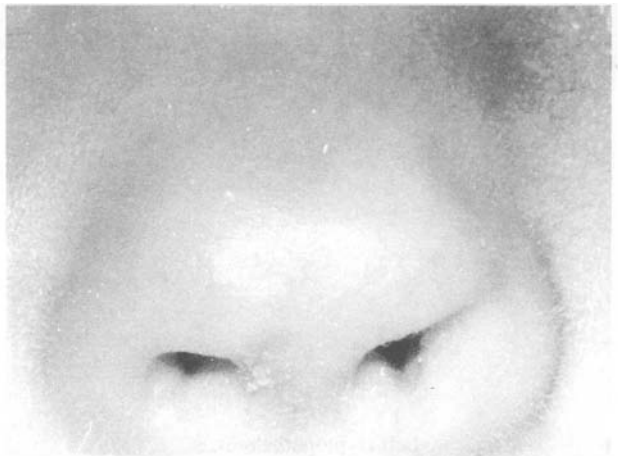

FIG. 2
Notched left nostril.

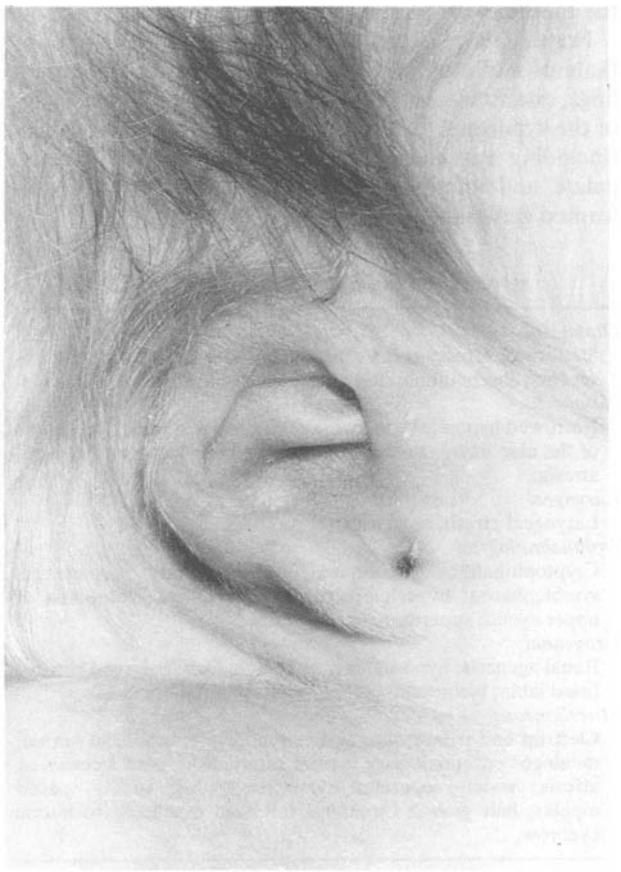

FIG. 3
Right meatal stenosis and low set ear.

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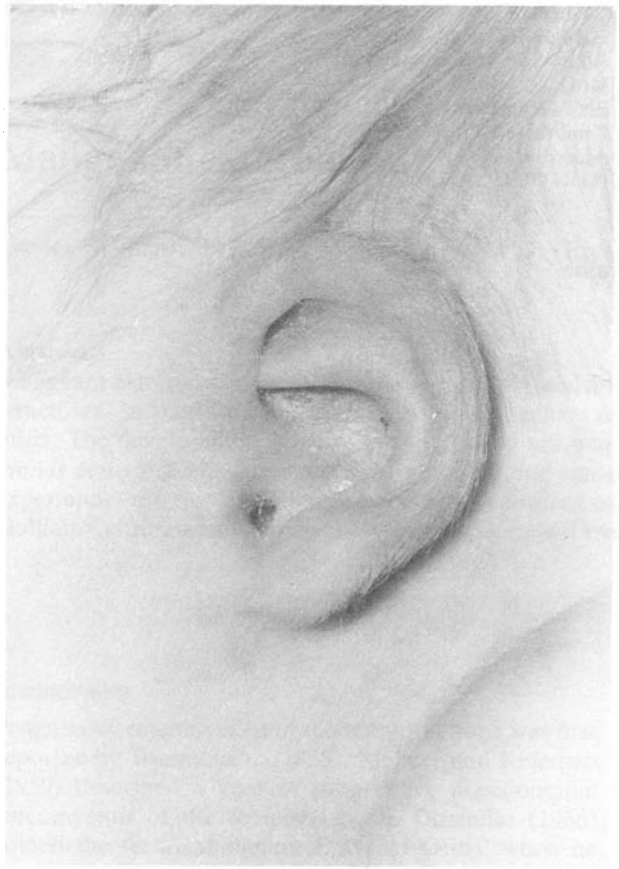

