

Cardiovascular malformations in Fryns Syndrome



A case report

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Abstract

Fryns syndrome is characterized by multiple congenital anomalies including congenital diaphragmatic hernia (CDH), and congenital heart disease (CHD). The prognosis of infant with Fryns syndrome and left sided CDH when associated with pulmonary hypoplasia is grave. We report a 2- year old boy with Fryns syndrome who had right sided CDH, Tetralogy of Fallot, and other multiple congenital anomalies. The patient survived a successful operation of both heart and diaphragmatic defects.

Key words: Diaphragmatic hernia, Fryns syndrome, Tetralogy of Fallot

Introduction:

The anteromedial or retrosternal diaphragmatic defect through the foramen of Morgagni accounts for 2-6% of diaphragmatic hernias. Failure of the sterna and crural portions of the diaphragm to meet and fuse produces this defect. These defects are more commonly right sided(90%) but may be bilateral. The transverse colon or small intestine or liver is usually contained in the hernia sac. The majority of children with these defects are asymptomatic and are diagnosed beyond the neonatal period .The diagnosis is usually made on chest X-ray (1). Associated anomalies have been reported in up to 30% of cases of CDH. These include central nervous system lesions, oesophageal

atresia, omphalocele, and cardiovascular lesions. CDH is recognized as part of several chromosomal syndromes; Trisomy 21, Trisomy 13, Trisomy 18, Fryns, Brachman-de-Lange, Pallister-killan, and Turner(1).

Fryns syndrome is an apparently rare (one in 10.000 birth) autosomal recessive disorder with a high rate of stillbirth and early neonatal mortality. This syndrome is a genetically-determined condition with variable expression. A significant inter and intra familial phenotype variability as well as discordant phenotype in monozygotic twins may be seen. As originally described, the major diagnostic criteria include abnormal facies, small thorax with widely spaced hypoplastic nipples, distal limb and nail hypoplasia, brachytelephalangy, and diaphragmatic hernia with pulmonary hypoplasia. The cause of lethality in most cases is due to pulmonary hypoplasia (2). Fryns syndrome is the most common multiple congenital anomaly associated with CDH. The diagnosis is strongly suggested when CHD and brachytelephalangy are associated. Internal malformations included, central nervous system, cardiovascular, gastrointestinal, urogenital, and skeletal anomalies (3). The co-occurrence of CDH and cardiovascular malformations has important clinical, genetic and developmental implications. The frequency of cardiovascular malformations (CVM) associated with

isolated CDH was 11-15%. A careful analysis of CVM indicates that atrial and ventricular septal defects, conotruncal defects, and left ventricular outflow tract obstructive defects were the most common type of CVM, but proportional to the frequency of occurrence in the general population. The combination of CVM and CDH results in a poorer prognosis than would be expected with either malformation alone (4). We report a case of right sided diaphragmatic hernia accompanied with congenital heart disease (Tetralogy of Fallot). Associated anomalies in other organs suggest the diagnosis of Fryns syndrome.

Case report:

A 2 - yr old boy was admitted at paediatric ward of Shahid Modarres hospital on June 2008. The chief complaint was cyanosis. The patient was the product of nonconsanguineous marriage and had been delivered by full term spontaneous vaginal delivery. The previous pregnancy of his 21- year old mother was aborted. On physical examination the weight was 10 kg, There was central cyanosis .The facies was slightly abnormal (long and prominent forehead and prominent eyes), figure 1. There was mild lingual developmental delay. Examination of chest showed wide hypoplastic nipples. Heart auscultation revealed a grade 3/6 ejection systolic murmur at upper left sternal border. The breath sounds was normal. Examination of genitourinary system showed hypospadias and left sided undescended testis. There was brachyphalangy of first toes and clubbing of nail beds. Chest X- ray showed intestinal loops at the right hemithorax. The heart size was normal with prominent right ventricle, concave pulmonary segment, and decreased pulmonary blood flow. ECG showed right axis deviation and right ventricular hypertrophy. Echocardiography revealed a large ventricular septal defect, overriding of aorta, and severe pulmonary stenosis. Cardiac catheterization confirmed the diagnosis of Tetralogy of Fallot, figures 2 and 3. A combination of right sided diaphragmatic hernia, congenital heart disease, abnormal facies, with mild mental retardation, hypoplastic nipples, genitourinary and skeletal abnormality, suggested the diagnosis of Fryns syndrome. The patient underwent cardiac surgery. The chest was opened by mid sternotomy. There was a substernal right diaphragmatic hernia. The diameter of defect was 6 cm. The hernia sac contained small intestine, transverse colon and peritoneal fat .Diaphragmatic defect was repaired by Dacron patch. The heart was opened by right ventriculotomy. The incision continued up to pulmonary artery. The right ventricular tract obstruction was relieved by transannular pericardial patch. The size of VSD was 2cm and the defect was repaired with Dacron patch .The patient transferred to postoperative cardiac surgery intensive care unit. The postoperative course was uneventful. The

patient was discharged from hospital in good condition. In the last outpatient follow-up the general condition was good and the patient was acyanotic and gained weight.

