

Original Article

Analysis of cystic hygroma diagnosed in the first trimester: single-center experience

Yakıştıran et al. Analysis of cystic hygroma

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DOI: 10.4274/jtgga.galenos.2019.2019.0032

Received: 20 February, 2019

Accepted: 10 July, 2019

Abstract

Objective: To evaluate the obstetric outcomes of fetuses with cystic hygroma other than karyotype abnormalities and structural malformations.

Material and Methods: We conducted a retrospective study based on the review of medical records of pregnant women in whom ultrasonographic diagnosis of fetal cystic hygroma was established in the first trimester from January 2014 to October 2018. All patients were offered genetic counselling and prenatal invasive diagnostic procedures to obtain fetal karyotype. For ongoing pregnancies fetal echocardiography and detailed second trimester sonographic anomaly screening was performed by a perinatologist/pediatric cardiologist. Demographic characteristics of the women and results of the karyotype analysis were obtained from the database of our hospital and correlated with the obstetric outcome.

Results: Within five-year period, there were 106 cases of fetal cystic hygroma. Of those, fetal cardiac malformations were detected in 4 and micrognathia in one. 85 women underwent fetal invasive procedures and in 52 of the cases, karyotype abnormalities were detected. Fetal outcomes of 33 cases with normal karyotype and 21 cases in whom karyotyping analysis were not performed due to patient refusal were enrolled into the study. Obstetric outcomes of 21 women who refused karyotyping consisted of 13 livebirths, 7 missed abortions and one fetal death, whereas those of 33 women with normal karyotype were; 12 livebirths, 12 missed abortions, 2 hydrops fetalis and 5 fetal deaths. 19 of 33 fetuses with normal karyotype and 8 of 21 fetuses in whom karyotyping were not performed were terminated.

Conclusion: The presence of cystic hygroma carries a high risk for fetal karyotype abnormalities and cardiac malformations. Postnatal outcomes of the fetuses with cystic hygroma appeared to be correlated with the absence of structural malformations and karyotype abnormalities.

Key words: cystic hygroma, perinatal outcomes, prenatal diagnosis

Introduction

Cystic hygroma is a congenital malformation characterized by the presence of abnormal fluid collection at sites of lymphatic-venous collection within neck, mediastinum, abdomen, and axillary region (1). It is also defined as a subgroup of lymphangiomas with the cystic variety, filled with protein-rich fluid (2). Cystic hygroma is classified as septated and non-septated. The overall incidence of cystic hygroma is approximately 1/1000-6000 births and 1/750 spontaneous abortions (3).

Cystic hygromas of nuchal origin are reported to be associated with fetal aneuploidy and structural anomalies in 50-80% of cases (1). Association with aneuploidy and/or fetal structural abnormalities worsens the prognosis. This condition can be diagnosed with sonography during fetal nuchal translucency measurement in the mid-sagittal plane in the first or early second trimester. When a cystic hygroma is diagnosed, the fetus should have a thorough anatomic scanning for other system anomalies. In the next step, the parents should be offered invasive procedures for fetal karyotype analyses in order to detect any chromosomal abnormality (4). If they accept karyotype analyses, chorion villus sampling (CVS) or amniocentesis should be performed by a perinatologist.

Previous studies have reported poorer perinatal outcomes in pregnancies with fetal cystic hygroma and associated aneuploidy (5,6). We carried out this retrospective study to evaluate the pregnancy outcomes of fetuses with cystic hygroma either with normal karyotype or with no karyotype analysis in the prenatal period.

