Rare association of hypoplastic left heart syndrome(HLHS) with partial monosomy X (Turner syndrome) and partial trisomy 14 (14q11.2 microduplication syndrome) in the neonate.

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Abstract

Hypoplastic left heart syndrome is a fatal congenital complex heart defect where the left side of the heart is critically undeveloped. HLHS with complex partial monosomy and partial trisomy are rare conditions that have not reported to occur together.

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1 Key message

Hypoplastic left heart syndrome (HLHS) is a fatal congenital complex heart defect where the left side of the heart is critically undeveloped.

HLHS with complex partial monosomy and partial trisomy are rare conditions that have not reported to occur together.

Keywords

Hypoplastic left heart syndrome, congenital heart disease, translocation, chromosome, Turner syndrome, 14q11.2 microduplication syndrome.

2.Case presentation

A term, no dysmorphic baby girl, was a product of consanguineous marriage born to a 29-year-old primigravida mother by spontaneous vaginal delivery. At 30 weeks of gestational age, fetal echocardiography revealed the presence of hypoplastic left heart, atrial septal defect, and patent ductus arteriosus. Amniocentesis requested at 32 weeks of gestational age, and chromosomal microarray analysis (CMA) sent and revealed partial monosomy and partial trisomy. An approximately 63 Mb large pathogenic one copy loss (heterozygous deletion) encompassing the entire small arm of the chromosome X (Xp) and extending to the long arm of chromosome X (Xq), X p22.33q11.2 as well as an approximately 50 Mb large pathogenic one copy gain (duplication) of the chromosomal region 14q11.2q 24.2 were detected.

These findings are suggestive of a chromosome translocation involving the chromosomes X and 14.

There was no family history of similar conditions and no history of radiation exposure or drug intake in any trimester.

The baby cried immediately after birth and required only the initial steps of resuscitation.

Apgar scores were 8, 8, and 9 on the 1st, 5th, and 10 minutes. Birth weight was 2270 gram (below 5th percentile), length of 48cm (25^{th} centile), and head circumference of 32 cm (below 5^{th} percentile). No apparent dysmorphic features.

Clinical examination revealed mild tachypnea (respiratory rate 65 per minute), tachycardia (heart rate 170 per minute), blood pressure (62/40 mmHg), and oxygen saturation of 90% on room air.

Arterial umbilical blood gases showed pH-7.3, PaCO2 47 mmHg, and BE-2.

She had vesicular breath sounds with fine basal crepitations and equal chest expansion. The first and second heart sounds auscultated with normal intensity. Systolic murmur grade 3/6 maximal intensity at the lower sternal edge heard.

An echocardiogram 2 hours after the birth confirmed HLHS with the hypoplastic left ventricle, mitral atresia, aortic atresia, and moderate tricuspid regurgitation (Figures 1, 2 and 3).

Continuous intravenous infusions of prostaglandin E1 started. Physical examination of other systems on admission was normal with stable hemodynamic values.

Laboratory blood tests showed normal ranges of white blood cells, hemoglobin, and platelets counts.

The patient further investigated with an abdomen ultrasound and magnetic resonance imaging of the brain, which were unremarkable.

A diagnosis of hypoplastic left heart syndrome and complex partial monosomy and partial trisomy made.

The infant's poor prognosis explained to the family who refused further intervention, and comfort care management was applied.

The patient died on day 7 of life.

3 Discussion .

HLHS is a congenital heart defect constituting 2% to 9% of all congenital heart diseases[1].

This cardiac malformation includes varying degrees of the left ventricle's underdevelopment, hypoplasia of the aorta, aortic valve, and mitral valve stenosis or atresia[2]. It is more common in males than in females[3]. The mortality rate is high, and accounts for 23% of neonatal deaths from congenital heart malformations[2,4].