Discussion:

Fryns syndrome is an autosomal recessive syndrome of multiple congenital anomalies described by Fitch et al in 1978 and Fryns et al in 1979. As originally described the major diagnostic criteria included abnormal facies, small thorax with widely spaced hypoplastic nipples, distal limb and nail hypoplasia, and diaphragmatic hernia with pulmonary hypoplasia. Malformation involving other system occurred irregularly in published reports (5). In a review of 45 cases of Fryns syndrome by Pinar et al 88% of cases had congenital heart disease and 72% had CNS malformations. They concluded that CNS anomalies and CHD should be added to the major diagnostic criteria of Fryns syndrome (5). The abortion of previous sibling of our patient may be due to presence of Fryns syndrome in other offspring of his parents and suggested an autosomal recessive pattern of inheritance .The lingual developmental delay of our patient corresponded with minimal brain dysfunction. Patients with Fryns syndrome have a high rate of CVM. Conotruncal CVM were found more commonly than in the general population. The possible association between conotruncal CVM and Fryns syndrome may provide additional support for an etiologic role of genes related to neural crest cell development in the pathogenesis of Fryns syndrome and hence ,congenital diaphragmatic hernia (6). In a study by Neville et al in USA, a total of 1833 patients with CHD were entered in the database. 23 of these patients had Fryns syndrome (1.3%).Ten patients (43%) were found to have other major anomalies (7).Congenital heart disease and congenital diaphragmatic hernia are frequently associated (8).Cardiovascular abnormalities were present in 11 of 48 (23%) patients with CDH (9).A case of right diaphragmatic hernia associated with a complex congenital heart disease (double outlet right ventricle ,transposition of the great arteries ,and left isomerism) was reported previously by Bianchi et al (10). Another case of right sided CDH associated with a complex heart disease (VSD, ASD, left pulmonary artery atresia) described by Jog et al in an Australian newborn. Their patients had multiple congenital anomalies compatible with Fryns syndrome (11). In a review of literature, Slavotinek concluded that CDH with brachytelephalangy and /or nail hypoplasia is strongly suggestive of the diagnosis of Fryns syndrome, and that pulmonary hypoplasia, craniofacial dimorphism, orofacial clefting, and polyhydramnios are sufficiently frequent to be diagnostically useful. Other distinctive malformations that are consistent with Fryns syndrome include CNS malformations, urogenital and skeletal abnormalities (12).

Our patient with right diaphragmatic hernia, CHD, abnormal face, mild mental retardation, wide and hypoplastic nipples, brachyphalangy of both first toes, and urogenital malformation fulfills the criteria of Fryns syndrome. Our case survived the successful operation of heart and diaphragmatic defects. The incidence of recurrence for future child of family was discussed with parents.

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Figure 1



Legends

Fig 1: Note the long forehead, prominent eyes, hypoplasia of nipples. The midsternal incision is evident

Fig 2: Angiocardiography showed hypertrophy of right ventricle (RV), obstruction of right ventricular outflow tract (RVOTO), appearance of aorta (AO), and bowel loops at right hemi thorax.

Fig 3: Angiocardiography showed right ventricle (RV), left ventricle (LV) and aorta (AO) appeared via VSD. Bowel loops are evident at right hemi thorax.

Figure 2

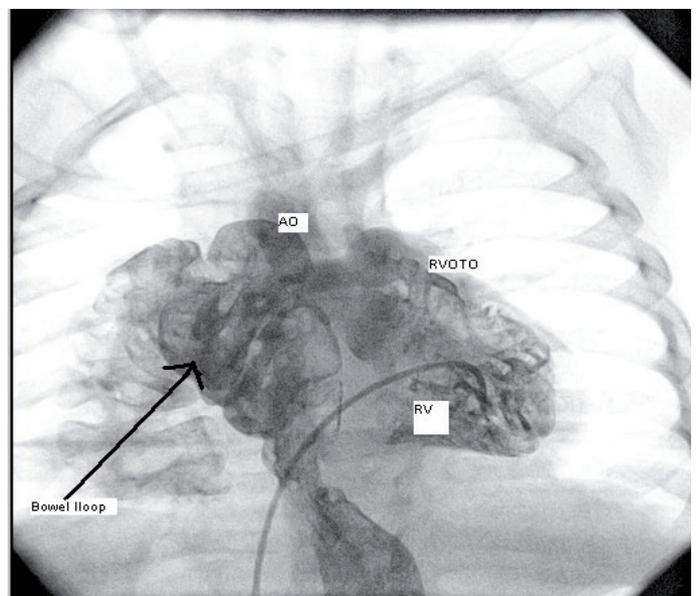


Figure 3