Methods

A retrospective cohort based on the review of medical records of patients with fetal cystic hygroma, diagnosed and/or referred to our hospital, between January 2014 and October 2018 was carried out. All scans were performed with a Voluson™ 730 Pro (GE Healthcare, USA) multifrequency convex transducer at 2.0-7.0 MHz. Cystic hygroma was defined as an enlarged sonolucency with clearly visible septations extending along the fetal body axis, in contrast to nuchal translucency, which was described as a non-septated sonolucent area confined to the fetal neck. They were differentiated from nuchal edema by the presence of the nuchal ligament. Upon diagnosis of cystic hygroma, all patients were provided genetic counselling. Prenatal invasive diagnostic procedures were offered for fetal karyotyping. A complete fetal anomaly scanning was then performed for the detection of other associated structural anomalies. Women who wanted to continue their pregnancies with cystic hygroma with normal karyotype and undetermined karyotype/ due to the fact that parents did not accept the invasive procedures were enrolled into the study. For those women, fetal echocardiography and second trimester detailed sonographic evaluation were performed by a perinatologist.

Demographic characteristics of the patients, results of the fetal karyotypes were recorded from electronic database of the hospital. Pregnancy outcomes were tabulated from electronic records of the hospitals and for women who did not deliver at our hospitals telephone interviews for the pregnancy outcome were made. Moreover, physical examination findings of the infants were also performed by inviting them to to the hospital.

Statistical analysis

Data were calculated using the SPSS 11.5 software package for Windows (SPSS Inc., USA). Descriptive statistics were presented as mean \pm standard deviation and median (minimum-maximum) and percentages.

Results

Within this five-year period, there were 106 cases of fetal cystic hygroma. 85 women underwent karyotype analysis, whereas 21 refused karyotype analysis.

Demographic characteristics of the women were depicted in Table 1. Median maternal age was 35 years (range: 22-40). Among them a normal karyotype was revealed in 33 (38.8%) cases. In the remaining 52 (61.2%), fetal karyotype abnormalities were detected; and they were excluded from the study. Thus the study population included the outcomes of 54 fetuses with cystic hygroma in whom invasive diagnostic procedures were either not performed (n=21) or normal (n=33).

The flow chart of the evaluation of the women with hydrops fetalis together with the details of the karyotype abnormalities, fetal structural abnormalities and pregnancy outcome were summarized in Figure 1. Associated structural anomalies were present in 7 (12.9%) cases., including hydrops fetalis (n:2; 28.6%), transposition of great arteries (TGA) (n:2; 28.6%), perimembranous VSD (n:1; 14.3%), atrioventricular septal defect (n:1; 14.3%) and micrognathi (n:1; 14.3%).

In the group which had refused karyotype analysis (n:21), pregnancy outcomes were as follows: 13 live births (n: 11 vaginal birth; n:2 cesarean delivery), 7 missed abortion and 1 intrauterine death. In the other group with normal fetal karyotype (n:33), pregnancy outcomes included 12 live births (n:8 vaginal birth; n:4 cesarean delivery), 12 missed abortion, 2 hydrops and 5 fetal deaths. We were unable to get the results about pregnancy outcomes in two of the fetuses with cystic hygroma having normal karyotype. Second trimester pregnancy termination was performed on 19 women with fetal cystic hygroma having normal karyotype and eight of 21 women who refused karyotyping. Two newborns with cardiac malformation died within the first week of delivery.

Both of these cases were TGA. Follow-up of the 23 infants continued nearly 36 months. Only one infant was operated due to congenital hip dislocation. About the 13 live births that refused karyotyping in utero, were karyotyped postnatally; one infant was Trisomy 21 and the remaining 12 infants were euploid. No neurological developmental disorder were detected in any of the infants excluding the infant with Trisomy 21.

Discussion

This study once again confirms the fact that increased nuchal translucency in the first trimester screening is associated with chromosomal abnormalities, structural malformations and fetal demise. The overall probability of live births for both groups was 23.5%; and after the exclusion of aneuploid fetuses was 46.3%. Bilardo et al, reported this rates to be, 43.2% and 68.1%, respectively for increased nuchal translucency groups (7). On the other hand, live birth rates of women who refused karyotyping prenatally was 61.9% (n: 13/21); and the overall chance of live birth in the total group was 12.3% (n:13/106).

