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CASE REPORT

POTENTIAL AND PITFALLS OF FIRST-TRIMESTER SCREENING IN DETECTING CONGENITAL HEARTS DEFECTS – A CASE REPORT

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Abstract

Introduction. Early fetal morphology screening by ultrasound markers can be challenging in early diagnosis of congenital heart disease. Technical limitations of fetal echocardiography in the first trimester must be borne in mind, and follow-up at mid-gestational echocardiography is prudent in some high risk patients, like fetuses with increased nuchal translucency.
Case presentation. The author presents a case report of HLSL in fetus with increased nuchal translucency, normal tricuspid and ductus venosus flow on early fetal morphology scan, with resolution of NT thickness and diagnosed hypoplastic left heart syndrome later in the second trimester.
Conclusions. The presented case highlights the need to improve screening for heart anomalies by extending the first trimester cardiac examination beyond the assessment of heart rate and position. Early prenatal detection by "soft markers" such as nuchal translucency thickness gives the possibility for planning early fetal echocardiography, genetic analysis, and adequate perinatal management.

Résumé

Potentiel et pièges du dépistage du premier trimestre dans la détection des malformations cardiaques congénitale – rapport de cas

Potentiel et limites du dépistage du premier trimestre dans la détection des malformations cardiaques congénitales – rapport de cas d'un ECG chez un fœtus avec le syndrome d'hypoplasie du cœur gauche (SHCG) , une clarté nucale augmentée, un flux tricuspidien et ductus venosus normal.
Introduction. Le dépistage morphologique fœtal précoce à l'aide de marqueurs échographiques peut être difficile pour le diagnostic précoce des cardiopathies congénitales. Il faut garder à l'esprit les limitations techniques de l'échocardiographie fœtale au premier trimestre, et un suivi échocardiographique à mi-grossesse est raisonnable chez certaines patientes à haut risque, telles que les fœtus présentant une clarté nucale accrue.
Présentation du cas. L'auteur présente un rapport de cas d'HLSL chez un fœtus avec une clarté nucale <<augmentée>>, un flux tricuspidien et un flux du ductus venosus normaux lors du scan morphologique

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Keywords: congenital heart disease, HLSL, nuchal translucency, ductus venosus, first trimester screening.

List of abbreviations:
HLSL – hypoplastic left heart syndrome
CHDs – congenital heart diseases
NT – nuchal translucency
BMI – body mass index
DV – ductus venosus
U.S. – United States
NIPT – non-invasive prenatal test
2D – two dimensional

fœtal précoce, avec résolution de l'épaisseur de la clarté nucale et un diagnostic de syndrome d'hypoplasie du cœur gauche posé plus tard au cours du deuxième trimestre.

Conclusions. Le cas présenté souligne la nécessité d'améliorer le dépistage des anomalies cardiaques en étendant l'examen cardiaque du premier trimestre au-delà de l'évaluation de la fréquence et de la position cardiaques. La détection prénatale précoce par des <<marqueurs mous>> tels que l'épaisseur de la clarté nucale permet de planifier une échocardiographie fœtale précoce, une analyse génétique et une gestion périnatale adéquate.

Mots-clés: cardiopathie congénitale, HLSL, clarté nucale, canal veineux, dépistage au premier trimestre

Introduction

Congenital heart defects (CHDs) account for one-third of congenital anomalies and are the leading cause of death from congenital diseases. CHDs occur in 0.8–1% of term births and in 8.3% of prematurely born children. Abnormalities of the cardiovascular system are 6.5 times more common than chromosomal[1] abnormalities and 4 times more common than neural tube defects. Hypoplastic left heart syndrome (HLSL) is a form of severe congenital heart disease characterized by underdevelopment of the left-sided heart structures. It accounts for around 4% of cases of CHDs, but is responsible for 15–25% of the associated deaths. Depending on the time of diagnosis, presence of accompanying anomalies, and available treatment options in the region, three main variants of approach are possible: postpartum surgical correction, intrauterine intervention, termination of pregnancy for medical reasons, or heart transplantation. Cardiac examination became a routine part of the fetal anatomical assessment in the mid-trimester over 20 years ago. Due to the small size, fast fetal movements and complexity of the heart, prenatal diagnosis of CHDs is most often made in the second trimester of pregnancy. The association between cardiac anomalies and first trimester screening markers, as increased nuchal translucency, tricuspid regurgitation, and abnormal ductus venosus flow, has been widely envestigated during the last years[2-4].

