Fryns syndrome is a rare autosomal recessive disorder, with an estimated prevalence is 0.7 per 10,000 births. The syndrome, first described by Fryns in 1979, is characterized by dysmorphic facial features, diaphragmatic hernia, distal limb hypoplasia, and pulmonary hypoplasia. In this case report we describe the first recorded case of Fryns syndrome associated with Karyotype XO (Turner syndrome) in a newborn baby.

Case

A female baby was born at 36 weeks gestation. The mother was a 23-year-old Bahraini, admitted at 35 weeks of pregnancy for uncontrolled high blood pressure. A Doppler ultrasound carried out at 36 weeks of gestation showed an IUGR fetus of 35-weeks size and a right-sided diaphragmatic hernia. The baby was the second of a healthy first cousin parent. The first child was normal. Delivery was induced at 36 weeks, her birth weight was 2060 grams (third centile), the head circumference was 31 centimeters (third centile), and the length was 44 centimeters (third centile). Apgar scores were 6, 7, and 8 at 1, 5, and 10 minutes, respectively. She gasped and cried at birth but became cyanotic at 7 minutes, requiring intubation and ventilation. Her initial chest X-ray showed right-side diaphragmatic hernia with the liver occupying a right hemithorax (Figure 1). On examination, she had coarse facial features with micrognathia, a depressed nasal bridge, facial hair overgrowth (Figure 2), hypoplastic nails of both the left little finger (Figure 3) and the toe (Figure 4), a small rudimentary 4 terminal phalanx of the left fifth finger (Figure 3), and non-pitting generalized edema (Figure 4). The eyes were normal.

The patient was operated on on the second day of life. Intra-operative findings were right diaphragmatic hernial sac extending to the apex of the chest wall, with a thin membranous sac; the lower lip of diaphragm was well developed, while the upper lip was thin and underdeveloped with no muscle. The liver and small intestine were in the right chest. The right lung was hypoplastic and expanded after relief of the chest content. She was extubated on the 10th postnatal date, but reintubated the next day as she developed tachypnoea and CO2 retention. The chest X-ray showed right-sided lung collapse. Initial CBC showed polycythaemia (Hb=23.8 g%, PCV=0.74), for which a partial exchange blood transfusion was done. Platelets were 48X109 and dropped to 14X109. Because of this and other features of disseminated intravascular coagulation, she received fresh frozen plasma, Vitamin K, and a platelet transfusion. She developed hypoglycaemia requiring...
FRYNS SYNDROME ASSOCIATED WITH KARYOTYPE XO

**Figure 2.** Coarse facial features with micrognathia, depressed nasal bridge and facial hair overgrowth.

**Figure 3.** Hypoplastic nail of little finger.

**Figure 4.** Hypoplastic nail of the toe and non pitting generalized oedema.
Patients with Fryns syndrome have certain craniofacial features, including coarse facial features, hypertelorism, facial hair overgrowth, a broad flat nasal bridge, anteverted nares, microretrognathia, and cleft lip and palate. Our patient had coarse facial features, micrognathia, a depressed nasal bridge, and facial hair overgrowth (Figure 2). Premature erupted incisors, and natal teeth have been described in a preterm baby of 24 weeks gestational age.

The vast majority of patients (up to 90%) have diaphragmatic hernia, narrow thorax, hypoplastic nipples and abnormal lung lobation. However, more recent reports suggest that a diaphragmatic hernia is not necessarily a feature of the syndrome. Turner’s syndrome has never been reported with diaphragmatic hernia.

The most frequently observed skeletal abnormality in Fryns syndrome is distal digital hypoplasia commonly represented by absent or hypoplastic nails, and very short terminal phalanges. Occasional hand and finger abnormalities are seen (camptodactyly, prominent finger tippads, axial deviation of the fingers and single transverse
Fryns syndrome is associated with karyotype XO

palmar creases). Various thumb abnormalities have been reported (digitalizing proximal placement, wider club-shaped thumbs and small thumbs). In addition to extra pairs of ribs, a single transverse palmar crease and broad medial ends of the clavicles have been reported. Our patient had a broad medial end of the clavicles (Figure 6) and a hypoplastic distal phalanx of the left little finger.

The finding of delayed ossification of the basiocciput and cervical vertebral bodies, and histopathologic evidence of osteochondrodysplasia in two siblings with Fryns syndrome, suggests that osteochondrodysplasia could be a feature of Fryns syndrome. Our patient showed no occular abnormalities, but several eye changes have been described, including microphthalmos, cloudy cornea, irregularity of Bowman’s layer, thickened posterior lens capsule, cataract and retinal dysplasia. Corneal endothelial dysfunction might cause an abnormal composition of the interior descement’s membrane, which could contribute to a cloudy cornea.

Multiple CNS abnormalities have been reported, including agenesis of the corpus callosum, Dandy-Walker abnormality, cerebellar heterotopias, cerebellar hypoplasia, enlarged ventricles, arthrinencephaly, hypoplasia of the olfactory bulbs, malformation of gyration and sulcation and hypoplastic optic track. Profound mental retardation have been reported in survivors of Fryns syndrome.

Genitourinary abnormalities include bicornuate uterus, vaginal duplex, uterine and cervical atresia in females. Cryptorchidism, hypospadias, scrotalization of the phallus and bifid scrotum in males and cystic dysplastic kidneys have been reported. These features were not found in our patient. Intestinal malrotation and non-fixation, omphalocoele, Hirschsprung disease and anal anomalies, duodenal atresia, pyloric hyperplasia, common mesentery, Meckle diverticulum, multiple accessory spleen and ectopic pancreatic tissues have been reported. Cardiovascular anomalies include septal defects, aortic arch anomalies and persistent left superior vena cava.

The vast majority of affected individuals are stillborn, or die in the early neonatal period. In postneonatal survivors Rielaa et al described myoclonus appearing shortly after birth. Progressive cerebral and brain stem atrophy was noted on serial MRI scan at three months and six months of ages respectively. Patients surviving the neonatal period represent approximately 14% of reported cases. Characteristics of the survivors include less frequent diaphragmatic hernia, mild lung hypoplasia, absence of complex cardiac malformations, and neurological impairment with profound mental retardation.

To our knowledge, our patient is the first case report of Fryns syndrome and pedal edema at birth, a feature of Turner’s syndrome, which was confirmed by karyotyping.

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