CASE REPORT

Mosaic trisomy 14 and aorta-pulmonary window association: A case report

Mozaik trizomi 14 ve aorta-pulmoner pencere birlikteliği: Bir olgu sunumu

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Summary– Trisomy 14 mosaicism is a rare chromosomal abnormality with distinct and recognizable clinical features. Congenital heart anomalies can accompany in this syndrome. To the best of our knowledge, this is the first case of mosaic trisomy 14 with an aortopulmonary window to be described in the literature.

Özet– Mozaik trizomi 14, belirgin ve tanınabilir klinik özelliklere sahip nadir bir kromozom anomalisidir. Bu sendroma doğuştan kalp anomalileri eşlik edebilmektedir. Bu olguda literatürde daha önce yer almayan aorta-pulmoner ile pencere mozaik trizomi 14 birlikteliğini sunuyoruz.

Mosaic trisomy 14 was first described in 1970 as a chromosomal disorder associated with dysmorphic craniofacial features (such as microcephaly, large anterior fontanel, hypertelorism, dysmorphic nose, prominent over-lip, ear anomalies, cleft palate), finger anomalies, congenital heart and genitourinary abnormalities, as well as widespread psychomotor and growth retardation.[1] Mosaic trisomy 14 is a very rare chromosome disorder presented in approximately 30 cases in the literature.[2] Presently described is the first case of mosaic trisomy 14 with an aorta-pulmonary window (APW) to be added to the literature.

Abbreviations:

APW	*Aortopulmonary window*
ASD	*Atrial septal defect*
CT	*Computed tomography*
MRI	*Magnetic resonance imaging*
PH	*Pulmonary hypertension*
VSD	*Ventricular septal defect*

CASE REPORT

The patient was the first live birth and the result of the second pregnancy of a 24-year-old woman, and was delivered at 35 weeks' gestation. The patient was admitted to the neonatal intensive care unit due to prematurity and respiratory distress. Hypertelorism, micro and retrognathia, prominent forehead and nostrils, anteverted nostrils, pes equinovarus of the left foot, and arachno- and clinodactyly were observed in a physical examination. The measurements recorded included a weight of 1285 g (<third percentile), a length of 36 cm (<third percentile), and a head circumference of 29.5 cm (<third percentile) (Fig. 1). A 3/6 systolic murmur was heard in the third intercostal space on the left side of the sternum in the cardiovascular examination. It was determined that the patient's parents were distantly related and the patient's sibling died intrauterine due to hydrops. In a cytogenetic examination of the amniocentesis performed during the prenatal period, the patient was diagnosed with mosaic trisomy based on the following results: 47, X *, +14 [2] / 46, X *.[30] The patient was suspected of having Tetralogy of Fallot following an obstetric ultrasound examination revealing a medium-sized, perimembranous inlet malalignment ventricular septal defect (VSD) and a 25% overriding aorta. Antimicrobial therapy, non-invasive respiratory support, and oral and parenteral nutrition were initiated for the patient, since early-onset neonatal sepsis could not be excluded. A

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Figure 1. A photo of the patient illustrating findings of hypertelorism, micro and retrognathia, prominent forehead and nostrils, antevert position of the nostrils, pes equinovarus of the left foot, and arachno- and clinodactyly.