This article presents a case of missdiagnosed hypoplastic left heart syndrome in high-risk pregnancy, with increased nuchal translucency (NT), normal ductus venosus and tricuspid valve flow. The importance of first trimester screening is discussed as an advantage regarding the timing of further investigations, prenatal counseling, and access to management options in pregnancies with CHDs.

Case presentation

It is a case of a 28-year-old secundigravida who came for a routine first trimester screening with spontaneous pregnancy and a history of previous normal delivery of a healthy term newborn six years before. There was no history of accompanying diseases or previous surgeries. The initial sonographic evaluation revealed a single, live fetus, with a crown-rump length of 48.2 mm (11 weeks 4 days). The ultrasound examination showed increased NT of 5.2 mm, with visible hypoplastic nasal bone (Fig. 1, 2). There was no evidence of tricuspid regurgitation, and ductus venosus flow was normal. The cardiac assessment was difficult and insufficient because of retroverted uterus and inappropriate fetal position, with no suspected abnormalies during the examination.

The patient was adviced for non-invasive prenatal testing (NIPT), with suspiction for Down syndrome, which showed normal result. The follow up examination after 2 weeks showed resolution of nuchal translucency with measurable distance 1.5 mm. Targeted ultrasound examination scan at 20 weeks and fetal echocardiography at 22 weeks of gestation were planned.

The fetal morphology assessment found a single live male fetus with normal fetal growth at 20 gestational weeks. The cardiac screening showed left and right ventricular discordance at a four-chamber view of the heart (Fig. 3), without the presence of accompanying extracardiac anomalies.

The patient was referred for a cardiological consultation. The following sonographic findings were documented: a small, thick-walled, hyperechoic left



Fig. 1. 2D ultrasound image, sagital view of the fetus with measurement of increased nuchal translucency (NT) of 5.2 mm (red arrows)



Fig. 2. 2D ultrasound image, axial view of the fetus with measurement of increased nuchal translucency (NT) (red arrows)

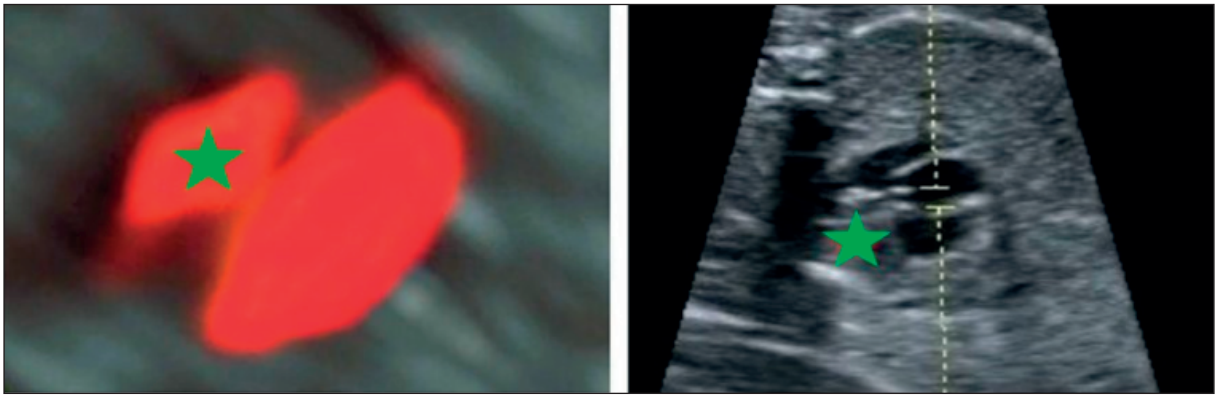


Fig. 3. Four-chamber view of the heart. Hypoplastic left ventricle on power Doppler (right image, *green star) and on color doppler (left image – green star)

