

Quiz

The importance of autopsy in fryns syndrome; a case report of a rare disease Aynaolu Yıldız et al. Fryns syndrome diagnosed by autopsy

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What is your diagnosis?

A 29-year-old 20-month pregnant woman was admitted to our center since she had a history of hydrocephalus and anencephaly in her previous pregnancy. There was no history of taking folic acid tablets before pregnancy, but she took them in the first trimester of her pregnancy. A detailed obstetric history was taken and it was determined that the patient had a consanguineous marriage with his second generation cousin. She has three pregnancy history. Two of them ended with birth of healthy babies and one of them was terminated because of hydrocephalus and anencephaly. As ultrasonographic findings; hyperechogenic cystic structure measuring 28x31 mm in the right lobe of the liver, hyperechogenic and polycystic left kidney, cystic hygroma, pulmonary hipoplasia and single umbilical artery were detected. It was seen that there were no cerebellar vermis and corpus callosum in magnetic resonance imaging (Figure 1). Informed consent was obtained and amniocentesis was performed. The patient decided to terminate the pregnancy without waiting for the result of amniocentesis, so the pregnancy was terminated and the fetus was sent for an autopsy examination. We have received a male fetus, weighing 476 g, for autopsy. The crown rump length, chest circumference and abdominal circumference were measured as 18cm, 19cm, 21cm, respectively.

It was seen that cerebellar vermis and corpus callosum was absent and the fetus has bulging eyes, broad nose, depressed nasal bridge, folded ears, large mouth with a protruding tongue, long philtrum, small chin and an increase in his nuchal fold thickness with the help of the external examination (Figure 2).

On the dissection and the internal examination, cardiac defect and diaphragmatic hernia were not observed. A serous cystic structure with a size of 28x31 mm was observed in the right

lobe of the liver (Figure 3). The left kidney parenchyma could not be observed. Amniocentesis reported as a normal karyotype.

Answer

Fryns syndrome is a rare autosomal recessive disorder with multiple congenital anomalies and about 0.7 prevalence per 10,000 births (1). It is characteristic with diaphragmatic defects, typical facial expression, distal digital or nail hypoplasia, pulmonary hypoplasia and some associated anomalies (polyhydramnios, cloudy corneas and/or microphthalmia, orofacial clefting, renal dysplasia/renal cortical cysts, and/or malformations including the cardiovascular system, gastrointestinal system, brain or the genitals). It is also closely related with consanguineous marriage. The diagnosis is based on clinical findings and made with the presence of 3 criteria (2,3). Regarding to genetic analysis, fetal karyotypes of cases are usually normal, so it is important to diagnose the syndrome at autopsy. Fryns syndrome, known as the most common single gene defect causing congenital diaphragmatic hernia, is responsible with 4–10 % of all patients with congenital diaphragmatic hernia. Diaphragmatic defects are found in almost all cases with fryns syndrome (4). A limited number of fryns syndrome without diaphragmatic hernia has been identified in the literature (5).

The purpose of this autopsy case report is to show that The Fryns syndrome can be diagnosed without congenital diaphragmatic hernia and to show its association with rare abnormalities such as cystic hygroma, agenesis of the corpus callosum and the cerebellar vermis.

Fryns syndrome is one of the most common syndromes associated with congenital diaphragmatic defect (CDH), reported in up to 10% of patients with CDH. Despite the fact that there wasn't any diaphragmatic defect, other findings of our patient were similar to the rest of the typical diagnostic findings, except for cystic hygroma and some other defects not previously described. Several chromosomal abnormalities show symptoms similar to Fryns Syndrome. Therefore, the diagnosis of Fryns Syndrome can only be made if the karyotype is tested normal and the diagnosis is confirmed by autopsy. In this case, autopsy findings have been very useful to make differential diagnosis. Based on the ultrasonographic findings, we thought about chromosomal anomaly at first. However, the amniocentesis was reported as normal. We did not recommend the non invasive prenatal testing as an alternative to amniocentesis. Because, non invasive prenatal testing is not suitable for genetic evaluation of ultrasound anomalies (6). Simpson-Golabi-Behmel Syndrome which is an X-linked overgrowth syndrome resulting from deletions or mutations in the GPC3 gene, and conditions with hypoplasia or absence of the distal phalanges such as DOOR syndrome (deafness, onychodystrophy, osteodystrophy, and mental retardation), Schinzel–Giedion syndrome, and Rudiger syndrome should be considered in differential diagnosis. Heterozygous de novo mutation in the SETBP1 gene is heredity characteristic of Schinzel-Giedion syndrome. None of the patients have diaphragmatic hernia in Rudiger syndrome. The diagnosis of Fryns Syndrome without diaphragmatic hernia is quite difficult. Although this patient is diagnosed as fryns syndrome, it cannot be clearly differentiated from Rudiger syndrome and Schinzel-Giedion syndrome. Therefore, these diseases can be called fryns-like syndromes (7). In the presence of cystic hygroma, other signs of fryns syndrome should be carefully monitored, since the risk of recurrence is 25 percent. It must be kept in mind during the next pregnancies.

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Figure 1. Magnetic resonance imaging of corpus callosum agenesis



Figure 2. Bulging eyes, broad nose, depressed nasal bridge, folded ears, large mouth with a protruding tongue, long philtrum, small chin and increase in nuchal fold thickness



Figure 3. Hyperechogenic cystic structure measuring 28x31 mm in the right lobe of the liver