large APW (7–8 mm in size) above the aortic valve, a 6-mm perimembranous inlet malalignment VSD and 6-mm atrial septal defect (ASD) were observed by a pediatric cardiologist on a postnatal echocardiography (Fig. 2a-d). The direction of the shunt from the APW was from left to right. The estimated systolic pulmonary artery pressure as a result of the tricuspid insufficiency jet was 57 mmHg, and while pulmonary stenosis was not present, pulmonary hypertension (PH) was recorded. The arcus aorta was evaluated as normal. A type I window, 7 mm in diameter between the main pulmonary artery and the ascending aorta was detected on a cardiac computed tomography (CT) angiography performed to determine a definitive diagnosis and surgical approach (Fig. 3a, b). On the 13th day of hospitalization, intubation and mechanical ventilator support were initiated due to increased respiratory distress. Diuretic and inotropic treatment (dobutamine) was introduced upon the development of heart failure symptoms. A consultation was held with the pediatric neurology clinic and the genetics department. A magnetic resonance image (MRI) of the brain was interpreted as normal. Based on the genetic results, the diagnosis was thought to be mosaic trisomy 14. On the 42nd day of hospitalization, the patient was transferred to the cardiovascular surgery clinic for surgery due to congenital heart disease. The APW, ASD, and VSD were closed. In the first postop-

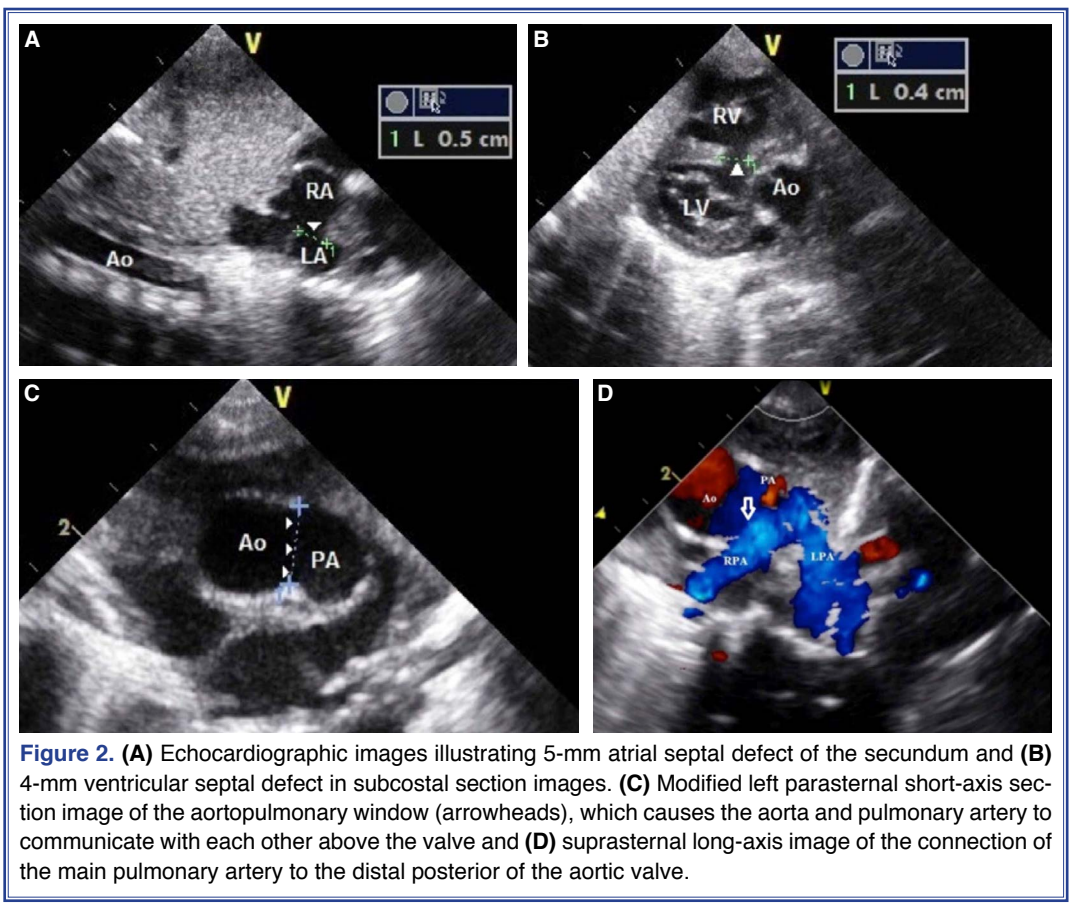

Figure 2. **(A)** Echocardiographic images illustrating 5-mm atrial septal defect of the secundum and **(B)** 4-mm ventricular septal defect in subcostal section images. **(C)** Modified left parasternal short-axis section image of the aortopulmonary window (arrowheads), which causes the aorta and pulmonary artery to communicate with each other above the valve and **(D)** suprasternal long-axis image of the connection of the main pulmonary artery to the distal posterior of the aortic valve.

