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Rare combination in an infant patient: trisomy 7p and tetralogy of fallot

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Brief Report

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Abstract

This case report presents an infant patient with the association of trisomy 7p and tetralogy of fallot (TEF). Patients diagnosed with trisomy 7p should certainly be scheduled for an echocardiographic exam and be scanned for any CHDs that may accompany it. The CHDs that most frequently accompany this syndrome include atrial septal defect, ventricular septal defect, and patent ductus arteriosis. Yet, it should be known that TEF may also be present, albeit rarely.

Trisomy 7p is a rarely seen genetic abnormality. Very few patients have been reported in the literature. The clinical signs associated with this abnormality have been clearly defined.[1] These include psychomotor retardation, a wide and protruding forehead, posterior fontanelle remaining open, hypertelorism, low-set ear, abnormal palmar lines, ocular, genital, and cardiovascular abnormalities.[1,2] Changes in the number of copes such as chromosomal duplications or deletions may be associated with cardiovascular abnormalities.[2] Various cardiovascular abnormalities may be seen in more than one-third of trisomy 7p patients.[3]

Tetralogy of fallot (ToF) is the most frequently observed cyanotic CHD and its incidence is 0. 34 per 1000 live births. Patients present with a wide perimembranous ventricular septal defect, overriding of the aorta, stenosis in the right ventricular outflow, and right ventricular hypertrophy.[4] The disease is also accompanied by various genetic or chromosomal syndromes in approximately 15% of patients.[5] In this case report, we present an infant patient with a combination of partial trisomy 7p and ToF.

Case report

The female infant was delivered through normal spontaneous vaginal birth by a 34-year-old healthy mother at week 36 as G4D2Y2 had a birth weight of 1940 g, which was small for her gestational age and an APGAR of 6/7. The mother's antenatal history did not include smoking, alcohol, warfarin or another drug use, or any other chronic conditions. The patient, who had fascial dysmorphism and whose parents were first cousins, underwent abdominal ultrasonography, and the result was normal. TEF was identified during echocardiographic exam (Fig 1). The brain magnetic resonance showed that both occipital lobes were hypoplasic, ectasia was present in the ventricular system, and there was widening of the peripheral cerebrospinal fluid distance in the frontotemporal anterior parts. The patient was identified to have severe sensorineural hearing loss during the hearing test. She was scheduled for chromosome analysis.

The chromosome analysis performed on the short-term lymphocyte culture derived from peripheral blood yielded the result of der(15)t(7;15)(p10;q10). On the meta-phases derived from the patient's materials, trisomy of the p arm of the chromosome number 7 was identified (Fig 2). The parents underwent chromosome analysis. While the mother had normal karyotype, the father's karyotype was 46,XY,t(7;15)(p10;q10). The patient received micro-array study and an increase of 57,963 kbp encompassing the 7p22. 3p11. 1 region was identified.

When the patient turned became 7 months old, her saturation values dropped to 60% and she began to experience spells. The patient, who had developmental retardation, underwent a left Blalock–Taussig aorto-pulmonary shunt procedure using a 4-mm Goretex graft. The patient's saturation levels were within the normal ranges. When the patient became 18 months old, she underwent cardiac catheterisation and it was decided to perform total correction. Afterwards, a total correction surgery was performed via sternotomy and trans-atrial approach using a transannular patch and mono-cusp. No problems were identified in the follow-up echocardiographic exam.

The patient's physical exam that was done at the age of 21 months revealed dolichocephaly, a wide and protruding forehead, hypertelorism, a depressed nasal bridge, anteverted nostrils, low-set and dysplastic ears, downturned corners of mouth, a high palate, micrognathia, brachydactyly, bilateral transverse single line on the hands, dimples on the hands, ankles, elbows, and back as well as hypotony. Furthermore, the patient's fontanelle had not yet closed (8 × 4 cm). The patient was observed to be behind in terms of neuromotor development steps. She could not

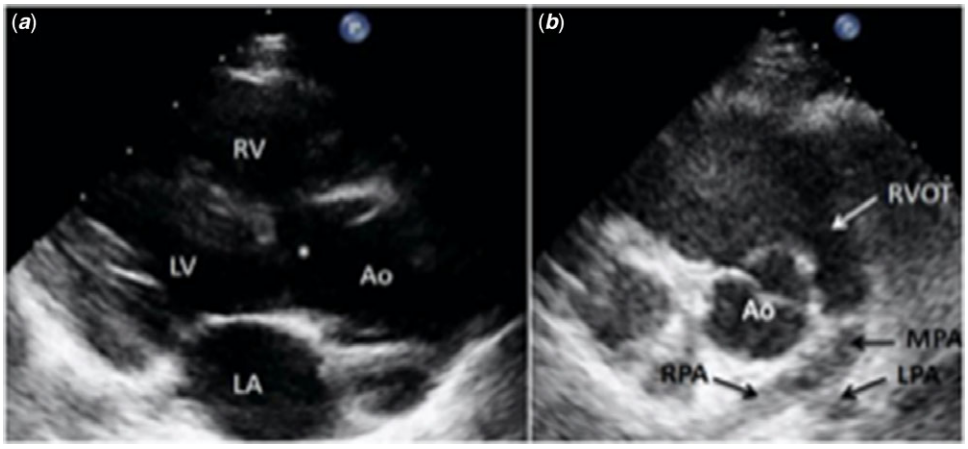

Figure 1. In echocardiographic examination; (***a***)**:** Dextroposition of the aorta and large perimembranous ventricular septal defect (star) are observed. (***b***)**:** Normal relationship between the aorta and pulmonary artery and RVOT are seen. It is seen that the pulmonary annulus and main pulmonary artery are hypoplasic, and the branches of the pulmonary artery are well developed and confluent. **Ao:** Aorta, **LA:** Left atrium, **LPA:** Left pulmonary artery, **LV:** Left ventricle, **MPA:** Main pulmonary artery, **RPA:** Right pulmonary artery, **RV:** Right ventricle, **RVOT:** Right ventricular outflow tract.

