Fraser Syndrome with Partial Anomalous Pulmonary Venous Connection

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ABSTRACT

Fraser syndrome is characterized by cryptophthalmos, cutaneous syndactyly, malformations of the larynx and genitourinary tract, craniofacial dysmorphism, orofacial clefting, mental retardation, and musculoskeletal anomalies. We report a case of a two day old neonate who presented with features suggestive of the diagnosis of Fraser syndrome. This child also had partial anomalous pulmonary venous connection and congenital hypothyroidism.

Key words: *Fraser syndrome, Hypothyroidism, Partial anomalous pulmonary venous connection.*

INTRODUCTION

The present report describes a case of Fraser syndrome(1) with partial anomalous pulmonary venous connection (PAPVC) and congenital hypothyroidism, not described till date.

CASE REPORT

A two-day-old female term neonate born to non-consanguineous parents by cesarean section for fetal distress presented with difficulty in respiration and refusal to breastfeed for the last 12 hours. On examination the neonate weighed 2.3 kg and measured 48 cm in length. She had a narrow forehead, a tongue of scalp hair descending on to the lateral end of eyebrows, pseudo-hypertelorism, fine hair over the nose which was slightly upturned and high arched palate. The palpebral fissures with the underlying eyeballs could not be appreciated on visual inspection (***Fig.* 1**). Both the ears were low set, posteriorly rotated with right external auditory canal stenosis. The right ear was dysplastic with folded helix. The left was not externally malformed. The upper and lower limbs were normal. The genitalia were well formed with passage of meconium from the vaginal orifice (low recto-vaginal fistula). The anal opening was normally situated with normal caliber.

Echocardiography revealed the presence of partial anomalous pulmonary venous connection (two pulmonary veins draining into the left atrium and the other two into the right atrium). Hearing screen with brainstem evoked response audiometry was normal. Ultrasound examination of the abdomen and brain were normal. Chest radiograph and

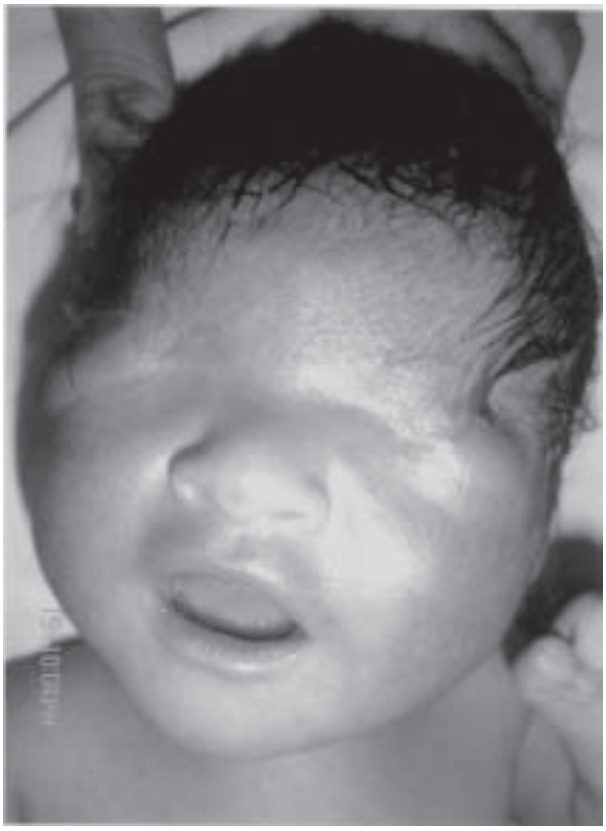

FIG. 1. *Facial features comprising of bilateral complete cryptophthalmos, narrow forehead, a tongue of scalp hair descending on to the lateral end of eyebrows, pseudo-hypertelorism and upturned nose.*

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skeletal survey did not reveal any significant abnormality.

Thyroid profile done on the seventh day of life was consistent with the diagnosis of congenital hypothyroidism [T4: 3.2 μg/L (normal: 4.8-11.6 μg/L); TSH: 48.4 μIU/L (normal: 0.28-5.6 μIU/L)]. The mother's thyroid profile was normal.

Colostomy was performed on the third day of life with definitive repair of the fistula after one month. Plastic repair of both the eyelids was performed on the tenth day of life. Corneal opacity was observed in both eyes at the time of surgery. Mutation studies were not carried out.

DISCUSSION

Fraser syndrome comprises of cryptophthalmos with defects of the eyes, especially the anterior segment, combined with anomalies of the ears, nose, limbs, urogenital system and other areas. It is inherited in autosomal recessive fashion and is caused by mutations in *FRAS1* gene located on the long arm of chromosome 4 (4q21). Our patient satisfied the diagnostic criteria proposed by Thomas, *et al.*(2) which require at least two major and one minor, or one major and four minor criteria for the diagnosis. The major criteria include cryptophthalmos, syndactyly, abnormal genitalia, and sibling with Fraser syndrome; the minor ones are (*i*) congenital malformations of the nose, ear, larynx, (*ii*) cleft lip and/or palate, (*iii*) skeletal defects, (*iv*) umbilical hernia, (*v*) renal agenesis and (*vi*) mental retardation.

The cardiac anomalies reported thus far in Fraser syndrome include hypertrophy of the left ventricle(3) a variant of Ebstein anomaly, coarctation of the aorta(4), an atrial septal defect(5), an interventricular communication(6), and a truncus arteriosus and a ventricular septal defect(4). One patient had complex heart disease with dysplasia of the pulmonary and aortic valves and endocardial fibrosis(7). A patent foramen ovale and patent ductus arteriosus were present in three cases and one patient had a patent ductus arteriosus and dilated coronary sinus(8). Dextrocardia and transposition of the great vessels are also reported. The present report is the first to describe the association of Fraser syndrome with partial anomalous pulmonary venous connection. We could not investigate the cause of congenital hypothyroidism in this child. It is possible that the observed finding is incidental. With cryptophthalmos, prognosis with regard to sight is uniformly poor. Otherwise the prognosis is dependent on the type and severity of the associated defects. Prenatal diagnosis by means of ultrasonography and fetoscopy is possible.

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