FIG. 4
Left meatal stenosis.

from the rectum to the fourchette. Further investigation revealed left choanal atresia (confirmed on CT scan), an absent right kidney, hiatus hernia and a widely separated symphysis pubis.

At the age of ten months she underwent surgery to the hands, and at intubation she was thought to have subglottic stenosis. A bronchoscopy was subsequently performed which confirmed subglottic stenosis, and this procedure was followed by stridor which settled after 48 hours of treatment with systemic steroids and nebulized adrenaline. At present she has intermittent mild stridor only occurring with upper respiratory tract infections. A hearing assessment has shown a threshold of 60–70 dB bilaterally.

Case 4

A 2-year-old boy presented at birth with left cryptophthalmos, bilateral meatal stenosis (Fig. 4), small nostrils with a broad nasal bridge, and hypospadias. Further investigation showed an absent left kidney.

A left eyelid reconstruction was performed at three months of age at which stage subglottic stenosis was detected at intubation. Two further eyelid reconstruction operations were performed, and then at the age of 14 months he developed severe laryngotracheobronchitis which necessitated tracheostomy. Follow-up microlaryngoscopy and bronchoscopy has shown a significant subglottic stenosis and a laryngotracheal reconstruction is planned. A hearing assessment has shown normal thresholds bilaterally.

TABLE III
FRASER SYNDROME—DIAGNOSTIC CRITERIA

Major	Cryptophthalmos
	Syndactyly
	Abnormal genitalia
	Sibling with Fraser Syndrome
Minor	Congenital malformation of the nose
	Congenital malformation of the ears
	Congenital malformation of the larynx
	Cleft lip and/or palate
	Skeletal defects
	Umbilical hernia
	Renal agenesis
	Mental retardation

Discussion

Over a hundred cases of Fraser Syndrome have been reported, with the majority being in the Ophthalmology or Genetic Literature. Only one case report which emphasizes the ENT abnormalities has been published (Mina *et al.* 1988).

There is an autosomal recessive inheritance of the syndrome, with just over a half of the cases being familial and the remainder sporadic. About one-quarter of the cases are stillborn and another quarter die within the first year of life, usually as a result of renal agenesis or laryngeal stenosis. A family history was not obtained in any of the cases presented. In all four the diagnosis was made within a few weeks of birth from the characteristic appearances of the eyelids, and in all cases there was a multiplicity of abnormalities.

Thomas *et al.* (1986) have proposed diagnostic criteria for the syndrome (Table III), requiring at least two major and one minor, or one major and at least four minor criteria for the diagnosis. All four cases presented fulfil these requirements. Bilateral meatal stenosis was a constant feature, with three out of the four cases also having abnormalities of the shape or position of the pinna. The external appearance of the nose was abnormal in all four cases with notched, small or widely set nostrils or a broad nasal bridge. In two patients there was also choanal atresia or stenosis. A degree of subglottic stenosis was present in all four cases and in three this was first diagnosed at the time of intubation for reconstructive procedures.

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