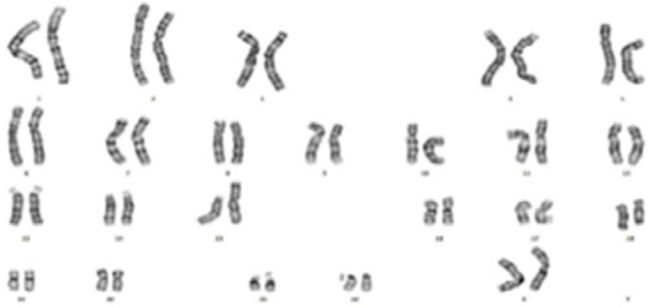

Figure 2. The karyotype image of the case.

hold her head upright or speak. The patient is still under outpatient follow-up. Signed informed consent forms were obtained from the family members to allow the use of clinical findings, laboratory test results, and images.

Discussion

Trisomy 7p is a rarely seen genetic disease that develops due to the partial or full duplication of the shorter arm of the chromosome 7, which involves many systems. It was reported for the first time in the year 1968 in the literature. Most cases develop as a result of the mal-segregation of parental balanced translocations.[2,6,7] For our case, it was identified that the father was the carrier of a balanced translocation and that the p arm of chromosome 7 was triplicated due to the inheritance of an imbalanced product by the child. Parentally inherited balanced-looking changes, regardless of gender, may present with different clinical pictures that may vary according to the chromosomal content after abnormal gamete formation. In our case, der15 was detected after abnormal gamete development in a balanced-looking healthy t(7;15)(p10;q10) father. Chromosome analysis should be done in such cases and families should be informed about possible situations before pregnancy.

The clinical findings of the trisomy 7p syndrome have been well-defined. Patients may present with abnormalities of the cranio-fascial, musculoskeletal, genital, ocular, and cardiovascular systems.[8,9] Half of the cases are lost during the infancy period and nearly half of them develop mental retardation.[9] While the clinical findings may vary per the size of duplication, the most frequent complications develop in the intrauterine period and as a result of the musculoskeletal system involvement associated with the abnormal muscle tone in post-natal life. Hypotony may be seen in one-third of patients.[7] Our patient also had hypotony. The primary cranio-fascial abnormalities seen in cases include micrognathia, hypertelorism, low-set and malformed ears, a large fontanelle, and wide sutures.[1,7,10] The findings in our case were also consistent with the literature. Severely large front fontanelles that do not close are specifically the most characteristic finding in patients with trisomy 7b syndrome.[1] The patient's front fontanelle was still open during her exam performed at 21 months of age and it was rather large. A large front fontanelle that closes late may also present with different genetic syndromes such as trisomy 13, trisomy 18, achondroplasia, and campomelic dysplasia; however, trisomy 7 should also be considered for differential diagnosis in such a situation.

Various cardiovascular abnormalities may be seen in more than one-third of trisomy 7 patients.[3] A study evaluating the trisomy 7 patients reported the presence of cardiovascular abnormalities in 43% of patients. The most frequently observed abnormalities include atrial septal defect, ventricular septal defect, and patent ductus arteriosus. In the literature, patients with trisomy 7b were also reported to have coarctation of the aorta, ToF, pulmonary and aortic valve stenosis, double inlet left ventricle, and dextrocardia. The spectrum of abnormalities suggests that multiple segments on 7p may be associated with normal development of the heart.[2,10] In our case, ToF was present and it was surgically treated with success. A literature review showed that the association of trisomy 7p with ToF is very rare.

Many genetic and chromosomal syndromes may accompany ToF. Approximately 15% of cases are syndromic cases. These may include the DiGeorge syndrome, trisomy 21, 18, and 13 as well as the VACTERL and CHARGE syndromes.[5] A study looking at patients with syndromic ToF reported that hypoplasic pulmonary arteries, aortic dilatation, and major aortopulmonary collateral arteries were more frequently compared to those without syndrome and that the cardiac phenotype was associated with the underlying genetic profile. Similarly, it was reported that patients with ToF had a higher need for staged surgery due to the high frequency of hypoplasic pulmonary artery.[5] In our case, it was also required to perform a systemic pulmonary arterial shunt procedure prior to total repair due to the low saturation in the early infancy period. Therefore, staged surgery was performed.

In conclusion, patients diagnosed with trisomy 7p should certainly be scheduled for an echocardiographic exam and be scanned for any CHDs that may accompany it. The CHDs that most frequently accompany this syndrome include atrial septal defect, ventricular septal defect, and patent ductus arteriosis. Yet, it should be

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known that ToF may also be present, albeit rarely. In patients diagnosed with ToF, one must act with caution with respect to the associated chromosomal and genetic abnormalities, as well. It should be taken into account that ToF, the most frequently encountered cyanotic disease, may be associated with many syndromes and such patients more frequently require palliative intervention.

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