Case Report

ULTRASOUND

Ultrasound
2017, Vol. 25(2) 115–119

DOI: 10.1177/1742271X16688235
journals.sagepub.com/home/ult

SAGE

Antenatal ultrasonography findings and magnetic resonance imaging in a case of Pena–Shokeir phenotype

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Abstract

Pena–Shokeir phenotype is a lethal anomaly characterized by neurogenic arthrogryposis, craniofacial anomalies, and pulmonary hypoplasia. This syndrome should be distinguished from trisomy 18 and arthrogryposis multiplex congenita for better counseling and establishing fetal prognosis. We present the case of a pregnant woman diagnosed with a Pena–Shokeir phenotype affected fetus at 24 weeks of gestation. Prenatal ultrasonography and fetal magnetic resonance imaging detected persistent hyperextension of the lumbar spine, micrognathia, absent septum pellucidum, and all characteristic features of Pena–Shokeir phenotype. Karyotyping was performed to exclude fetal chromosomal anomalies. Antenatal ultrasonography is an essential tool in the diagnosis of Pena–Shokeir phenotype while fetal magnetic resonance imaging is necessary to identify any associated anomalies of central nervous system.

Keywords

Arthrogryposis, hyperlordosis, micrognathia, Pena–Shokeir phenotype

Date received: 11 September 2016; accepted: 20 November 2016

Introduction

Pena–Shokeir phenotype (PSP), also called Pena–Shokeir syndrome type 1, is an autosomal recessive inherited disorder with an incidence estimated at one in 12,000 births.[1,2] Being different from the Pena-Shokeir type 2 (connatal Cockayne syndrome) described as the autosomal-recessive cerebro-oculo-facio-skeletal syndrome, the PSP is characterized by neurogenic arthrogryposis, pulmonary hypoplasia, and various craniofacial anomalies that could be diagnosed by fetal ultrasonography such as microcephaly, micrognathia, cleft palate deformity, ocular hypertelorism, low-set and malformed ears, and depressed nasal tip.[3,4] Most affected fetuses have a poor prognosis such as stillbirth (30%) or early death in the neonatal period due to complications of pulmonary hypoplasia.[5] It is not easy to diagnose PSP because it is not a clearly described syndrome[6] and its features have been shown to have a clinical presentation similar to trisomy 18,[7,8] Potter syndrome,[9] and Bowen–Conradi syndrome.[10] Therefore, the presence of pulmonary hypoplasia is helpful in distinguishing it from other syndromes as its presence means a likely diagnosis of PSP.[8,11] Nevertheless, this finding may not be observed as early as a prenatal diagnosis of arthrogryposis,[8] so the PSP may be misinterpreted as arthrogryposis multiplex congenita (AMC), in which the prognosis of the fetus is considerably better, with only mild to moderate orthopedic limitations.[8] To the best of our knowledge, an arthrogryposis affecting the fetal lumbar spine as extreme hyperlordosis is very rare in the PSP.[5]

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We present a case of PSP diagnosed at 24 weeks of gestation. Based on the antenatal findings, we review the pathogenesis of PSP and emphasize the important role of both prenatal ultrasonography and magnetic resonance imaging (MRI) in diagnosing this disorder.

Case

A 33-year-old pregnant woman, gravida 3, para 2, underwent a routine ultrasound scan examination at 24 weeks of gestation. There was nothing remarkable in her previous pregnancies: she had delivered two healthy girls in 2011 and 2013, weighing 3500 and 3200 g, respectively. The couple had no family history of skeletal, genetic, or congenital malformations.

First trimester combined screening (nuchal translucency, free β-hCG and PAPP-A) was performed at 12 weeks and the results showed a low risk for fetal aneuploidies. The routine second trimester ultrasonography (using 3D4-7EK transducer, Accuvix XQ, Medison Samsung, South Korea) was done at 24 weeks of gestation and revealed fetal micrognathia, absent septum pellucidum, and extreme hyperlordosis with reduced fetal movements (Figure 1). A very small stomach (diameter = 2.4 mm), small thorax, and the normal amniotic fluid index (AFI = 16) were also detected. Fetal biometry was consistent with the 11th percentile of gestational age. A fetal MRI confirmed absent septum pellucidum and persistent hyperextension of fetal lumbar spine (Figure 2). No further neurological abnormality was detected. The woman underwent an amniocentesis which revealed normal fetal karyotype (46, XY). Based on antenatal ultrasonography, MRI findings, and normal fetal chromosomes, a diagnosis of PSP was made. The couple was informed of the very poor prognosis and they decided to proceed to termination of pregnancy. Labor was induced with misoprostol (600 μg intravaginally) and a stillborn male weighing 600 g was delivered at 26 weeks of gestation. Postnatal examination revealed a neonate with growth restriction, limb anomalies (clenched hands and clubfeet), facial malformations (flat face, low ears, micrognathia), and skeletal deformity (extreme hyperlordosis) (Figure 3). A final diagnosis of PSP was confirmed following the presence of pulmonary hypoplasia detected in the postnatal ultrasonography

