Ultrasound diagnosis of recurring Jeune's syndrome: a case report

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Summary

Jeune's Syndrome or asphyxiating thoracic dystrophy (ATD) is a rare autosomal recessive skeletal dysplasia syndrome characterized by a small and narrow chest, short extremities, and often polydactyly associated with multiple organ manifestations. The severity of complications ranges from mild to lethal. This is a report of two cases of ATD diagnosed in successive pregnancies of a non-consanguineous couple. The contribution of sonography in prenatal diagnosis of the syndrome is highlighted.

Key words: Jeune's Syndrome; Asphyxiating Thoracic Dystrophy; Ultrasound diagnosis of Jeune's Syndrome.

Introduction

Jeune's syndrome or asphyxiating thoracic dystrophy (ATD) is a rare autosomal recessive skeletal dysplasia clinically characterized by a small and narrow chest, shortness of all four extremities, and postaxial polydactyly in 14% of cases, associated with multiple organ anomalies. Its estimated incidence is one in 100,000 to 130,000 live births [1]. The diagnosis is based on clinical and radiological findings. Pathognomonic radiological findings at birth include bell-shaped thorax with short horizontal ribs, square-shaped iliac wings, trident appearance of the acetabulae, "handlebar" clavicles, limb shortening with a rhizomelic pattern, and metaphyseal widening [1, 2]. This report demonstrates the importance of prenatal diagnosis of the syndrome and the ethical dilemmas that arose regarding poor prognosis and low quality of life of these patients. The authors are also attempting to highlight key points to antenatal sonographic diagnosis. The cases refer to the recurrence of the syndrome in consecutive pregnancies of a non-consanguineous couple.

Case Report

A 19-year-old woman was referred to this clinic for fetal evaluation. Detailed sonography at 24 weeks of gestation showed shortness of all long bones (below fifth centile) and a long and narrow chest (Figures 1 and 2). Clinical suspicion of Jeune's ATD syndrome was aroused. Serial ultrasonographic examination revealed a hypoplastic with short-rib thorax and shortness of all four extremities. The views of the heart showed normal situs solitus and the great arteries were normally-related. The fetal head, brain, spine, gastrointestinal tract, kidneys, and bladder appeared normal. As gestation progressed, bilateral brachydactyly, relative macrocephaly, and polyhydramnios were observed. The couple attended genetics team counseling and the pregnancy was terminated on the 26th week of gestation.

During patient's next pregnancy, ultrasound examination at 19 weeks of gestation revealed shortness of all extremities and small narrow thorax. Measurements of all long bones were below the third centile and the chest was small with short ribs. Serial scans confirmed the findings and also showed polydactyly of the left hand. Amniocentesis was performed and a normal male karyotype and normal alpha-fetoprotein levels were diagnosed. The couple opted once again for pregnancy termination.

Discussion

The syndrome demonstrates a variety of clinical manifestations that vary from mild to lethal. The prominent problem is hypoventilation caused by impaired chest expansion and subsequent pulmonary hypoplasia [3]. Pulmonary insufficiency or respiratory distress syndrome (RDS) is the main cause of death among patients before the second year of life with a percentage that reaches 80% [4]. Respiration is considered to be improved with age, as thoracic malformations become less pronounced but impairment of the respiratory system remains as a restriction pattern in spirometry [1, 4]. Young patients also suffer from recurrent pulmonary infections during neonatal period or infancy [1, 2].

Renal problems, which include secondary hypertension, polycystic kidneys, pelviectasia, and hypoplasia, exist in 34% of patients and 38% of those with renal involvement may develop end-stage renal disease (ESRD) [1, 2]. These complications are usually found after the second year of life [4].

Liver is impaired in < 30% of cases with ATD [1]. Common findings are prolonged neonatal jaundice with elevated direct bilirubin, elevated liver transaminases, hepatomegaly, polycystic liver disease, and portal hypertension [1, 5]. Histologically, portal fibrosis and bile duct proliferation which may lead to cirrhosis have been reported. Ursodeoxycholic acid administration appeared to control progression of liver disease [5].

Pancreatic and retinal complications are also noticed. The presence of fibrosis and cysts in the pancreatic parenchyma may obstruct normal exocrine function. Retinal dysplasia and retinitis pigmentosa have been described in 15% of patients [1, 2, 4]. The syndrome may

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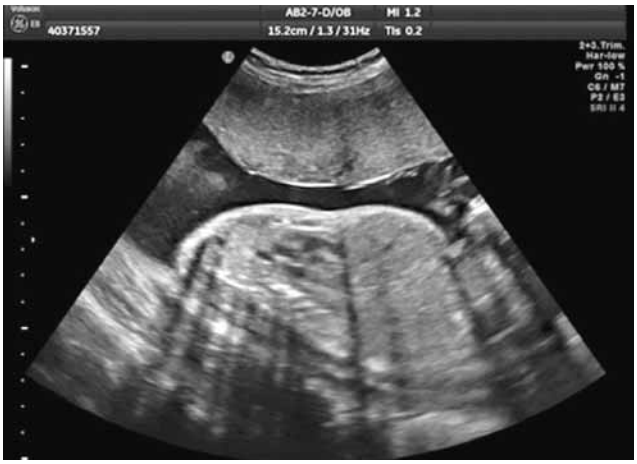
Table 1. — *Sonographic characteristics and differential diagnosis [7, 9, 10].*

