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Case Report
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Fryns Syndrome: Long Term Infertilty May Cause Teratogenicity/Mutation/Syndrome

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Abstract

Fryns syndrome is syndrome in which Congenital Diaphragmatic Hernia (CDH) is a characteristic feature. Fryns syndrome comprises CDH and pulmonary hypoplasia, brachytelephalangy with nail hypoplasia, craniofacial dysmorphism, and organ malformations. We report a case of Fryns syndrome with all characteristics and after a long infertility without any treatment in elderly parents.

Keywords: Fryns syndrome; Elderly Parents; Infertility; Syndrome

Introduction

Fryns syndrome is the commonest autosomal recessive syndrome in which Congenital Diaphragmatic Hernia (CDH) is a characteristic feature. FS comprises CDH and pulmonary hypoplasia, brachytelephalangy with nail hypoplasia, craniofacial dysmorphism, orofacial clefting, and organ malformations including cerebellar and neuronal heterotopias, ventricular septal defects, renal cysts, and bicornuate uteri [1-3].

Diagnostic guidelines have been established but there are no formal diagnostic criteria for FS or currently known biochemical or molecular markers for FS, and the aetiology has not been determined. Several different chromosome aberrations have been associated with a phenotype similar to FS [4,5]. For example, Pallister-Killian syndrome or tetrasomy 12p has frequently been the cause of a presentation resembling FS with CDH, pulmonary hypoplasia, coarse facial features, aortic stenosis and cardiac septal defects, anal abnormalities, and hypoplasia of the external genitalia [6]. CDH is associated with an underlying cytogenetic abnormality in 10%–33% of cases [4]. We report this case because our case is spontaneous conception product after a long infertility and elderly parents. It means long infertility and old age of parents may cause some genetic changes and leads to syndromic clinical features in newborn.

Case Presentation

A newborn admitted in neonatal nursery at Govt. Mahila chikitsalaya Ajmer. He was delivered as full term LSCS due to polyhydramnios and foetal distress. He had c/o difficulty in breathing, sluggishness just after birth with apgar 6/10 at 1 min, 7/10 at 5 min. Age of mother at the time of delivery was 45 years & fathers age 48 years. Age of mother at marriage was 20 years. She had undergone D&C procedure at age of 22 years with 7 year treatment of infertility but not conceived. At present document not available. She conceived at age of 45 years spontaneously without any infertility treatment. Mother had taken tab iron folic acid, calcium during pregnancy. No history of other medication. Second trimester USG shows polyhydromnios with multicystic kidney disease in fetus Last week USG shows polyhydromnios with multicystic kidney disease in fetus.

Gestational age assessment by new ballard score is 38+-2 weeks. On examination weight, length and head circumference were 2.8 kg, 43 cm, 32 cm. Child has scaphocephaly, large forehead, low set ear, broad nasal bridge, hypertelorism, microphthalmia, narrow palpebral fissure, distorted eyelashes, few hair at eyebrow, big nose, long philtrum, retognathia, high arched palate, short neck, loose fold of skin at bask of neck, widely spaced nipple, abnormally large fingers and toes with hypoplasia of nails, hypospadiasis, bilateral club foot and clinodactyly of 2nd toe bilaterally (Figure 1). Child has recurrent tearing with vomiting initially 3 days. Detail ophthalmic examination was normal.

X-ray shows high left dome of diaphragm (Figure 2). Other findings in whole body x-ray were normal. USG cranium was normal (Figure 3). USG abdomen and thorax shows eventration of

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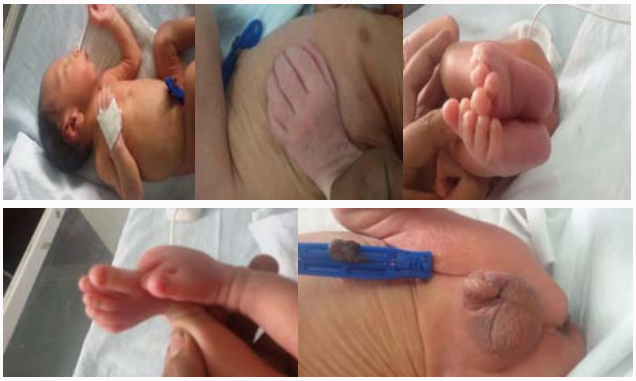

Figure 1: Physical examination of child.

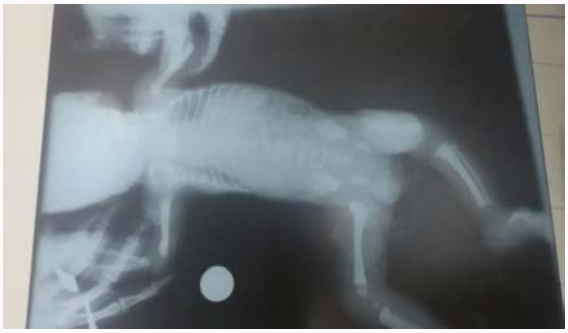

Figure 2: X-ray shows high left dome of diaphragm.

diaphragm on left side with multicystic dysplastic kidney right side (Figure 4). ECG was normal complete blood count within normal limits. Other blood investigation were normal including CRP, urea, creatinine, SGPT, sugar, blood culture.