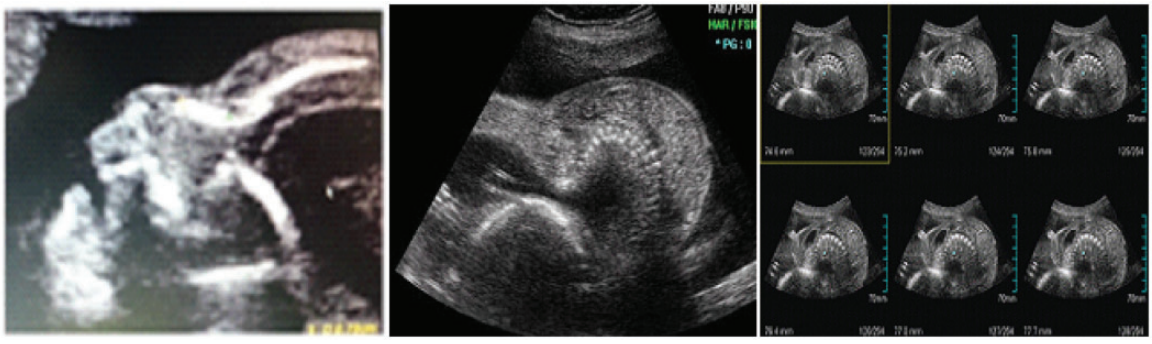

Figure 1. Fetal micrognathia and extreme hyperlordosis.

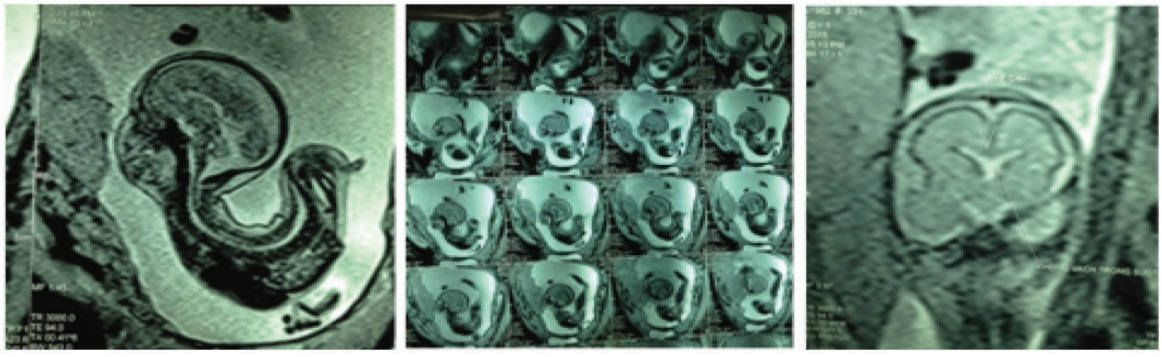

Figure 2. Persistent distorted spine with scoliosis and absent cavum septum pellucidum in MRI. MRI: magnetic resonance imaging.

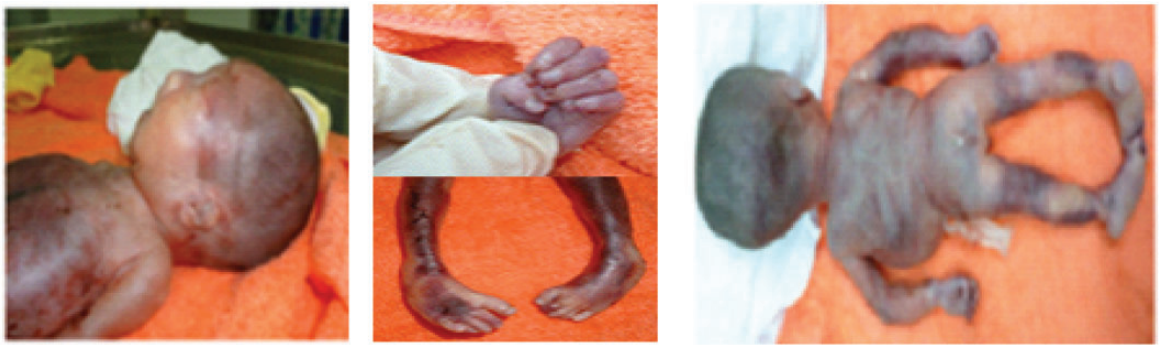

Figure 3. Postnatal examination showed micrognathia, low-set ears, clenched hands, clubfeet, and hyperextension of the lumbar spine.

with the reduced ratio of fetal lung to head circumference (lung area to head circumference ratio (LHR) = 0.62). Unfortunately, an autopsy for pulmonary hypoplasia was refused by the mother and her family for religious and cultural reasons.

