

CASE REPORT

Hypertrophic cardiomyopathy with Jeune syndrome: The first reported case

Jeune sendromu ile hipertrofik kardiyomiyopati birlikteliği: Literatürdeki ilk olgu

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Summary– Jeune syndrome (Asphyxiating thoracic dysplasia) is a rare dystrophy of the skeleton, inherited as an autosomal recessive condition. Patients develop a narrowed thorax, rhizomelic dwarfism, and hepatic, renal, and pancreatic abnormalities. High rates of pulmonary hypoplasia and pulmonary hypertension have been reported. Some patients die in early stages of life due to respiratory failure. The case of a patient referred with a history of severe asphyxiating birth, who had been diagnosed with Jeune syndrome and later hypertrophic cardiomyopathy (HCM) upon echocardiographic examination is described in the present report. This rare disease is discussed with respect to the current literature, as the present is the first reported case to be accompanied by HCM.

Jeune syndrome, or asphyxiating thoracic dysplasia (OMIM 208500), is a skeletal chondro-dystrophy rarely diagnosed in children, accompanied by extremity shortness and dwarfism, with possible involvement of organs including kidneys, liver, and pancreas.^[1,2] It is inherited as an autosomal recessive condition and characterized by a bell-shaped, narrowed chest wall. It was first defined in 1955 by Jeune et al., is diagnosed with equal frequency in both sexes, and has an incidence of 1 per 100,000–130,000 live births. A majority of patients die at an early stage after experiencing varying degrees of respiratory distress. Jeune syndrome is diagnosed on the basis of

Abbreviations:

HCM Hypertrophic cardiomyopathy
PHT Pulmonary hypertension

Özet– Jeune sendromu (Asfiktik torasik displazi), nadir görülen bir iskelet distrofisidir. Otozomal resesif olarak geçer. Hastalarda dar göğüs kafesi, rizomelik cücelik, karaciğer, böbrek ve pankreas anomalileri gelişir. Akciğer hipoplazisi ve pulmoner hipertansiyon yüksek oranda bildirilmiştir. Hastaların bir kısmı yaşamın erken dönemlerinde solunum yetersizliğinden kaybedilir. Bu makalede, ağır asfiktik doğum öyküsü ile kliniğimize sevk edilen ve Jeune sendromu tanısı konulan, ekokardiyografik incelemede hipertrofik kardiyomiyopati tespit edilen olgu sunuldu. Nadir görülen bu hastalık, hipertrofik kardiyomiyopatinin eşlik ettiği ilk olgu olması nedeniyle literatür bilgileri eşliğinde tartışıldı.

clinical and radiological findings.^[2–4] Heart involvement is not expected, and concomitance with hypertrophic cardiomyopathy (HCM) has never before been reported.

The case of a patient diagnosed with Jeune syndrome in the neonatal period and identified to have HCM upon transthoracic echocardiographic examination is described in the present report, and this rarely occurring disease is discussed.

CASE REPORT

A female patient was born at an external center following the first pregnancy of an 18-year-old mother of Syrian origin who had not been regularly moni-

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tored during pregnancy and was referred the same day. The patient was born at the end of 41 weeks with meconium. Her Apgar scores at 1 and 5 minutes were 1 and 3, respectively, and she received cardiopulmonary resuscitation. The patient's mother had no diseases and did not use medication. The mother and father were third-degree relatives, and there was no family history of a similar disease or unexpected sudden death. The patient was admitted to the newborn intensive care unit while intubated. Upon physical examination, her weight was 2100 grams (below the 3rd percentile), height was 38 cm (below the 3rd percentile), head circumference was 32 cm (below the 3rd percentile), chest circumference measured at breast line was 28 cm, body temperature was 35.8 C°, peak heart rate was 120 beats per minute, systemic blood pressure was 68/44 mmHg, and oxygen saturation was 93% (fraction of inspired oxygen [FiO₂]: 0.5). The patient had a narrowed thorax, shortened upper and lower extremities, and a swollen abdomen (Figure 1). Neither pathological murmur nor evidence of heart

failure were observed during cardiovascular examination. She did not have organomegaly, her outer genital structures appeared to be typical, and other systemic examination results were normal. In laboratory analysis, blood gas levels were as follows: pH: 7.26; pCO₂: 46 mmHg; pO₂: 58 mmHg; HCO₃⁻: 20 mmol/L. Whole blood count, liver and kidney function, bilirubin, serum electrolyte, blood glucose, and acute phase reactant values were within normal range, and lactic acid dehydrogenase was 1878 u/L (normal value: 126–222 u/L). In pulmonary and whole-body bone x-ray scans, front-rear thorax diameter was small, lungs were hypoplastic, ribs, iliac bones, humerus, and femur bones were short, and she had typical clavicles, similar in shape to a bicycle handlebar (Figure 2). Based on these assessments, the patient was diagnosed with Jeune syndrome. Results of abdominal and transthoracic ultrasonography and optometry were normal. On transthoracic echocardiographic assessment, interventricular septum was identified as thick, with a z score of 5, right and left ventricular cavities were



Figure 1. The newborn patient appeared to have a narrowed thorax, shortened upper and lower extremities, and a swollen abdomen.



