A Case of Left Isomerism With Hydrops Fetalis: A Case Report

İncim Bezircioğlu1, Mine Tunakan2, Ali Baloglu1, Burcu Çetinkaya1, Merve Biçer1

1Izmir Atatürk Eğitim ve Araştırma Hastanesi, 1. Kadın Hastalıkları ve Doğum Kliniği, İzmir
2Izmir Atatürk Eğitim ve Araştırma Hastanesi, Patoloji Kliniği, İzmir

Abstract

Objective: The purpose of this study is to emphasize that heterotaxy syndrome should be kept in mind in any case with hydrops fetalis.

Case: Ultrasound findings were skin edema, hypoplastic thotax, pericardial effusion, ascites. Fetal biometry was consistent with 16 weeks of gestational age. There was fetal bradicardia with 80 beats per minute. There was no Rh alloimmnization and diabetes mellitus. Parvovirus B19 was negative for IgM.

Conclusion: Heterotaxy syndrome is a complex condition usually associated with significant cardiovascular disorders. There was a few published data on fetal heterotaxy syndrome presenting the spectrum of cardiovascular disturbances, the accuracy of prenatal diagnosis, and neonatal outcome.

Keywords: Left isomerism, hydrops foetalis, heterotaxy, polisplenia.

Introduction

Hydrops fetalis is a condition characterized by excess accumulation of fluid at extravascular compartments in fetal body and tissue edema of the fetus. Mortality rate depends on underlying cause. It may be formed by immune (Immune Hydrops Fetalis, IHF; %12,7) and non immune (Non-immune Hydrops Fetalis, NIHF; %87,3) causes. The main five cases of NIHF are cardiovascular, chromosomal, thorasic, twin to twin transfusion syndrome (TTTS) and anemia.1 Most parts of the human body are symmetric according to the sagittal plane. Asymmetric organs begin developing as midline structures and than lateralize their position in later stages.
The usual positioning of these organs are ‘situs solitus’ and a mirror-image reversal of this arrangement is ‘situs inversus’. Situs ambiguous (Heterotaxy syndrome) results from left-right asymmetry failure of the developing embryo and occurs in 1.44 in each 10000 live births. At heterotaxy syndromes, typical manifestations include abnormal symmetries and malpositions of the thoraco-abdominal organs and vessels. Two groups of anomalies are determined: Right isomerism and left isomerism. Right isomerism (Ivemark Syndrome, asplenia, bilateral right sidedness) is characterized by bilaterally trilobed lungs, bilaterally eparterial bronchi, an absent spleen, a midline liver, right or left sided stomach and gallbladder, complete atrioventricular septal defect, juxta positioning of aorta and vena cava, cono-truncal cardiac anomalies. Left isomerism (polisplenia, bilateral left sidedness) is characterized by bilaterally bilobed lungs, bilaterally hyparterial bronchi, symmetrical liver, multiple splenules, right or left sided stomach, malrotation of the bowels, atrial septal defect, ventricular septal defect, bilaterally superior vena cava, interruption of the inferior vena cava with azygos continuation, and heart blocks. However thoracic and abdominal organs can take part of these pathologies at different degrees. Cardiac anomalies are reported in 99% of right isomerism and 90% of left isomerism cases. Isomerism cases form about 1% of congenital heart defects. Heterotaxy syndrome is a complicated anomaly group associated with important cardiovascular pathologies. There are few studies about prenatal diagnosis and neonatal prognosis of the spectrum of the cardiovascular pathologies in fetal heterotaxy syndromes. In this study, it is purposed to emphasize keeping in mind of heterotaxy syndrome in antenatal diagnosis of fetal hydrops.