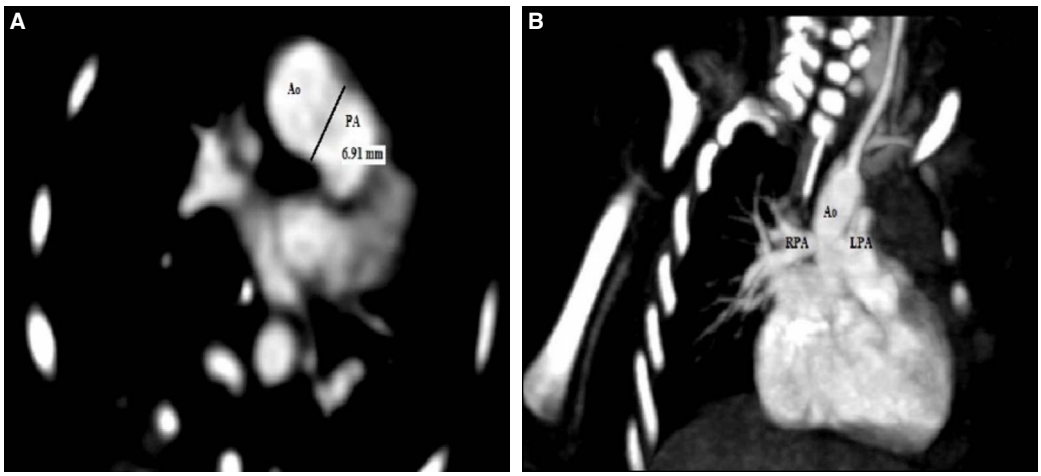

Figure 3. **(A)** Computed tomography angiography images of the thoracic aorta revealing the 6.91-mm aortopulmonary window between the aorta and the pulmonary artery and **(B)** a separation of the right and left pulmonary artery branches from the distal posterior of the aortic valve.

erative week, the thoracic tubes were withdrawn, the inotropic support was gradually terminated, and oral feeding was initiated. Unfortunately, the patient died due to sepsis on postoperative day 12.

DISCUSSION

Chromosome 14, which contains between 800 and 1300 genes, constitutes between 3% and 3.5% of the human genome. Partial trisomy 14, or mosaicism, is the result of numerical or structural abnormalities in this gene region. Complete trisomy 14 is diagnosed with spontaneous abortions and is incompatible with life.[3] A limited number of cases diagnosed with mosaic trisomy 14 through amniocentesis have been reported in the literature.[4] Our case is one of the rare few in this group to be diagnosed in the prenatal period.

Clinical presentations are nonspecific and vary widely; therefore, they cannot provide a decisive definition of the disease. Findings such as intrauterine and extrauterine growth retardation, psycho-motor retardation, microcephaly, large forehead structure, low and dysmorphic ears, micro/retrognathia, dysmorphic palpebral fissures, short neck, micropenis, undescended testis, clitoromegaly, hyperpigmentation of the skin, and cardiac defects are commonly seen. Though rare, it may be accompanied by diaphragm hernia, omphalocele, and severe scoliosis.[2] The clinical characteristics of our case were intrauterine growth retardation, microcephaly, dysmorphic facial findings (hypertelorism, micro and retrognathia, prominent forehead and nostrils, antevert position of nostrils), pes equinovarus, arachnodactyly, clinodactyly, and cardiac defects (ASD, VDS, APW). Cardiac anomalies often accompany phenotypic features of this disease, but the presently described case of mosaic trisomy 14 with APW is valuable in that it appears to be the first identified in the literature.

