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Pena-Shokeir 증후군

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Pena-Shokeir Syndrome

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Pena-Shokeir syndrome is a rare disease that characterized by intrauterine growth restriction, polyhydramnios, multiple contractures, facial anomalies, lethal pulmonary hypoplasia and decreased or absent in utero movements. We report the fetus with polyhydroamnios, decreased in utero movement, clenched hands at 28 weeks of gestation but large biparietal diameter (BPD) and no intrauterine growth restriction untill term. The diagnosis in our case was made on the basis of characteristic findings by ultrasonography. Cesarean section was done due to non-reassuring fetal heart rate pattern at 40 weeks of gestation. The female neonate had a depressed nasal tip, low-set ear, cleft palate, hypoplastic dermal crease, pulmonary hypoplasia, thoracic kyposis and scoliosis, varus deformity, rocker bottom feet and joint contracture of fingers. She died of respiratory failure at 21 weeks after the birth. Compared to typical Pena-Shokeir syndrome, this case showed large BPD and no intrauterine growth restriction.

Key words: Pena-Shokeir syndrome, Polyhydroamnios, Clenched hand, Pulmonary hypoplasia

Pena-Shokeir syndrome is characterized by arthorogryposis, intrauterine growth restriction, polyhydramnios, multiple contractures, facial anomalies, and lethal pulmonary hypoplasia. It was first described by Pena and Shokeir in 1974, as an early lethal disorder of neurogenic arthrogryposis, lung hypoplasia, and hypertelorism.[1] The prevalence was reported one out of 12,000 births.[2] It has been postulated that phenotypic manifestations are no-specific and may be caused by decreased or absent in utero movements, thus resulting in the fetal akinesia deformation sequence. Prenatal diagnosis is based on the ultrasonographic findings such as the absence in fetal movements and abnormal limb position.[1-3] We report a case of Pena-Shokeir variant without intrauterine growth restriction until term gestation, which was diagnosed at 28 weeks of gestation.

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CASE REPORT

A 26-year-old Korean woman, gravida 2 para 1, who had got antenatal care in our institution from early gestation came for routine prenatal care at 26 weeks of gestation. She did not have any history of skeletal, genetic, or congenital diseases. She delivered her first baby through the vaginal route at term.

Until 26 weeks of gestation, her perception for fetal movement was normal, and level II obstetric ultrasound at 18 weeks of gestation was also unremarkable. The present pregnancy had no obstetric complications. At 26 weeks of gestation, a sonographer reported a fetus with contractures of the lower limbs. Both upper

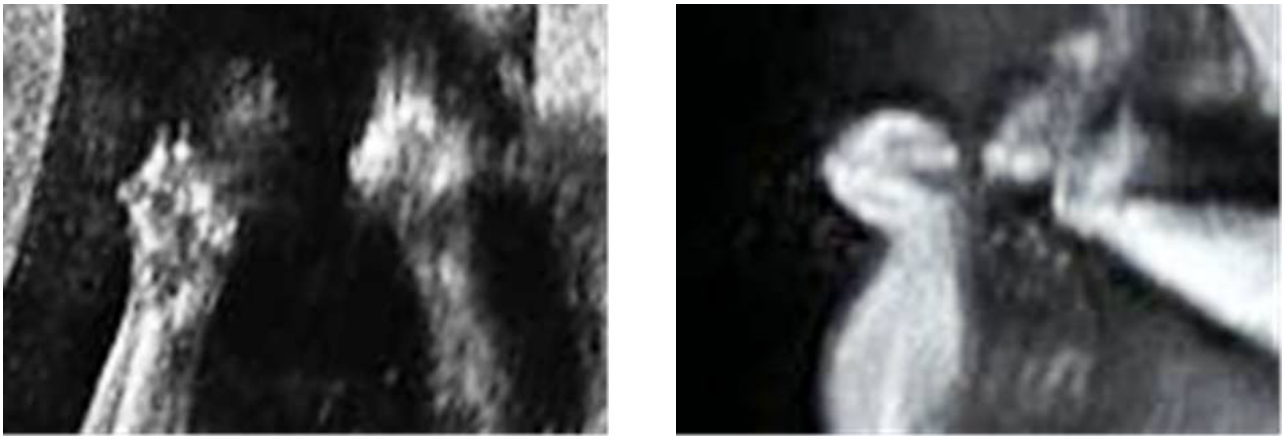

Fig. 1. Ultrasound of the fingers showed joint contractures. Such images of the fetal hands are features of clenched hands, and may raise the suspicion of trisomy 18.

