CASE REPORT

A Case With Dextrocardia and Multiple Cardiac Anomalies in a Family With Congenital Heart Malformations

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Abstract

In this case; an interesting example of family with recurrent congenital heart defects due to situs ambiguous has been presented. The parents were relatives and had a history of termination because of complex congenital cardiac malformations in the first pregnancy. Dextrocardia and complex malformations of the heart and great vessels were detected in the second pregnacy by fetal echocardiography at 23rd weeks of gestation. Postmortem evaluation confirmed prenatal findings on fetal echocardiography and also revealed medially placed liver, dextrocardia and a spleen on normal location. We suggest that all cases with complex congenital malformations of heart and/or great vessels must be assessed for the heterotaxy disorders because of the findings in this family.

Keywords: dextrocardia, heart defects, congenital, pregnancy, genetic counselling, prenatal diagnosis

Özet

Konjenital Kalp Malformasyonları Olan Bir Ailede Dekstrokardi ve Multipl Kardiyak Anomalili Bir Olgu

Bu olguda; situs ambigusdan kaynaklanan tekrarlayan konjenital kalp defektleri olan ilginç bir aile örneği sunulmuştur. Ebeveynler akrabaydı ve kompleks kardiyak malformasyonlar nedeniyle ilk gebelikte bir tahliye öyküsü mevcuttu. İkinci gebelikte, 23. haftada yapılan fetal ekokardiyografide, dekstrokardi, kalp ve büyük damarların kompleks malformasyonları tespit edildi. Otopsi değerlendirmesi prenatal ekokardiyografi bulgularını doğruladı ve ek olarak orta hat yerleşimli karaciğeri, tek normal lokalizasyonlu dalağı ve dekstrokardiyi ortaya koydu. Bu ailedeki bulgular nedeniyle kalp ve/veya büyük damarları içeren kompleks konjenital malformasyonlu bütün olguların heterotaksi bozuklukları açısından değerlendirilmesini öneriyoruz.

Anahtar sözcükler: dekstrokardi, kardiyak malformasyon, gebelik, genetik danışmanlık, prenatal tanı

Introduction

Human body is a harmony of symmetry and asymmetry. Symmetry is a normal finding for some of the organs like extremities while asymmetry is normal for the others like liver and spleen. Mechanisms organizing symmetry/ asymmetry are so complex and many genes have been identified and described so far (1).

Abnormalities of these complex mechanisms are responsible for some disorders. Situs solitus is the normal placement of all organs and in usual atrial arrangement (situs solitus), the aorta lies on the left of the spine and the inferior vena cava on the right, the opposite being the case in situs inversus (2). Situs ambiguous is an intermediate phenotype between situs inversus and situs solitus. Isomerism denotes duplication of left or right side completely or partially (3). Heterotaxy, a Greek word which means "other arrangement", is a term in use to describe all types of situs abnormalities. These abnormalities might occur in the family circle and different family members might have situs ambiguous or situs inversus or situs solitus (4).

Prevalence of situs inversus appears to be in a range between 1/8000- 1/25 000 (5).

Other than X-linked visceral heterotaxy (OMIM 306955) most familial cases are thought to be autosomal recessive.

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Digilio et al. (6) reported four cases with situs ambiguous of del (18p). On the other hand, organ discordance observed in situs ambiguous suggests that the pathways determining the left-right orientation of different organs are separable (1). Dextrocardia is the most frequent situs abnormality. The frequency of this disorder is 1/10 000 (7). Nearly 1-2% of cases with congenital cardiac malformation have dextrocardia (8). Dextrocardia may be isolated or a part of heterotaxy syndromes. 71.4% of dextrocardia cases also have other cardiac malformations. Dextrocardia was most commonly seen with situs inversus (39.2%) and it is followed by situs solitus (34.4%) and situs ambiguous [26.4% (right isomerism in 18.4% and left isomerism in 8.0%)] (9).

Case Report

A 20-year-old pregnant woman was referred to Obstetrics and Gynecology Department of Kahramanmaraş Sütçüimam University Hospital with a history of complex cardiac malformation detected in her first pregnancy. In spite of the fact that it had not had a dextrocardia on fetal echocardiography previously, there was no information about other situs abnormalities. There was consanguinity in parents.

