CASE REPORT

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A Rare Disease with Arthrogryposis: Pena-Shokeir Syndrome

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ABSTRACT Pena-Shokeir syndrome (PSS) type 1 is an autosomal recessive disease, characterized by arthrogryposis, facial anomalies, fetal growth restriction, polyhydramnios and pulmonary hypoplasia. Ultrasound features are varied and may overlap with those of trisomy 18. The neuromuscular abnormality of the diaphragm and intercostal muscles causes pulmonary hypoplasia, and consequently pulmonary hypoplasia is the primary cause of early death. PSS is a very rare syndrome and should be considered when indicators of the condition are encountered in fetal ultrasonic examination. It is important to perform an invasive procedure appropriate for the gestational week for the differential diagnosis of the condition. Our aim is to share the prenatal and postnatal process of the PSS case we diagnosed at 28 weeks of gestation.

Keywords: Arthrogryposis; diagnostic imaging; Pena-Shokeir syndrome; ultrasonography; trisomy 18 syndrome

Pena-Shokeir syndrome (PSS) type 1 is also known as fetal akinesia deformation syndrome. The disease is extremely rare and often results in death in the intrauterine or early neonatal period. It is described by joint contractures, decreased fetal movements, intrauterine growth restriction and features of pulmonary hypoplasia. It indicates autosomal recessive inheritance and has a prevalence of 1/12,000 births.[1,2]

The aim in sharing this case is to contribute to the literature on the prenatal findings regarding the condition, and the issues to be considered in the differential diagnosis and postnatal process.

CASE REPORT

A 21 years old, gravida 2, para 1, 28 weeks pregnant was referred to our clinic due to the lack of fetal movements and polyhydramnios. The family had not undertaken the 1st and 2nd trimester screening tests, and there was a first-degree consanguineous marriage between the mother and father. The mother was using insulin due to gestational diabetes. There was no alcohol, cigarette or teratogen drug exposure.

In the 28th week, ultrasound examination revealed a bilateral flexion deformity in the elbow and knee, and contractures in the wrists (Figure 1). Both feet had a rocker bottom deformity and overlapping toes. Micrognathia and low ears were observed in the fetal face. It was observed that estimated fetal weight and abdominal circumference were lower than the 3rd percentile for gestational week. Amniotic fluid was evaluated as being 12 cm in one pocket and 31 cm as index, indicating polyhydramnios. Fetal stomach and fetal movement were not observed during ultrasound examinations performed 45 minutes apart.

Cordocentesis was recommended to the family and information was given about the option for termination of the pregnancy. The family did not accept termination. The family wanted to assess the situation and reapplied 4 days later. Cordocentesis was performed. Fetal bradycardia developed after cordocentesis. Despite intrauter-

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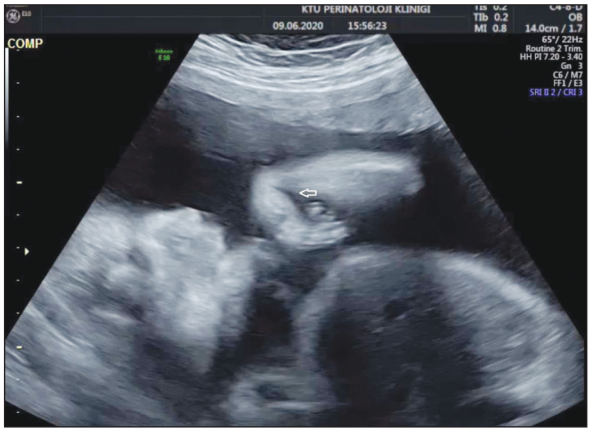

FIGURE 1: Gray-scale ultrasonography at the 28 weeks of gestation, the contracture of the wrist (arrow).

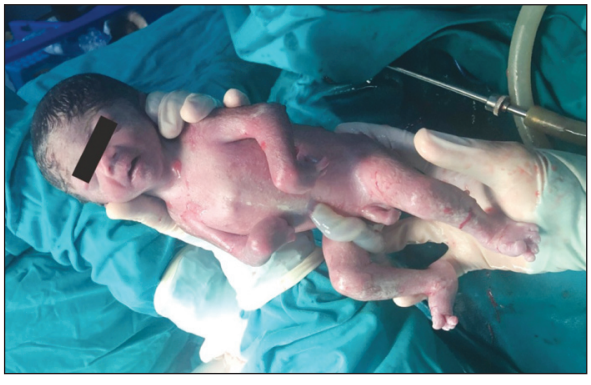

FIGURE 2: Macroscopic image of the delivered baby (micrognathia, bilateral flexion deformity in the elbow and knee, and contractures in the wrists, overlapping toes).

ine resuscitation, bradycardia did not recover, so a cesarean decision was made. A male baby, weighing 910 g, with an Apgar score of 1-1 for 1 and 5 minutes was delivered (Figure 2). The newborn died on the same day because of pulmonary hypoplasia. The family refused to have their baby an autopsy.