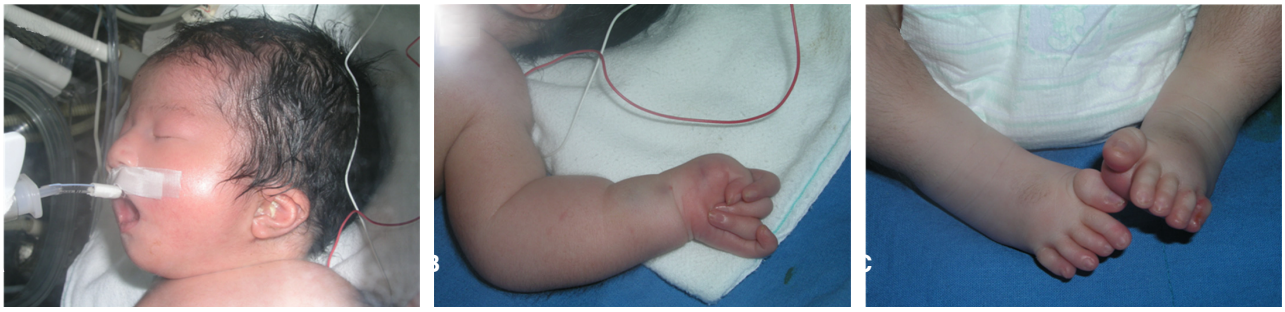

Fig. 2. Postnatal gross findings showed low-set ear (A), joint contracture of fingers and toes (B, C).

limbs were fixed with flexion at the wrist and elbow joints. The fingers were flexed looking like clenched hands (Fig. 1). There was no movement and amniotic fluid index was 26 cm. But, estimated body weight was adequate for gestational age. One week later, repeated ultrasound exam showed the same findings and behavior. Gastric fluid was not visible on either examination. The brain and spine was unremarkable. The ultrasonographic findings were also similar at 28 weeks of gestation. No breathing was visualized over 2 hours of observation. In spite of them, fetal growth followed the trend within normal range.

The ultrasonographic manifestations were consistent with the Pena-Shokeir syndrome phenotype. The parents were informed of the diagnosis and the possibility of other diagnosis. They decided to refuse the prenatal chromosomal evaluation and to continue with this pregnancy.

Cesarean section was done due to non reassuring fetal heart rate pattern at 40 weeks of gestation. Birth weight was 3.45 kg, Apgar score was 3 and 6 at 1 and 5 minutes, respectively. In the physical examination, the female neonate had a depressed nasal tip, low-set ear, cleft palate, hypoplastic dermal crease, pulmonary hypoplasia, thoracic kyposis and mild scoliosis, varus deformity, rocker bottom feet and joint contracture of fingers (Fig. 2). Chromosomal study was performed, with the result of 46, XX. She died of respiratory failure 21weeks after birth. Based on the chromosomal study and clinical features, we report a female neonate with Pena-Shokeir syndrome.

DISCUSSION

Pena-Shokeir syndrome is not a homogeneous syndrome but has various etiologic mechanisms. It is heterogeneous both with regard to the specific anomalies present and with regard to the cause. The

etiology may include many environmental agents and multiple genetic forms.[2]

Pena-Shokeir syndrome type I is considered to be a lethal form in most cases, although some affected children may reach the age of one year. Most of them die from neurogenic arthrogryposis with pulmonary hypoplasia within the first few weeks.[4] The lethality makes the prenatal diagnosis to be important. In 1985, MacMillan et al. diagnosed Pena-Shokeir syndrome type I prenatally using ultrasound.[3] Ultrasonographic diagnosis is mainly based on absent fetal movement and abnormal limb position.[5] In spite of various characteristic ultrasonographic features of Pena-Shokeir syndrome, the prenatal diagnosis may be difficult because of the complexity of the clinical findings. Table 1 summarizes the distinctive features of the syndrome and describes incidence of each feature.[4, 6]

The phenotypes of Pena-Shokeir syndrome are usually similar with those of trisomy 18, from which it must be distinguished. Therefore, fetal karyotyping is necessary in order to reach a definite diagnosis. If the karyotype is normal and there is micrognathia, absent of active fetal movements, arthrogryposis of lower extremities, rocker bottom feet, a diagnosis of Pena-Shokeir phenotype can be made.[6] In most case reports, prenatal or postnatal chromosomal study was performed to rule out trisomy 18. In this case, chromosomal analysis after birth was done to fulfill the diagnosis. Other major differential diagnosis include Freeman Sheldon syndrome, multiple pterygium syndrome, trisomy 13, Potter syndrome, Neu-Laxova syndrome, restrictive dermopathy, Larsen syndrome, and cerebro-ocular-facial-skeletal syndrome (Pena-Shokeir syndrome type II).[7, 8]