Nuchal translucency is an essential part of the screening for chromosomal anomalies on routine or indicated first trimester fetal sonographic assessment. During fetal nuchal translucency measurement in the mid-sagittal plane, we should keep in mind the association between increased nuchal translucency and chromosomal abnormalities, congenital malformations or several genetic syndromes (8). When a cystic hygroma is diagnosed, detailed ultrasound examination and fetal chromosomal analyses are indicated due to high rates of fetal aneuploidy and

coexisting structural malformations (9). Although, invasive prenatal diagnostic procedures for fetal karyotyping and parental counseling about poor fetal prognosis; sometimes parents refuse these procedures due to religious beliefs, increased risk of abortion with invasive fetal procedures. Even if normal karyotype is reported due to the limited treatment modalities and possibility of unfavorable consequences, the parents can opt for elective termination.

Previous studies have indicated that, cystic hygroma with fetal structural abnormalities is associated with poor fetal outcomes (1-6). The most frequent fetal structural malformation is cardiac defects within euploid groups. TGA is with the highest incidence (90%) in this group. Septal or valvular defects are present in 43% and aortic valve/isthmus stenosis is present in 86% of cardiac abnormalities (7). We found that the overall frequency of cardiovascular anomalies in our study group was 7.4%. Within cardiac defects, TGA, perimembranous VSD and atrioventricular septal defect were detected with a frequency of 28.6%, 14.3% and 14.3% , respectively, emphasizing the fact that in the second trimester, targeted fetal echocardiographic examination is important and essential diagnostic tool in euploid fetuses with cystic hygroma (1,7).

Hydrops fetalis is another important prognostic marker; Bernard et al, reported that mortality rate of 96.5% in hydropic fetuses (10). Our findings showed that the incidence of fetal death with coexisting hydrops was 100%. Generalized edema and hydrops may be the reason of left atrium dysfunction and aorta due to compression effect leading to fetal death. In literature, only a few studies have been reported that resolution of hydrops and healthy newborns (11); majority of the studies demonstrate that hydrops is associated with poor fetal outcomes (6,10,12,13). On the other hand, resolution of the nuchal edema with a normal karyotype is a good prognostic marker in the absence of any coexisting malformation. Two fetuses with hydrops fetalis were present in our study. Cardiac malformations were detected more frequently than hydrops fetalis. Cardiac malformations, arrhythmia, aneuploidy, fetal structural malformations may lead to non-immune hydrops fetalis (14). Our findings showed 25 live births in all included groups of which two of them with TGA died postnatally; one of the newborns was Trisomy 21; of the remaining 22 (88%) newborns had normal postnatal neurologic development. Similarly Sanhal et al, reported 90% of fetuses (euploid and structurally normal) with septated cystic hygroma had normal neurologic outcomes.

Other than fetal karyotyping, chromosomal microarray analysis (CMA) is an advanced technology with the ability to survey the entire genome and to identify chromosomal abnormalities, submicroscopic genomic alterations. Increased NT and cystic hygroma are associated with different conditions not only aneuploidy but also structural abnormalities. Shaffer et al, reported that the detection rate of CMA for the fetuses with cystic hygroma was 17.1% (15). CMA should be offered for any patient undergoing invasive sampling to identify all clinically significant alterations.

Though previous studies focused on cases with karyotyping, our study also investigated cystic hygroma with unknown karyotype in prenatal period. The refusal rate of karyotyping was higher (19.8%) than the published data from European countries; this condition might be due to lower socio-cultural levels and religious beliefs. We think, our findings may be helpful to clinicians providing parental counseling for women who refuse karyotype analysis. Fetuses with cystic hygroma with normal karyotype and in whom no structural malformations are present pregnancy outcomes may be favorable as reported in the literature (5).

The small number of cases with cystic hygroma and unknown karyotype in 21 cases are the main limitations of this study.

In conclusion; the presence of cystic hygroma carries a high risk for aneuploidy and major structural malformations. Invasive prenatal karyotyping procedures, fetal echocardiographic examination and parental counselling are necessary for the prediction of the prognosis. Until multicentric and large- sample sized studies have been published; these results might be helpful in providing parental counselling for those with fetal cystic hygroma.