APW is a rare congenital cardiac anomaly with an incidence of 0.1% to 0.2% in which there is a connection between the aorta and the pulmonary trunk.[5] Mori et al.[6] classified the cardiac anomaly in 3 groups considering features such as the location of the defect and the relationship to the aorta and pulmonary artery. Type I is a simple defect between the pulmonary artery and the ascending aorta. A type II defect is localized more distally and opens into one of the pulmonary artery branches. A type III defect is characterized by an abnormal origin from the pulmonary artery to the aorta.[6] Echocardiography is an important method to be used in the determination of a definite diagnosis and prognosis, but cardiac catheterization can be performed if the diagnosis is uncertain or to ascertain shunt direction. Cardiac angiography with CT is also helpful in determining the diagnosis and the surgical method to be applied in patients whose general condition is not suitable for catheterization. A type II APW was seen in the echocardiography results of the current patient performed on postnatal day 1, which was consistent with the result of cardiac CT angiography. The survival of these patients is largely related to the size of the defect and the presence of

PH. Since it is known that large defects lead to heart failure and concomitant PH, surgery is recommended as soon as possible. Perrin et al.[7] reported on a patient with distal trisomy 14 accompanied by APW who was successfully operated on at the end of the first month in the postnatal period. Our case was also operated on successfully within a reasonable period of time without the development of PH. Since our patient was still in the neonatal period, no specific PH treatments were carried out before or after the surgery.

Surgical correction of the APW immediately after diagnosis is imperative to avert irreversible PH, which may develop earlier than in other cases of left-to-right shunt. Once significant PH has set in, surgical intervention for the APW can lead to pulmonary hypertensive crisis and right-sided heart failure.[8]

In the absence of associated anomalies, transcatheter closure of APW should be considered when the anatomy is favorable in terms of the location and size of the defect.[9]

In the present case, surgical repair was chosen rather than transcatheter occlusion because the defect was quite wide and very close to both the aorta and the pulmonary valve (Type-I/proximal type). The literature reports describe patients closed with a transcatheter approach with a defect located more distally than the semilunar valve and coronary arteries, and these APWs were not very wide, which was not the case in our patient. The type of APW most suitable for device closure is a small APW located between the 2 great arteries, away from the origin of the left coronary artery and the right and left main pulmonary arteries, and with no associated congenital anomalies.[10]

Surgery is the traditional treatment; however, defects located sufficiently far from coronary arteries and from the origin of the pulmonary arteries (at least 5 mm each) can be successfully occluded with a transcatheter approach. The intermediate type is the least common, but the best-suited for device closure.[11]

Nutritional problems associated with craniofacial anomalies and neuromotor retardation, and respiratory failure associated with intrauterine growth retardation directly affect the duration of intensive care unit stay. Families are typically most curious about life expectancy and neuro-cognitive development. Although the mechanism is not clear, based on the literature, it is possible to say that this disease is likely to be accompanied by mental retardation.[12] Even if the brain MRI result is normal, an early neurological evaluation during hospitalization is important to assess for mental retardation. Life expectancy varies with the severity of accompanying anomalies, and complicated cardiac defects particularly increase the risk of mortality.

It is important to know that patients with mosaic trisomy 14 can survive. Appropriate management of multiple congenital anomalies is critical. Mosaic trisomy 14 cases may be accompanied by APW. Surgery before the development of irreversible PH in APW cases is important to obtain the best long-term results. A prenatal diagnosis and delivery performed at an appropriate center increase the chances for the best outcome.

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Keywords: Aortopulmonary window; mosaic trisomy 14; neonatal; survival.

Anahtar sözcükler: Aorta-pulmoner pencere; mozaik trizomi 14; yenidoğan; sağkalım.