Fetal echocardiographic evaluation at 23rd weeks of gestation displayed that cervical cystic hygroma, dextrocardia, interrupted inferior vena cava, bilateral superior vena cava, cetrallly placement of enlarged liver, abnormal localization of the aorta in the front of the pulmonary artery (Double outlet left ventricle), hypoplastic left ventricle, complete atrioventricular septal defect, coarctation of aorta and hyperechogenic bowel (Figures 1 and 2). Chromosome analysis performed by chordocentesis was normal (46, XX). As the cardiac malformations were lethal, pregnancy was terminated with the permission of the family. Autopsy confirmed echocardiographic findings. Apart from medially placed liver and dextra position of the heart, other organs in abdomen were in their normal localizations and there was only one spleen on normal location (Figure 3). The parents were normal and there were no situs abnormality. The diagnosis for the fetus was situs ambiguous.

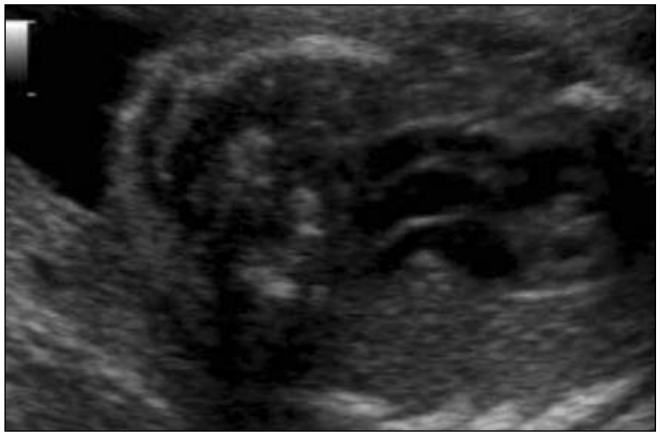

Figure 1. Aorta and pulmonary artery merges out from left ventricle.

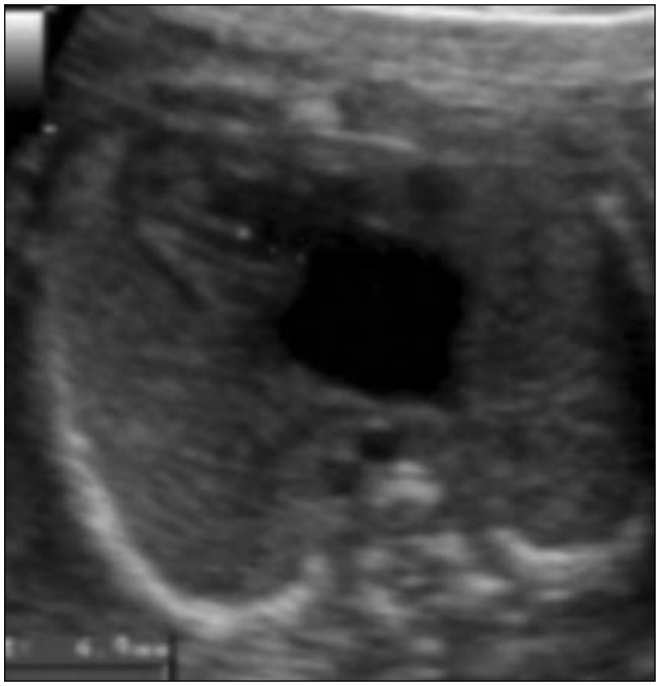

Figure 2. Transabdominal sonography (transvers section) showing the complete atrioventricular septal defect.