Discussion

PSP, also called Pena-Shokeir syndrome type 1, is a lethal autosomal recessive syndrome which is characterized by arthrogryposis, facial anomalies, intrauterine growth restriction, and pulmonary hypoplasia.[3,8] Mutations in RAPSN and DOK7 genes have been determined as the cause of this phenotype.[1,12] A positive family history and several environmental factors, including maternal cocaine abuse, trauma, and hypotension are considered as risk factors for this disorder. Maternal thrombophilia has been said to be an association.[8,13]

According to Chen, PSP is a primary motor neuropathy which results in fetal akinesia deformation sequence (FADS).[12] The abnormal neuromuscular function causing the absent or reduced fetal movement leads to stiff joints (secondary arthrogryposis) and skeletal deformities (scoliosis, kyphoscoliosis, congenital hip dislocation, and rocker-bottom feet).[1,8,12] Besides neuromuscular dysfunction, fetal pulmonary hypoplasia and polyhydramnios occur as a result of inadequate diaphragmatic and intercostal muscle development and decreased fetal swallowing.[1,8,12]

In clinical practice it is not easy to diagnose PSP in pregnancy because FADS also occurs in many other congenital malformations, including trisomy 18 (arthrogryposis and micrognathia),[7,8] Potter syndrome (renal agenesis with oligohydramnios sequence),[9] and Bowen–Conradi syndrome (a lethal autosomal recessive disorder of microcephaly, micrognathia, intrauterine growth retardation, and joint deformities including clinodactyly, camptodactyly).[10] It is therefore necessary to combine prenatal imaging (ultrasonography and MRI) and fetal karyotyping to make a differential diagnosis.[2,5,13,14]

In our case report, the extreme persistent hyperlordosis of fetal lumbar spine was the first characteristic feature of congenital arthrogryposis and was detected at 24 weeks of gestation. This finding may be a clinical sign of AMC in which neurogenic atrophy develops with a later onset, after 20 weeks gestation.[8] According to Ajayi et al., the earliest possible diagnosis of PSP was at 14 weeks of gestation.[15] However, we do not consider the onset of fetal akinesia as sufficient evidence to diagnose Pena–Shokeir because a variable onset of arthrogryposis has been reported.[13] Because of this, we felt it necessary to perform subsequent ultrasonography to evaluate the presence of other fetal abnormalities, including facial anomalies, pulmonary hypoplasia, and polyhydramnios.[5,8,11]

Following detailed ultrasonography, we detected fetal micrognathia associated with an isolated absence of septum pellucidum, a very small stomach (diameter = 2.4 mm), an extreme hyperlordosis, a small thoracic diameter, and small for gestational age fetus (11th percentile). In addition, the atrophy of lumbar muscles and persistent hyperextension of fetal lumbar spine were also identified using T1-weighted MRI images. Therefore, based on the combined findings of multiorgan malformations associated with neuromuscular dysfunction, we suspected the presence of a trisomy 18. A normal fetal karyotype (46XY) helped us to distinguish PSP from trisomy 18 and other congenital arthrogryposis. Furthermore, postnatal examination findings of facial, limb, and skeletal malformations and presence of lung hypoplasia based on LHR < 1 confirmed the prenatal diagnosis of PSP.

Although the presence of pulmonary hypoplasia is necessary in definitively identifying PSP,[8,11] this finding is often detected in the final stage of fetal akinesia.[8] Therefore, we suggest that PSP can be diagnosed earlier

based on prenatal ultrasound and MRI findings including arthrogryposis of the fetal lumbar spine associated with craniofacial and gastrointestinal malformations. In Vietnam, and other resource limited settings, it is not yet possible to perform genetic tests to identify mutations of RAPSN and DOK7 genes, and, in this case, autopsy was not possible to determine the presence of pulmonary hypoplasia. Nevertheless, we emphasize the important role of prenatal ultrasonography, especially when combined with three-dimensional ultrasonography in rendering mode, in detecting PSP, as it can assess a detailed pattern of fetal akinesia. Besides ultrasonography and fetal karyotyping, fetal MRI may be used to exclude chromosome abnormalities as well as to look for any anomalies of central nervous system and better demonstration of distorted spine with scoliosis. The combined information from these three sources can then be used to plan appropriate clinical management and assist in counseling for likely fetal outcomes.

Conclusion

PSP is generally considered a lethal disorder because of the severe pulmonary hypoplasia. The recurrence risk is estimated to be 10–25%, so the early diagnosis of this disease should be suspected in pregnancies with affected fetus in previous pregnancy and detailed morphology scanning by ultrasonography should be carried out.

Acknowledgments

The authors are grateful for the permission from the family concerned in this case to publish the information and data contained here. We would like to thank Professor Jean-Pierre Schaaps (University of Liege, Belgium), Professor Pierre-Simon Jouk, Doctor Fréderique Nugues, and Doctor Dominique André-Marchand (CHU Grenoble, France) for their assistance in counseling the couple. We also thank Doctor Sarah Hoskins and Doctor Ludwig Marquet for their help in editing this manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethical approval

Local approval was provided on 20 December 2012 by Ethnic Committee of Medic Medical Center, Ho Chi Minh City, Vietnam.

Guarantor

DW.

Permission from patient obtained in writing

The patient and her husband were medical staffs and they gave their consent (by the agreement letter) to use the data and images of their fetus for this publication.

Contributors

RW and NL researched literature and conceived the study. RW, NL, DW designed the audit. RW, NL, and DW did the data analysis. RW wrote the first draft of the manuscript. RW and NL wrote the final version of the manuscript. All authors reviewed and approved the final version of the manuscript.

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