ventricle (Fig. 3) with 4 mm anterior mitral leaflet, enlarged right ventricle with increased excursion of tricuspid valve, absence of antegrade flow through the aortic valve with poor motion, ascending aorta hypoplasia. A congenital heart malformation was diagnosed, with hypoplasia of all segments on the left heart—the mitral valve, left ventricle, and aorta hypoplasia. The options for surgical correction after delivery, the expected average life expectancy, and the lack of definitive treatment were explained to the family. Amniocentesis, to rule out concomitant chromosomal abnormalities, was refused, with a subsequent request to terminate the pregnancy on medical grounds due to the impossibility of a definitive surgical correction.

Discussion

The majority of CHDs can be suspected by first trimester screening in high-risk groups, such as fetuses with increased nuchal translucency. A detailed cardiac assessment requires specialized scanning, performed by an expert sonographer and usually reserved to tertiary referral centers. The examination must be adapted in accordance with the stage of pregnancy and requires adequate training and experience[4]. This may be particularly relevant in challenging technical conditions such as a retroverted uterus, suboptimal fetal position, or increased maternal body mass index. The overall success rate at obtaining correct cardiac views in the first trimester increases progressively with advancing gestational age and is the highest after 13 weeks[2]. Only apical four-chamber view of the heart in 11-13 weeks can achieve up to 30% of congenital heart diseases, like HLSL, but in some cases, such as the presented case, an appropriate image is not possible. This is the reason why the challenges of an early diagnosis of CHDs is still debatable and researchers try to increase the suspiction and reduce the false-negative rates of first trimester screening.

More frequently, HLHS is diagnosed with fetal morphology scan at 18–23 gestational weeks by visualization of an abnormal four-chamber image of the heart:

1. With evidence of ventricular size discordance, concomitant aortic stenosis, and/or coarctation of the aorta.
2. Left outflow tract and aortic arch with abnormal image and arcus size < 5mm, hypoplastic or atretic aortic valve.
3. Left ventricular size tends to decrease as pregnancy progresses, while the right ventricle and right atrium tend to dilate due to increased volume loading.

Several pathologies can remain undetectable in the first trimester and it is therefore important to inform patients of the limitations of an early examination and highlight the importance of subsequent anatomical ultrasound assessment[3]. However, there are some markers that put the pregnancy in high-risk group for congenital and chromosomal anomalies. Syngelaki et al. studied 44,859 singleton pregnancies, 85 of which were diagnosed with CHD, and found the presence of increased nuchal translucency (NT) in 35.3% of cases. NT was tickened in 64.3% of all 28 fetuses diagnosed with cardiac abnormalities at 11–13 weeks, compared with 15.4% of the remaining 57 cases of CHD diagnosed in the second trimester or after delivery[5]. The risk of cardiac defects is six-fold higher in case of a NT above the 99th percentile, one of the strongest indirect markers of CHDs in the first trimester[6].

Abnormal blood flow through the ductus venosus (DV) in the first trimester is an independent predictor of CHD and is an indication for early fetal echocardiography. In 2019, an analysis of 6,120 pregnancies in 11–13+6 weeks reported an 11% increased rate of early detection of heart structural defects when examining DV compared to detection based on NT thickness alone. Pathological blood flow through DV has been found to occur more frequently in cases in whom CHD manifests with other sonographic findings, such as fetal hydrops. The absence of DV is associated with HLSL, ventricular, and atrial septal defects[7,8]. Analysis of data from first-trimester aneuploidy screening of 53,349 pregnancies in 2021 found that on early fetal echocardiography, 37.7% of CHDs were diagnosed at 11–13 weeks, more than 50% of which were major heart defects. The authors confirm that the most important factor in improving the sensitivity of first-trimester ultrasound screening is the use of a standardized scanning protocol[9]. Unfortunately, in our case ductus venosus blood flow was normal, wich reduced the suspiction for congenital heart abnormality.