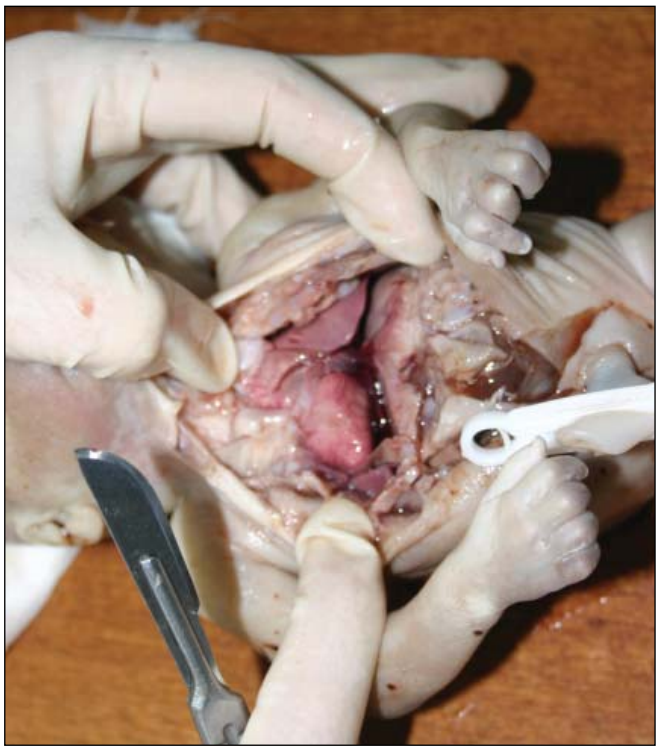

Figure 3. Autopsy of the cases showing medially placed liver and dextrocardia.

Discussion

Other structural malformations are not common in situs inversus but common with situs ambiguous. Especially, cardiac malformations and defects of great vessels, abnormalities of liver and biliary tract, and malrotation of bowel increased in

situs ambiguous cases. The patients in this group usually have either congenital asplenia or polysplenia (5).

Our case presented multiple cardiac malformations, dextrocardia and medially located liver with normally localized gall bladder. There was no spleen abnormality. Findings of previously reported cases suggest that isolated birth defects such as congenital heart disease, anal atresia, diaphragmatic hernia etc. may be caused by the genes that are involved in left-right axis determination tracts (10). Casey et al. (11) identified a family in which 4 individuals from 3 generations showed laterality defects. Two had situs inversus, while the others had asplenia, midline liver, and complex cardiac malformations (situs ambiguous). Two obligate gene carriers were anatomically normal (situs solitus). Male-to-male transmission confirmed autosomal inheritance.

Isolated heart malformations also occur among individuals with situs ambiguous; one might entertain the hypothesis that some cases of isolated heart malformations may be the result of abnormal laterality (12). Morelli et al. (13) reported situs abnormality families with the members just with congenital heart defect and cases with single asymmetric organ such as dextrocardia. Bamford et al. (10) reported cases with CRYPTIC gene mutation in cases that have only transposition in the great arteries, i.e., isolated congenital heart disease without any other sign of abnormal situs determination. Megarbane et al. (14) reported a family with ZIC3 mutation in which affected males have transposition of great vessels and midline anomalies but no obvious left right malformations. Furthermore, there is a male with mutation but anatomically normal in this family. There are other reports of such families presents both autosomal recessive and X-linked inheritance in the literature (Debrus et al. (15), Soltan and Li (16). Belmont et al. (17) also described the effects of these genes).

As there is consanguinity between healthy parents with two affected children, a boy and a girl, likelihood of autosomal recessive inheritance is present in this family. On the other hand consanguinity rate is so high in Turkey and association by chance is also possible.

There are numbers of syndromes reported both with dextrocardia and congenital heart malformations like Catel Manzke syndrome, Kartagener syndrome, Marden Walker syndrome etc. These syndromes also have other dysmorphic findings which are not present in our cases. Due to the fact that the case also had midline liver, we suggest that this case is an example of situs ambiguous.

This family is an interesting example of familial cases with congenital heart defects. One of the affected children did not have dextrocardia but complex congenital heart anomalies while the other affected child had dextrocardia together with congenital heart and great vessel abnormalities.

Nevertheless, this family points out the clinical variability of cases with heterotaxy and the necessity of the investigation of the genes that are involved in left-right axis determination pathways. This is also important during the counseling and evaluation of prenatally diagnosed cases. The most effective way of prenatal diagnosis of such cases is ultrasonography and echocardiography as the molecular studies is not enough to cover all cases with these syndromes.

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