**Case**

The case who was 20 years old and 18th week’s pregnant (gravida 1-para 0) with diagnosis of fetal hydrops was hospitalized in our clinic. In family history, there wasn’t any baby with anomalies or marriage with a relative. There was no exposure to teratogen drugs and chemical agents during pregnancy. In ultrasonographic evaluation, edema in fetal subcutaneous tissue, ascites, hypoplasia in thorax, and pericardial effusion were determined (Figure 1). Fetal biometric measurements were consistent of 16 weeks gestation. Fetal bradicardy was determined. Fetal heart rate was 80 beats/minute. Rh isoimmunisation and diabetes weren’t found. Parvovirus B16 IgM antibody was negative. The case was presented at the council of perinatolgy and making amniocentesis and termination of the pregnancy were advised to the family. Pregnancy was terminated after amniocentesis by family consent at 18th weeks of gestation. Karyotype was normal (46,XY) as a result of genetic amniocentesis. A 200 grams, 19 centimeters, hydropic, non viable, male fetus was delivered (Figure 2). Autopsy findings included hypoplastic lungs, bilaterally bilobed, with bilaterally hyparterial bronchi. Levocardia was established. The examination of the heart revealed that the atrial situs showed left isomerism, both atria and ventricules were equal sized, foramen ovale was closed at atrial septa, ventricular septal defect and atrioventricular valves were normal, atrioventricular connection was concordant. Abdominal wall was

**Figure 1.** Ultrasonographic appearance.
overstretched by ascites. Symmetrical liver, three splenula in right side, malrotation of the bowel were found when abdomen was opened. (Figure 3, 4) Parents were evaluated for isomerism after the autopsy of the baby. Echocardiograms were normal in both parents. Polysplenia at the left side of abdomen was found in mothers’ abdominal ultrasonography.

Discussion

The case we presented showed almost whole findings of left isomerism including bilaterally bilobed lungs, hyparterial bronchi, bilaterally morphologic left atrial appendages, symmetrical liver, polysplenia, and malrotated bowel. 0.4 to 2% of the infants born with congenital heart disease were diagnosed as left or right isomerism. 6% of these cases could be diagnosed antenatally. Various chromosomal abnormalities were reported at situs inversus and ambiguous cases. Chromosomal rearrangements may lead repetition or over expression and loss of some genes. Established chromosomal abnormalities were various and spontaneous. Experimental studies established some locuses determining laterality, but more studies are required in this field. Amniocentesis is not proposed according to current knowledge. In our case, amniocentesis was performed for fetal anomalies and normal fetal karyotype was established. CRYPTIC gene and Hensen node regions were established for laterality determination. It is emphasized that teratogene exposure during 30 to 32nd days of pregnancy when formation of spleen, atrioventricular canal and conotruncal separation are seen in these gene regions may cause mutation. The most accused environmental factors are diabetes mellitus and retinoic acid exposure. There weren’t any exposure to teratogens and diabetes mellitus in our patient. Isomerism cases are usually seen sporadically. Because of recurrence in some families, mendelian patterns and genetic mechanisms responsible for laterality determination has been investigated. Autosomal recessive and X-linked recessive inheritance patterns have
been suggested. The case presented was thought not to be sporadically because of maternal polisplenia. Characteristics of heterotaxy syndromes are described postnatally. The diagnosis of atrial appendages, lobulation of lungs, and branching of bronchi are difficult by ultrasonography. Spleen could be discriminated after 20 weeks of gestation. Stomach, gallbladder and spleen could be added to the picture at various degrees. Determination of viscerocardiac situs can provide the prenatal diagnosis of heterotaxy syndromes, but it is not a mandatory finding. However cardiovascular findings compose more important clues for diagnosis of heterotaxy syndromes. For this reason, only fetal echocardiography centers have series on antenatal diagnosis of heterotaxy syndromes. High risk cases with suspected cardiac anomalies apply these centers.