Figure 2. On straight x-ray, the thorax appeared to be small and narrow, the ribs short and horizontally oriented, the extremities short, the clavicles similar in shape to a bicycle handlebar, and the pelvis similar in shape to a trident harpoon.



Figure 3. (A) On TTE, IVS appeared to be thickened, and a small left ventricular cavity was observed, (B) significant pulmonary hypertension was observed on continuous-wave Doppler measurement of the tricuspid valve. IVS: Interventricular septum; LV: Left ventricle; RV: Right ventricle; TTE: Transthoracic echo-cardiography.

extremely small, left ventricular outflow tract was not constricted, and ventricular functions were normal and accompanied by severe pulmonary hypertension (PHT) (Figure 3). In spite of mechanical ventilator support, the patient's clinical condition did not improve, and she died from respiratory failure on the sixth day of hospitalization.

DISCUSSION

Jeune syndrome is a disease of the ciliopathy group. It develops as a result of mutations in genes that code the proteins of the cilium microtubule structure. Most frequently occurring are mutations in genes *TTC21B* and *DYNC2H1*, which code intraflagellar transport proteins.^[4] The patient died before genetic studies could be performed. Patients with Jeune syndrome develop a small, narrow, bell-shaped thorax, and chest circumference measured after birth is generally smaller than head circumference.^[1,5] Ribs are short and horizontally oriented, and costochondral cartilages are prominently swollen in an outward manner, resembling rachitic rosaries. The abdomen is noticeably swollen, compared to the thorax, and arms and legs are marked by rhizomelic dwarfism, with varying degrees of shortness.^[5,6] Radiological findings are characteristic narrowed thorax, shortened ribs, shortened extremities, and harpoon-shaped pelvis (due to hypoplasia in the iliac wings and straightening of the acetabular angle). Jeune syndrome is diagnosed on the basis of clinical and radiological findings.^[7,8] The present patient was diagnosed based on typical thoracic and pelvic abnormalities, and clinical and radiological findings. Because the patient did not have polydactyly, ectodermal dysplasia, or complex congenital cardiac disease, such as that involving a single

atrium, Ellis–van Creveld syndrome was not considered. Prenatal diagnosis is possible in cases of Jeune syndrome, as typical bony changes can be observed with ultrasonography, though definitive diagnosis is difficult.^[2,3,9]

Prognosis is determined by severity of chest wall deformity and respiratory problems.^[1,3] Respiratory movements and pulmonary ventilation are inadequate, due to the narrow thorax and short, wide ribs. Patients often present with recurrent respiratory tract infections, pulmonary hypoplasia, and respiratory troubles. Bronchial development is generally normal, while alveolar development is deteriorated. Signs of pulmonary infection are increased, including cyanosis, and respiratory troubles such as tachypnea and dyspnea. A majority of patients die from respiratory failure within the first year of life, while surviving patients tend to have fewer respiratory problems over time,^[7,10] suffering from retarded growth. Organs may fail, resulting in the need for transplant, due to renal involvement such as cyst or stone growth, interstitial fibrosis, glomerulosclerosis, or hypertension, hepatic involvement such as hepatomegaly, cholestasis, hepatic fibrosis, biliary cirrhosis, or portal hypertension, or pancreatic involvement such as cyst or fibrosis. Renal failure is the most common cause of mortality between the ages of 3 and 10,^[10–12] and may be accompanied by ocular findings such as retinal pigmentation or dystrophy, agenesis of the corpus callosum, spinal cord compression, or hydrocephalus.^[2,8,13] No hepatic, renal, pancreatic, or ocular abnormalities were observed in the present patient.

No reports or collective reviews related to Jeune syndrome have included descriptions of patients with congenital heart diseases, though cardiomyopathy with unknown etiology and unspecified type was reported in a 32-year-old patient.^[14] The possibility of patients developing increased pulmonary vascular resistance, congestive heart failure, and PHT due to narrowed thorax, as well as alveolar and pulmonary hypoplasia, has been reported. Concomitance of severe congenital heart disease with Ellis–van Creveld syndrome is quite common, and Ellis–van Creveld syndrome may be mistaken for Jeune syndrome, requiring differential diagnosis.^[2,8,15] The present patient was diagnosed with HCM and significant PHT secondary to pulmonary hypoplasia via transthoracic echocardiography; no treatment was prescribed for

cardiomyopathy, as it did not cause constriction in narrow ventricular outflow, and PHT regressed with medical treatment.

In conclusion, Jeune syndrome should be considered when respiratory trouble is accompanied by a narrowed thorax, shortened extremities, and pelvic bone abnormalities in Turkey, where kin marriage occurs very frequently. The present case is considered to be the first of its kind, as concomitance of Jeune syndrome and HCM has never before been reported.

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Anahtar sözcükler: Asfiktik torasik displazi; kardiyak anomali; hipertrofik kardiyomiyopati; Jeune sendromu; yenidoğan.