	Case 1 (24th week)	Case (19th week)	Jeune Syndrome	Ellis van Creveld	SRPS I	SRPS II	SRPS III	SRPS IV
NT			Reported increase	Reported increase	Increased			Increased
FL (centile)	< 5th (33.6 mm)	< 3rd (21.8 mm)	< 5th	< 5th	< 3rd	5th/< 3rd	< 10th	< 5th
HC	Normal (229.3 mm)	Normal (165.9 mm)	Normal	Normal	Normal	Normal		
Thorax	Long and narrow, short, ribs	Small, short ribs	Narrow, short ribs	Small	Small, short ribs	Small	Small	Small
Visceral Anomalies			Pancreatic cysts	Cardiac anomaly, posterior fossa cyst	Hydrops	Exomphalos, bladder outflow obstruction, hydrops	Urogenital anomalies, hydrops	Exomphalos
Other characteristics	Polyhydramnios (26th week)		Polydactyly	Polydactyly	Severe micromelia, polydactyly	Polydactyly	Postaxial polydactyly	Tibia > fibula
Inheritance			Autosomal Recessive	Autosomal Recessive	Autosomal Recessive	Autosomal Recessive	Autosomal Recessive	Autosomal Recessive



Sonography at 24 weeks gestation showing shortness of all long bones (below fifth centile).
Figure 1. — Thorax and abdomen.

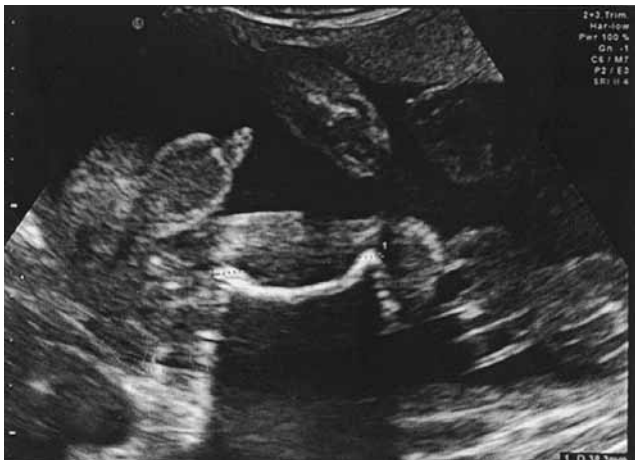


Figure 2. — Femur.

also be correlated with ciliopathy, malrotation, and Hirschsprung disease. Spinal cord stenosis and C1-C2 compression are life-threatening, although rare complications [1, 2]. Partial agenesis of corpus callosum (1.6%), situs anomalies, and cardiomyopathy have also been reported but they are rare complications [1].

Genetic heterogeneity exists in ATD patients. The main genetic mutation is located in a locus at chromosome 15q13 with a negative mutation analysis for genes GREMLIN and FORMIN1. Furthermore, a mutation in the intraflagellar transport 80 gene on chromosome 3 indicates that ATD may belong to the ciliopathy group. Indentifying a cytoplasmic dynein 2 heavy chain mutation (DYNC2H1) on chromosome 11q in five families with ATD or SRP type III supports this finding [1, 2, 4]. Another heterozygous mutation in INVS (NPHP2) gene found in a patient with ATD strengthens the thought of the heterogeneity of the disease [1].

Prognosis of the syndrome is difficult to be made because of the variability of its manifestations [2]. Pulmonary and renal function tests could have a prognostic value as long as RDS and ESRD are the main causes of death [1, 2, 4]. It is reported that only 20% of patients survive beyond infancy [2].

Poor prognosis of the syndrome and low quality of life of these patients is the reason that prenatal sonographic diagnosis is important. An accurate diagnosis can be made between 19-35 weeks of gestation [6]. Although, there have been reported cases with early prenatal diagnosis at 14th and 16th week in both high- and a low-risk pregnancies, respectively [7, 8]. It is suggested that confirmed antenatal diagnosis is possible at the first-trimester especially in high-risk pregnancies because the risk of recurrence is as much as 25% in skeletal anomalies inherited in an autosomal recessive pattern [9]. Most evaluated measurements are femur length (FL), biparietal diameter (BPD), head circumference (HC), thoracic circumference (ThC), and abdominal circumference (AC).

The major sonographic findings are shortness of all four extremities with a rhizomelic pattern, long and narrow thorax and postaxial polydactyly in some cases. Biometric parameters are best-evaluated when expressed as Z-scores[6]. In cases of ATD, polyhydramnios is an often sonographic finding [3]. Increased nuchal translucency (NT) has recently been associated with Jeune's syndrome case but it is not yet confirmed as a key point to sonographic diagnosis [7]. Pancreatic cysts were found during an ultrasound examination at 15 weeks of gestation in a pregnancy with Jeune's syndrome [10]. Differential diagnosis of the syndrome must exclude intrauterine growth restriction, chromosomal abnormalities, and especially syndromes such as Ellis-van Creveld syndrome, Verma-Naumoff syndrome, and other short-rib polydactyly syndromes (SRPS) [3, 7] (Table 1).

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