Table 1. Summary of clinical features of Pena-Shokeir syndrome

Characteristic	Reported frequency (confirmed cases/ Suspicious cases)
Obstetric features	
Growth retardation	28/30
Polyhydroamnios	18/28
Short umbilical cord	6/7
Perinatal death	27/31
Pulmonary hypoplasia	29/31
Dysmorphology of face	
Hypertelorism	27/29
Low set deformed ears	30/30
Decreased tip of nose	25/26
Micrognathia	29/29
Dysmorphology of extremities	
Camptodactly	28/30
Hypoplastic dermal ridge/crease	15/16
Clubfoot or rocker-bottom foot	27/29
Arthrogryposis	31/31
Male infants	14
Female infants	17
Cryptorchidism	14/14

Most infants reported as Pena-Shokeir syndrome had intrauterine growth restriction and microcephaly. This case was diagnosed with Pena-Shokeir syndrome type I because she had various typical features such as pulmonary hypoplasia, hydroamnios, and kyphoscoliosis with normal karyotype, and died from pulmonary hypoplasia. But, she was unusual as she had large biparietal diameter and normal intrauterine growth pattern until term. Two brothers with similar pattern of Pena-Shokeir were reported before. First baby had the macrocephaly may have resulted from obstructive ventricular enlargement due to the posterior extra-axis cyst. Second baby, however had neither a cyst nor ventriculomegaly and did not have any structural central nervous system (CNS) abnormalities.[9]

As a result of the abnormal neural development, a decrease in fetal movement was induced and secondary arthrogryposis and skeletal dysplasias were developed. Neuropathologic findings include hypoplasia of the cerebellum and thin cerebral and cerebellar cortices. Facial abnormalities are prominent. Due to the failure of normal deglutition, polyhydroamnios appeared. A neuromuscular deficiency in the diaphragm and intercostalis muscle leads to pulmonary hypoplasia. A lack of fetal movement also led the short umbilical cord and muscle joint contractures.[4]

There was experimental evidence in animals that fetal breathing movements are essential for normal lung development.[10] Absence of fetal breathing led to severe degrees of pulmonary hypoplasia. A valid diagnosis of Pena-Shokeir syndrome must include some

degree of pulmonary hypoplasia. If absent, another related member of the arthrogryposis complex needs to be a diagnosis.[11]

Approximately 30% of affected infants are still born. Most live-borns with Pena-Shokeir die as a results of the complications of pulmonary hypoplasia within a few weeks of birth.[2] Even though early prenatal diagnosis appears to be the only realistic approach because no specific treatment is available and most cases are lethal, it must be performed to parental counseling. Furthermore, a 0-25% risk for recurrence seems most appropriate in a sporadic case.[2]

Ultrasound together with fetal karyotyping, can lead to a relatively correct diagnosis of Pena-Shokeir syndrome type I, with the earliest reported diagnosis at 14 weeks of gestation.[12] Ultrasound plays an important role by demonstrating the characteristics and diagnostic features of Pena-Shokeir phenotypes, and is a valuable screening tool for prenatal diagnosis. In recent studies, the properties of magnetic resonance (MR) imaging have been reported. Fetal MR imaging can be used to document abnormalities throughout the body in addition to CNS, which gives more accurate clinical information.[7]

In our case, prenatal diagnosis of Pena-Shokeir syndrome was based on sonographic characteristics, which was confirmed by normal karyotype and clinical features postnatally. In our knowledge, this is the first reported case of Pena-Shokeir syndrome type I in Korea. This case was typical in the phenotypes, but showed extraordinary normal growth pattern. Thus, we report the case as a variant of Pena-Shokeir syndrome type I.

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「국문초록」

Pena-Shokeir 증후군은 자궁 내 태아지연, 양수과다증, 다발성 골절, 태아 안면기형, 치명적인 폐형성부전, 태동 감소를 특징으로 하는 희귀한 질환이다. 본 증례보고에서는 태령 28주에 확인된 양수과다증, 태동 감소, 꽉 쥔 주먹에 반해 만삭까지 유지된 정상적인 자궁 내 성장과정을 보였던 Pena-Shokeir 증후군에 대해 보고하고자 한다. 임신 중 초음파 검사를 통해 진단되었다. 태령 40주에 안심할 수 없는 태아 심박동 양상을 보여 제왕절개수술을 통해 태어난 여아는 낮은 코, 낮은 귀 위치, 구개파열, 피부주름 형성 부전, 폐형성부전, 척추 후만증 및 측만증, 내반슬, 흔들의자바닥기형, 손가락 및 발가락 구축 소견을 보였다. 여아는 생후 21주에 호흡부전으로 사망하였다. 전형적인 Pena-Shokeir 증후군과 비교하여 이번 증례에서는 정상 자궁 내 발육을 보여 보고하는 바이다.

중심 단어: Pena-Shokeir 증후군, 양수과다증, 꽉 쥔 주먹, 폐형성부전