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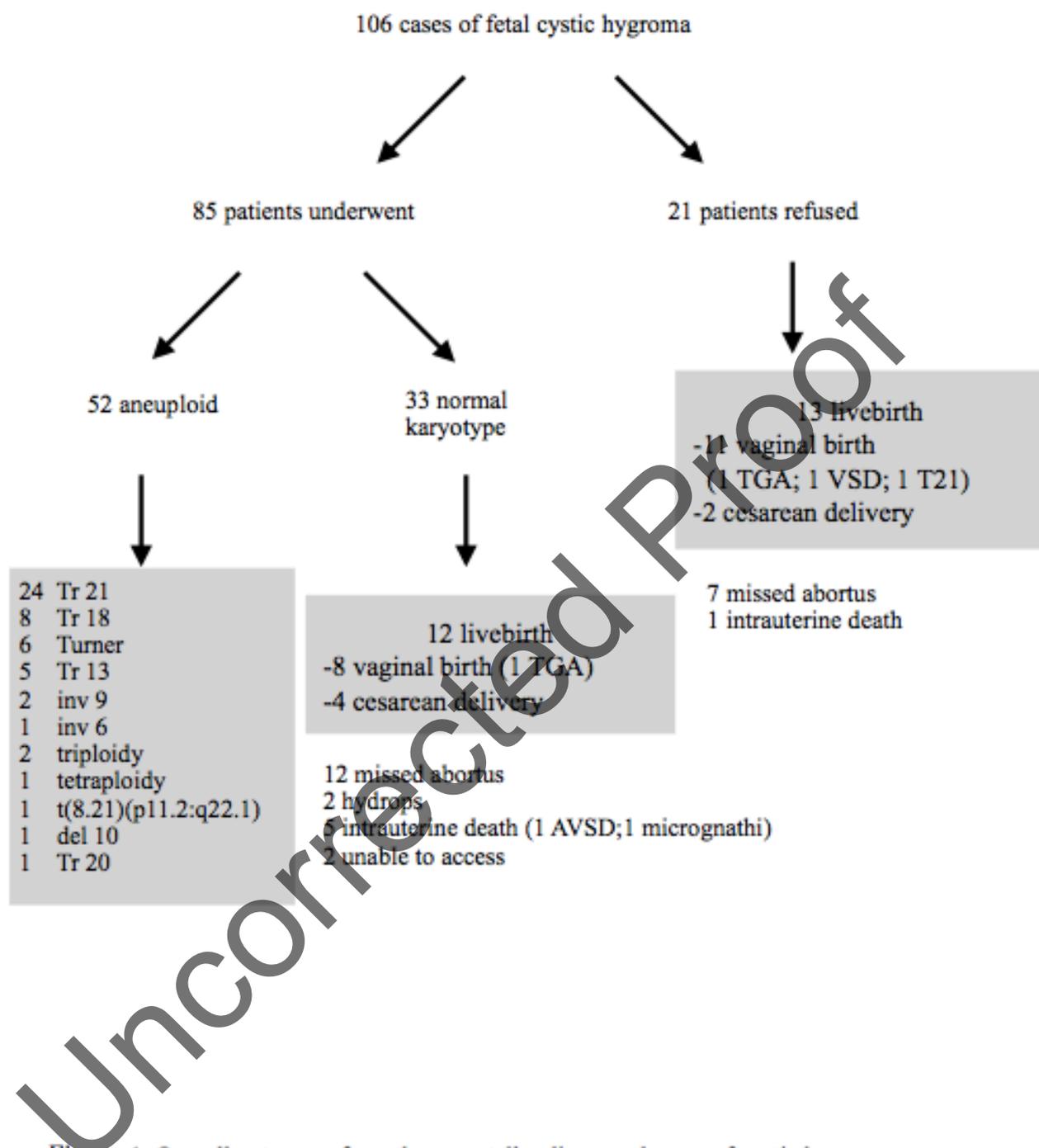


Figure 1: Overall outcomes from the prenatally diagnosed cases of cystic hygroma