Khalil and Nicolaides reported 45% identification of CHDs at 11 weeks versus 90% at 13 weeks, and that the detection rate for four-chamber cardiac view was only 20% at 11 weeks and 92% at 13 weeks[10].

Sonographers' experience and time allowed for a heart examination are among the most important factors that influence the ability to appropriately assess cardiac structures in the first trimester[11]. Botelli et al. identified human error as the primary cause of false negative diagnoses. The frequency of successful examinations grows with the number of scans performed and a learning curve of 180 ultrasound appears necessary to appropriately visualize the heart in most cases[12].

HLHS is a term describing a spectrum of abnormalities of the left half of the heart, with varying degrees of hypoplasia of the mitral valve, left ventricle, aortic valve, ascending aorta, and aortic arch. It occurs in 1 in 10,000 live births and causes 22% of mortality in the first year of life[13]. The risk of a recurrence of HLSL is 4%[14].

The frequency of HLSL is 9% of CHDs, with concomitant chromosomal abnormalities (monosomy X, trisomy 12, 18, 21, DiGeorge syndrome, Jacobsen syndrome) observed in 5% and extracardiac defects in 10–25% (holoprosencephaly, agenesis of the corpus callosum, diaphragmatic hernia, omphalocele)[10]. HLSL is a ductus-dependent lesion. Physiological shunting of the small circle of blood circulation through the foramen ovale and ductus arteriosus compensates for hypoplasia of the left ventricle during fetal life. Undiagnosed prenatally, HLHS often presents with clinical signs of low cardiac output and compromised systemic perfusion when the ductus arteriosus begins to close. In addition, a restrictive foramen ovale accompanied by HLHS will require surgical intervention in utero or immediately after birth[15].

The 30-day postoperative survival after surgical reconstruction exceeds 90%, and the 5-year survival rate ranges between 18.8% and 72%. In 2021, an analysis of data from 343 cases of children born with left-sided heart hypoplasia syndrome in England found 68% survival to age 5 years and 32.6% survival to age 15 years, due to improvements in surgical techniques for correction and the improvement of intensive care facilities[16]. The success rate after surgical correction varies between countries and regions, which is reflected in the frequency of medically terminated pregnancies, from 20% in the U.S. to 70% in European countries[17]. Heart transplantation is the only option for definitive treatment, especially in neonates who are at high risk for postnatal reconstruction or develop Fontan circulatory complications. Intrauterine fetal intervention, such as balloon atrial septostomy and stenting or balloon dilatation of the aortic valve, may also be necessary in severe cases of HLHS[18,19]. In Bulgaria, newborns with HLSL are stil in poor prognostic cathegory, with really shortened survival rate, so frequently the preffered family option

is termination of pregnancy. This poses the need for increase the knowlegde of potentials and pitfalls of first trimester screening and detection of CHDs, also in cases with increased NT in euploid fetuses.

Conclusions

The diagnosis of critical CHDs is possible as early as the first trimester morphology scan between 11 and 13+6 gestational weeks. NT thickness and the blood flow in DV increase the diagnostic suspicion, but the absence of abnormalities does not rule out the diagnosis. First trimester cardiac assesment can be challenging in some patients, but in high risk pregnancies like in fetuses with increased NT, a detailed cardiac examination should be planned earlier by a trained sonographer. Early detection of HLSL allows for fetal karyotyping and genetic counseling, evaluation of accompanying extracardiac anomalies, and planning the follow-up, delivery, and postoperative surgery as needed. It enables families to make informed decisions and allows, if desired, timely termination of pregnancy, which is safer for mother and has fewer psychological consequences.

Author Contributions:

S.A. was responsible for the diagnostic procedures, clinical diagnosis, and treatment decisions. S.A. wrote the manuscript. The author has read and agreed to the published version of the manuscript.

Compliance with Ethics Requirements:

"The author has no conflict of interest relevant to this article"

"The author declares that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008, as well as the national law. Informed consent was obtained from the patient included in the study"

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