Child was kept on O2 by hood for initial 36 hours. IV cefotaxime was given for 7 days. Catori and spoon feed started at age of 48 hour. Initially child has vomiting problem after each feed. Domperidone drops and head end elevation done. Now child take catori and spoon feed as well as mother feed well with no vomiting. Sample for Chromosomal and genetic study was normal. Child discharged successfully after 10 days of hospital stay. After 7 days on follow up gained appropriate weight and well. 2d- echocardiography shows complex congenital heart disease (ASD and multiple VSD). Later on child admitted with breathing difficulty at age of 3 month with diagnosis of pneumonia and successfully discharged. At age of 6 month child again of severe respiratory distress required ventilator and dopamine, dobutamine support with diagnosis of severe pneumonia, respiratory failure with shock and died.

Discussion

Fryns syndrome is an autosomal recessive hereditary disease, characterized by diaphragmatic defects (diaphragmatic hernia, eventration, hypoplasia or agenesis); characteristic facial appearance (coarse facies, ocular hypertelorism, broad and flat nasal bridge, thick nasal tip, long philtrum, low-set and poorly formed ears, tented upper lip, macrostomia, micrognathia); small thorax with widely spaced hypoplastic nipples, distal digital hypoplasia (nails, terminal phalanges); pulmonary hypoplasia; and associated anomalies (polyhydramnios, cloudy corneas and/or microphthalmia, orofacial clefting, renal dysplasia/renal cortical cysts, and/or malformations involving the brain, cardiovascular system, gastrointestinal system,

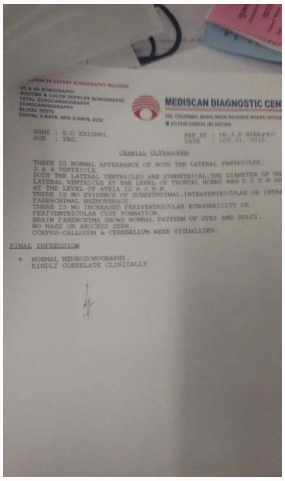

Figure 3: USG of cranium.

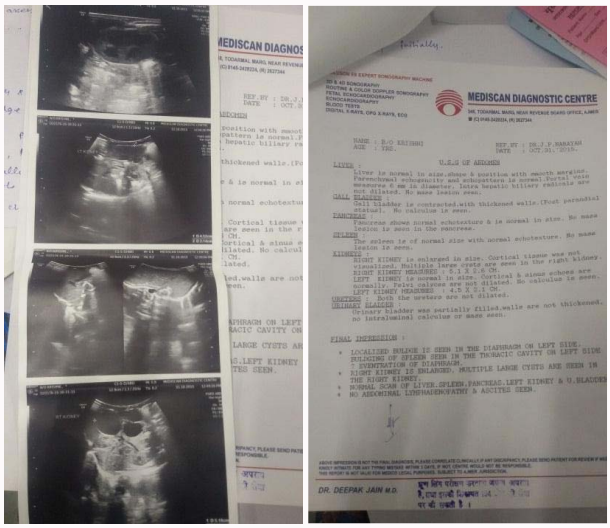

Figure 4: USG abdomen and thorax.

genitalia). Survival beyond the neonatal period has been rare. Data on postnatal growth and psychomotor development are limited; however, severe developmental delay and intellectual disability are common.

Fryns syndrome is the one of the most common syndromes associated with Congenital Diaphragmatic Defect (CDH), reported in up to 10% of patients with CDH. Although no eye abnormality was seen in our patient, other findings were similar to the other typical diagnostic findings. Fryns et al. [1] first described this syndrome in 1979 with the major diagnostic criteria include abnormal facies (coarse face, abnormal ear shape, cleft lip, cleft palate, large mouth, microretrognathia, and broad nasal bridge), small thorax with widely spaced hypoplastic nipples, distal limb and nail hypoplasia, and diaphragmatic hernia with pulmonary hypoplasia [1,3]. Diaphragmatic hernia is a leading diagnostic feature in Fryns syndrome, recorded in more than 80% of cases [4]. The rate of mortality in the lethal phenotype has changed, considering the past, and a 15% chance of survival is reported today [7]. Classically, Fryns syndrome is characterized by distal limb hypoplasia. The spectrum of distal limb hypoplasia includes short and broad hands, short digits, short or absent terminal phalanges, hypoplastic or absent nails and

clinodactyly [8]. Our patient showed short digits and nail hypoplasia.

Our case does not have diaphragmatic hernia, small thorax pulmonary hypoplasia; and associated anomalies (cloudy corneas and/or microphthalmia, and/or malformations involving the brain, cardiovascular system, gastrointestinal system). Other characteristic findings are similar to cases reported by other authors.

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