Informed consent was obtained from the parents about the use of data.

DISCUSSION

Pena and Shokeir first reported this rare disease in 1974 in two sisters with facial anomalies, knee and hip ankylosis, clubfoot, severe camptodactyly and pulmonary hypoplasia, resulting in death in the perinatal period.[1] It is also one of the possible clinical expressions of the fetal akinesia deformation sequence defined by Moessinger in 1983.[3] Ultrasound findings in the antenatal period are joint contractures, decreased fetal movements, short umbilical cord, intrauterine growth restriction and pulmonary hypoplasia. Severe equinovarus or clubfoot can be observed in the feet. Facial features of the disease include low-placement ears, hypertelorism, micrognathia and collapsed nose tip. Polyhydramnios usually becomes apparent in the second half of pregnancy.[4,5]

Dysfunction of the neuromuscular system is the underlying pathology of the condition, which leads to decrease in fetal movements in the intrauterine period. It results in spinal cord, brain, neuromuscular junction, motor neuron and neurotransmitter defects.[6] PSS can also be caused by blocking the neuromuscular transmission, as shown in recent observations with women developing antibodies to the fetal acetylcholine receptor. Brueton et al. reported 8 cases of Pena-Shokeir phenotypes (5 males and 3 females) born from 2 sisters.[7] Acetylcholine receptor antibody titers had increased in both mothers, but neither displayed neurological symptoms of myasthenia gravis. The authors noted that several babies born from mothers with clinically severe myasthenia gravis had the Pena-Shokeir phenotype. In the case of maternal myasthenia gravis, the risk of recurrence of PSS is high, consequently, there have been no examples of a normal child born after the affected pregnancy. For this reason, acetylcholine receptor antibody test was performed in our case, although the mother did not have a family history or any neurological symptoms. The result was negative (<0.10 nmol/L).

Paladini et al. diagnosed PSS in 3 consecutive pregnancies of the same patient at 18, 12 and 16 weeks of gestation, respectively, and there are also cases diagnosed in the third trimester in the literature.[8,9] The reason for the variation in the weeks of diagnosis are the variable start times of the phenotype of the condition.

PSS has a variable phenotype. The differential diagnosis includes Trisomy 18, cerebro-oculo-facio-skeletal (COFS) syndrome and mucopolysaccharidosis (MPS).[6,8] The features that distinguish PSS from trisomy 18, COFS and MPS are that it has a normal karyotype, absence of microphthalmia and microcephaly, and does not have pterygium that causes flexion contractures.[7,8] If the karyotype is normal and other conditions are excluded, a possible diagnosis of PSS can be

made.[8] In our case, the karyotype result was 46, XY, and there were no clinically significant changes in the chromosomal copy number as a result of microaarray [.arr (1-22) x2]. We thought that our case was compatible with PSS because the antenatal period ultrasound findings were compatible, the differential diagnosis could be made with other diseases, and the karyotype was normal.

The final prognosis of PSS depends on the underlying cause, but this condition almost always ends up fatal; 30% of fetuses are stillborn, while the rest are mostly born live but die within the first month of life.[10] The neuromuscular abnormality of the diaphragm and intercostal muscles causes pulmonary hypoplasia, and consequently pulmonary hypoplasia is the primary cause of early death. Families should be informed about the prognosis by a multidisciplinary team consisting of perinatologists, medical genetics and neonatologists. Comprehensive counseling should be provided regarding both diagnosis and prognosis including the antenatal period, intrapartum period, postnatal period and subsequent pregnancies.

Serial ultrasonographic follow-up should be performed on pregnant woman with a history of birth with PSS. This will allow early detection of abnormalities. However, since the phenotypic condition is due to heterogeneous causes, the calculation of the recurrence risk of the condition is uncertain. The recurrence risk is estimated to vary between 0% and 25%.[6]

In conclusion, PSS is a very rare syndrome and should be considered when indicators of the condition are encountered in fetal ultrasonic examination. It is important to perform an invasive procedure appropriate for the gestational week for the differential diagnosis of the condition.

Source of Finance

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Miraç Özalp, Ömer Demir;* ***Design:*** *Miraç Özalp, Mehmet Armağan Osmanağaoğlu;* ***Control/Supervision:*** *Mehmet Armağan Osmanağaoğlu, Miraç Özalp;* ***Data Collection and/or Processing:*** *Miraç Özalp, Ömer Demir;* ***Analysis and/or Interpretation:*** *Miraç Özalp, Ömer Demir;* ***Literature Review:*** *Ömer Demir;* ***Writing the Article:*** *Miraç Özalp, Ömer Demir;* ***Critical Review:*** *Mehmet Armağan Osmanağaoğlu;* ***Materials:****Miraç Özalp, Mehmet Armağan Osmanağaoğlu.*

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