The most frequently encountered cardiac pathologies at left isomerism cases are bilaterally superior vena cava, interruption of the inferior vena cava with azygos continuation, complete atrioventricular defect, common atrium, ventricular septal defect, partial anomalous connection pulmonary veins, and complete heart block. More serious cardiac defects impairing ventriculoatrial relationship are seen at right isomerism including complete atrioventricular septal defect, total anomalous connection pulmonary veins, and transposition of the great arteries, double outlet right ventricle. Interruption of continuation of vena cava inferior is an important marker for left isomerism. This marker is reported 55 to 85% of cases in postmortem series. Berg C et al reported that left isomerism could be diagnosed when there are at least two of criteria for left isomerism. These criteria are 1) Complete atrioventricular septal defect 2) Interruption of the inferior vena cava with azygos continuation 3) Early fetal heart block 4) Visscerocardiac heterotaxy. There are fetal bradicardia and visserocardiac heterotaxy in the presented case. It is not possible to interprete cardiac findings because of absence of fetal echocardiography. Vissserocardiac situs anomaly in the case couldn't be determinated by prenatal ultrasonography. Heart block may result from immaturity of conduction system, absence of connection to atrioventricular node or abnormal positioning of atrioventricular node. Above half of the complete atrioventricular block cases are together with structural anomalies as isomerism or atrioventricular discordance. Complete atrioventricular block may lead to diminished cardiac flow and congestive heart failure because of important bradicardia. In left isomerism, there is an abnormal development between the atrioventricular node and ventricular conduction tissues resulting in complete heart block. Berg et al reported that fetal heart block in fetal echocardiogram could be detected after 14 weeks' gestation in 13% of isomerism series. Bartram et al reported that complete heart block was found in about 22% of survived left isomerism cases. Heart block in left isomerism cases is described as a poor prognostic factor. The structural heart defects together with the low ventricular rate lead to congestive heart failure and hydrops fetalis develops. Berg et al stated that hydrops fetalis developed at 18 of 24 fetuses with heart block. In these cases complete heart block is the most important reason of hydrops fetalis and intrauterine fetal demise. Left heart failure, regurgitation of tricuspid valve, hypoplastic left heart, and supraventricular tachycardia are seen in isolated closed foramen ovale cases depending on obstructive defect. Fetal hydrops secondary to supraventricular tachycardia develops in these cases. Even though foramen ovale was closed in our case, there was no difference in ventricular size. It was thought that ventricular septal defect made right heart drainage.

Furthermore when fetal bradicardia was considered, it was accepted that the reason of fetal hydrops was not closed foramen ovale, but heart block. Left isomerism cases can be detected at early stages of pregnancy because of nuchal translucency, hydrops fetalis and fetal disrythm. Right isomerism cases could be detected later. Berg et al reported in their series that they could diagnose all of the right iso-
merism cases after 20 weeks of pregnancy. Left isomerism cases are mostly diagnosed antenatally, whereas right isomerism cases mostly diagnosed postnatally. This finding may be related to higher rate of intrauterine demise and termination of pregnancies after early intrauterine diagnosis of left isomerism cases. Because ventriculoatrial connection is normal left isomerism cases usually have a better prognosis at postnatal period. In isomerism cases, cardiac defects determine perinatal mortality and morbidity, visceral anomalies also affect postnatal long term prognosis. The prognosis is better and intrauterine demise is rare both of isomerism forms in the absence of heart block and hydrops fetalis. Lim et al performed cardiac correction surgery at 166 cases and analyzed 86 of them with antenatal diagnosis and suggested that overall prognosis wasn’t affected by antenatal or postnatal diagnosis. Finally, left isomerism is rare syndrome, which could be diagnosed by carefully done prenatal ultrasonography. Fetal heart block and hydrops development contribute to early diagnosis of left isomerism. Vissero-cardiac situs should also be evaluated, while the investigation of cardiac anomalies in non-immune hydrops fetalis cases. Heterotaxy syndromes should be remembered when cardiac anomalies and abnormal visseral situs are established.

**Conclusion**

Heterotaxy syndrome is a complex condition usually associated with significant cardiovascular disorders. There was a few published data on fetal heterotaxy syndrome presenting the spectrum of cardiovascular disturbances, the accuracy of prenatal diagnosis, and neonatal outcome.

**References**