The etiology of HLHS is multifactorial and includes maternal, infectious, immunosuppressive, and genetic factors[5]. Most of the cases with HLHS occur sporadically with no family history; however, some occur with autosomal recessive or autosomal dominant inheritance[6,7].

HLHS can be detected by prenatal ultrasonography between 18 and 22 weeks of gestation.

The management options of HLHS include comfort care, palliative surgery, and cardiac transplantation. Even with surgical intervention, life expectancy may be affected[8].

It is generally known that HLHS may have a genetic predisposition, but no specific gene has been identified until now[9].

Some reports have concluded that HLHS is genetically multigenic and heterogeneous in etiology[10].

Also, several genetic disorders like Holt-Oram, Noonan syndrome, trisomy 21, trisomy 13, trisomy 18, and Turner syndrome may coexist with HLHS[3,11].

The association of the hypoplastic left heart syndrome with Turner syndrome reported being 13.2 %[12], however, only 2.5% of HLHS cases presented with Turner syndrome[13].

The presence of chromosomal and other noncardiac abnormalities influence the mortality rate in neonates with HLHS.

Interestingly, it was observed both a strong association of the HLHS with Turner syndrome and a significant mortality rate in this group of neonates[13,14].

The association of Turner syndrome with HLHS is well known; however, isolated 14q11.2 microduplication syndrome was not described with HLHS.

14q11.2 microduplication syndrome is a rare chromosomal condition characterized by hypotonia, mental retardation, developmental delay, epilepsy, and dysmorphic craniofacial features like micrognathia, short nose, abnormally rotated ears, broad nasal bridge, and narrow upper lip[15].

Cranio-facial dysmorphic features were not so distinctive in the presented case that underscores the need for a genetic investigation in all cases with HLHS, even in non-dysmorphic neonates.

Ertürk et al. described the case of 14q11.2 microduplication with West syndrome (infantile spasms, hypsarrhythmia, and intellectual disability)[16]. Other manifestations of 14q11.2 microduplication including microcephaly, behavior disturbance, obesity, and speech delay[17].

Depending on the size of the duplication, clinical manifestations and degree of mental retardation may vary from case to case. The size of duplication varies from small size (e.g., 35KB) to large size (e.g., 50MB).

The presence of deletion and duplication in the reported case indicates these abnormalities may result from a balanced translocation in one of the parents, and we sent chromosomal analysis for parents to prove it.

Remarkably, a combination of Turner syndrome (partial monosomy X), 14q11.2 microduplication syndrome (partial trisomy 14), and HLHS to date unreported to the best of our knowledge.

4 Conclusion

We described the first case of HLHS reported in the literature to date, which carries a combination of microduplication of the chromosomal region 14q11.2q 24.2 and chromosome translocation involving the chromosomes X and 14.

Reported case suggested that HLHS may appear in a modular style, through the multiple mutations.

Timely provided prenatal ultrasonography and prompt genetic investigation for each case of HLHS may reveal the natural origin of this complex congenital heart disease that is essential for determining the optimal decision-interventions options for physicians and parents.

Conflict of interest

None declared

Informed consent was obtained from parents for reporting this case.

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Author Contribution

Roya Arif Huseynova wrote the clinical report, collected and analyzed the data.

Oqtay Ilham Huseynov participated in the drafting and critically revising the manuscript.

Latifa A Bin Mahmoud participated in the drafting and critically revising the manuscript.

Abduljabbar Alshenqiti participated in the critically revising the manuscript.

Khalid A. AlOmran in the drafting the manuscript.

Nabeel Abduallah Alodaidan in the drafting the manuscript

All authors approved the manuscript as submitted.

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Figure Legends:

(Figure 1) Long axis view shows severe hypoplastic left ventricle, aortic arch, aortic atresia and mitral atresia.

(Figure 2) 4 chambers view shows severe hypoplastic left ventricle, mitral atresia and dilated right ventricle.

(Figure 3) Short axis view shows dilated main pulmonary artery with large patent ductus arteriosus.