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Horseshoe Kidney as a New Anomaly in Pagod Syndrome: Case Report

Pagod Sendromunda Yeni Bir Bulgu: Atnalı Böbrek Anomalisi

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ABSTRACT PAGOD Syndrome is a rare condition with multiple congenital anomalies associated with very high mortality. Here, we present an infant who was born from 21 years old mother on the 37th week of gestation by caesarean-section. Physical examination of the patient revealed an omphalocele sac, small rib cage, asymmetry between the hemithoraces, cleft palate. The heart was in the epigastric region, and the pulmonary arteries were hypoplastic on the echocardiographic examination. The patient died in the sixteenth hour of life. On autopsy there were no ovaries, and she had horseshoe kidneys. Her cytogenetic analysis result was 46,XX. This is one of the rarely seen PAGOD Syndrome cases in the literature and it differs from the others with the existence of horseshoe kidney. It is also important as being the first case reported from Turkey.

Key Words: Hernia, umbilical; dextrocardia; Kennerknecht Sorgo Oberhoffer syndrome


Anahtar Kelimeler: Fıtık, umbilikal; dekstrokardiya; Kennerknecht Sorgo Oberhoffer sendromu


PAGOD syndrome is a rare condition with multiple congenital anomalies and is associated with very high mortality. Its aetiology and incidence are not well known.1 In this report, we present a case of PAGOD syndrome with a new finding: the horseshoe kidney.

CASE REPORT

A female patient was born to a 21-year-old mother whose pregnancy history was gravidity 2, parity 1. The patient was delivered by Caesarean section (C/S) on the 37th week of gestation and weighed 2.625 g, the C/S indication was the anomalic fetus. Except for the abortion of her first preg-
nancy, the mother had an unremarkable history. However, the parents were cousins. The father was 29 years old and had no significant health problems. The Apgar scores were 5 and 6, on the 1st and 5th minutes respectively. The patient was intubated and admitted to the neonatal intensive care unit (NICU). An omphalocele sac, a small rib cage, and asymmetry between the hemithoraces were noted on physical examination. The patient’s legs changed position from the hip through the back with a hyperextension posture, and the right knee joint was immobile. The length of the right leg was measured 17.5 cm; the left leg was 21 cm. There was clubfoot on the right foot (Figure 1). Phenotypically, the patient looked like a female, but the labia majora were immature, and located proximally from the expected position.

The x-ray showed kyphoscoliosis, tightened rib cage, and because of the anatomic limitations, reduced lung volume (Figure 2). Echocardiography demonstrated that the heart was in the epigastric region and the apex of the heart was located horizontally. The left ventricle was smaller than the right one, the right ventricular outflow tract was narrowed because of muscular bands, and the pulmonary artery branches were hypoplastic. Cytogenetic analysis showed 46,XX and no significant genetic defect was detected. An autopsy revealed that sensory organs had completed their maturation and there was an omphalocele sac measuring 13x9x7 cm in the abdominal region. In the genital region, the patient also had anomalies, such as immature labia majora, that made the external female genitalia different. In addition, no ovarian tissue was detected. The liver, spleen, stomach, and intestines were inside the omphalocele sac when dissected. Opening the thorax revealed the lungs to be hypoplastic, and the left hemithorax was narrower than the right one. The right and left lungs weighed 7 grams and 5 grams, respectively. The thymus was reported to be 5 grams in weight. The patient also had horseshoe kidneys, and there were no other concomitant renal anomaly (Figure 3).

An informed consent was given by the parents of the baby.
DISCUSSION

PAGOD syndrome is a rare condition characterized by multiple congenital anomalies, including pulmonary artery and lung hypoplasia, agonadism, diaphragmatic abnormalities, cardiac defects, omphalocele, and various genital anomalies. The first cases for two phenotypic sisters with genetic analyses of 46,XY and 46,XX with the anomalies identified above were reported in 1993. The acronym, PAGOD, was then suggested, standing for [hypoplasia of the] lung and pulmonary artery, agonadism, omphalocele/diaphragmatic defect, and dextrocardia. The occurrence of a similar set of malformations in twins of the opposite sex is interpreted as evidence for autosomal recessive inheritance. In our region, consanguineous marriages are common and, in this case report, the parents were cousins, so that this might be a clue for autosomal recessive inheritance. The ninth case of PAGOD syndrome in the literature was only reported in 2007, which clearly emphasizes the rarity of this syndrome. A case report published in 2002 emphasised that the condition might resemble the malformation complex associated with a developmental deficiency that results from a lack of vitamin A or retinoic acid, as described in animal models. There may be an association between PAGOD syndrome and vitamin A deficiency. Also, in a case report of PAGOD syndrome that was published in 2009, the patient’s free vitamin A level was low, but the maternal plasma vitamin A level was normal. It is known that, during pregnancy, maternal vitamin A is taken up by retinol binding protein 4 (RBP4), which is expressed in the embryonic visceral endoderm from pregastrulation stages. The transport is mediated through the specific membrane receptor for RBP and stimulated by retinoic acid 6 (STRA6), which is expressed in human organ systems and includes the placenta during embryonic development. Mutations in the STRA6 gene cause Matthew-Wood syndrome, which demonstrates a significant phenotypic overlap with PAGOD syndrome. In the case report, no mutations were detected and, as a hypothesis, a metabolic defect resulting from vitamin A deficiency, where transport is not mediated by the STRA6 receptor, might have played an aetiological role in the development of this syndrome of multiple congenital anomalies. Vitamin A deficiency (VAD) during pregnancy has been shown to be associated with a decrease in nephron number and kidney weight of the offspring. In recent studies, maternal VAD during pregnancy has been shown to decrease renal size in the infant at birth. It is also reported that renal tRA/RAR activity is confined to the ureteric bud (UB) and collecting duct (CD) cell lineage, suggesting that endogenous tRA/RARs primarily act through regulating gene expression in these cells in embryonic and adult kidney, respectively. Since we here report the concomitant renal anomaly with PAGOD Syndrome, this may partially support the hypothesis of VAD may result with renal anomaly. Since our patient lived only 16 hours, we could not obtain blood samples for vitamin A levels. A spherical spleen had already been shown as a new and additional finding in a case report in the literature. However, in this case, we added another new finding: a horseshoe kidney. Horseshoe kidney is a fusion defect of the kidney that has an incidence of approximately 1:400, and one-third of the patients with horseshoe kidney have other urogenital, gastrointestinal, skeletal, cardiac, or pulmonary anomalies. As a result, our report not only shows a case of PAGOD syndrome, which is rarely seen in the literature, but identifies horseshoe kidney as a new coexisting anomaly in this syndrome. This case is also important since it is the first to be reported from Turkey. Further genetic studies should be performed in order to explain the aetiology of PAGOD syndrome.
REFERENCES


