Management and outcomes of cystic hygromas: experience of a tertiary center

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Abstract

Purpose Cystic hygroma (CH) is a fetal sonographic finding with an incidence of 1%. Chromosomal abnormalities and structural malformations are commonly related with CH. We aimed to describe our experience and determine the association between diagnosis of CH and adverse pregnancy outcome.

Methods We retrospectively reviewed data of prenatal CH diagnoses over a ten-year period. Cases were evaluated for maternal age, gestational week at CH diagnosis, invasive procedure, karyotype result, associated abnormality and perinatal outcome. We categorized cases into two groups to understand the impact of maternal age on perinatal outcomes, and the cut-off was 35 years old.

Results Totally 28 individuals were enrolled in the study. The median maternal age at birth was 27.5 years old, and 7 patients were over 35 years old. Karyotype results were available for all individuals, and 15 had an abnormal chromosome (53.5%). Five fetuses had structural abnormalities, and they were all observed within patients under 35 years old. Healthy fetuses (without any problem at antenatal screening and birth) were found to be only 14.3% in advanced maternal age (AMA) group and 33.3% in young mothers.

Conclusions Women with AMA and CH had a higher risk of having a baby with a chromosomal abnormality, as compared with younger women.

Keywords Advanced maternal age · Cystic hygroma · Prenatal screening

Sommario

Scopo L'igroma cistico (CH) è un reperto ecografico del feto con una incidenza dell' 1%. Esso è comunemente associato ad anomalie cromosomiche e malformazioni strutturali. In questo lavoro abbiamo voluto riportare la nostra esperienza e correlare la diagnosi di igroma cistico con l'esito infausto della gravidanza.

Metodi Con uno studio retrospettivo abbiamo analizzato i dati di 10 anni relativi a diagnosi prenatale di igroma cistico. I casi sono stati valutati sulla base dell'età materna, della settimana gestazionale al momento della diagnosi, della procedura invasiva, dell'esame del cariotipo, delle anomalie associate e dell'esito perinatale. Abbiamo classificato i nostri casi in due gruppi per capire l'impatto dell'età materna sulla nascita ed il cut-off è stato di 35 anni.

Risultati Nello studio sono stati inclusi 28 casi. L'età materna media alla nascita era di 28,6 anni, e sette pazienti avevano più di 35 anni. Tutte le pazienti si erano sottoposte all' esame del cariotipo fetale e 15 di esse avevano avuto come risultato un cromosoma anomalo (53,5%). Cinque feti avevano anomalie strutturali, tutte rilevate in soggetti sotto i 35 anni di età. Solamente il 14,3% dei feti sani (senza alcun problema allo screening prenatale ed alla nascita) è risultato essere appartenente al gruppo di madri con età avanzata (AMA) mentre il 33,3% a quello delle giovani madri.

Conclusioni Le donne di età avanzata e con diagnosi di igroma cistico avevano un rischio maggiore di avere un bambino con anomalie cromosomiche rispetto alle giovani madri.

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Introduction

Ultrasonography has become a routine part of pregnancy follow-up in recent clinical practice, as early diagnosis of fetal malformations is important to decide how to manage the pregnancy. Moreover, nuchal translucency (NT) measurement is commonly performed in all pregnant women as a part of aneuploidy screening programs [1].

Cystic hygroma (CH) is a sonographic finding that can be described as increased fluid in the nuchal region of the fetus. The underlying pathophysiology of this phenomenon is a developmental abnormality of the lymphatic vessels that occurs at the beginning of embryogenesis [2]. The incidence of CH is approximately 1%, and detection is very easy with recent improved technology and experienced clinicians [3].

There is not a recommended screening program for CH, but its diagnosis is simple and possible during routine ultrasonography. Diagnosis of CH is more frequent during the first and early second trimesters; however, there are some cases that are detected in earlier gestational weeks (<10th gestational week), even when crown rump length (CRL) is smaller than 45 mm [2]. Patients should be well informed following CH diagnosis, and clinicians should offer all necessary consulting procedures as soon as possible. The most common etiologic factors associated with CH are reported to be chromosomal abnormalities and structural malformations. For this reason, prenatal invasive tests and detailed anatomy scans are mandatory [4]. The favorable pregnancy outcomes of fetuses with CH depend on multiple variables, and are only possible with a normal karyotype and without any structural anomalies [5].

It has been reported that there is an increased risk of adverse pregnancy outcome (i.e., miscarriage, sudden fetal death, hydrops fetalis) among fetuses with CH [6]. Nevertheless, spontaneous resolution of the CH is also possible, leading to a satisfactory pregnancy outcome. Regression of CH is reported to be about 20% [7, 8]. Thus, pregnancy termination should only be offered after all other necessary interventions have been completed. Management of fetuses with CH is difficult, and pregnancies involving this condition must be referred to experienced centers immediately.

Herein, we aimed to describe our experience and determine the association between diagnosis of CH and adverse pregnancy outcome.

Materials and methods

We retrospectively reviewed pregnancies with prenatal diagnoses of CH in our tertiary hospital between January 2005 and December 2015. CH was identified as an increased fluid collection with septations in the fetal neck

(Fig. 1). Two clinicians who are experienced with fetal abnormalities performed all of the ultrasonographic examinations, and confirmed the CH diagnoses. We have used the Aplio™ XG ultrasound system (Toshiba, Tokyo, Japan) for fetal morphology scanning in our maternal fetal medicine unit for the last ten years.

Information on maternal age, invasive procedure type, fetal karyotype result, pregnancy outcome (i.e., delivery, termination, intrauterine exitus) and neonatal outcome (i.e., postpartum exitus, liveborn) was obtained from the computerized system of “Hacettepe University Faculty of Medicine”. Ultrasonography findings, such as number of fetuses (singleton/twin), gestational week at diagnosis, associated abnormalities (if any), and fetal echocardiography results, were collected from the perinatology database.

This study considered 28 pregnancies with the prenatal diagnosis of CH. Amniocentesis (AC) or chorionic villus sampling (CVS) was applied to all patients after provision and receipt of the informed consent form. Second trimester ultrasonography (at 18–22 gestational weeks) and fetal echocardiography (at 20–24 gestational weeks) were performed in the ongoing pregnancies with normal karyotype. All patients were included in a special antenatal care program for their pregnancy follow-up. A termination of pregnancy option was offered to patients if “aneuploidy and/or lethal congenital malformation” existed in combination with the diagnosis of CH. All patients ($n = 20$) with a prenatally diagnosed abnormality accepted pregnancy termination.

We categorized our cases into two groups to understand the impact of maternal age on perinatal outcome, with a cut-off age of 35 years (Table 1). Advanced maternal age (AMA) was determined to be a maternal age of 35 years or older at delivery [9]. Fetal outcomes were classified as three groups: abnormal karyotype, structural anomaly and normal (without any problem at antenatal screening or birth). Fetuses with chromosomal abnormalities were also categorized in two groups according to the first CH diagnosis time, and aneuploidy types were noted to comprehend the CH distribution in the first and second trimesters (Table 2). Early onset was defined as a CH diagnosis before the 14th gestational week. On the other hand, fetuses with a normal first trimester ultrasonography but who presented with CH in the second trimester (≥ 14 weeks of pregnancy) were classified into a late onset group.

Results

The median maternal age at delivery was 27.5 years, ranging between 19 and 41 years of age. CH was diagnosed in 20 cases (71.4%) during routine NT measurement.

Fig. 1 Images of cystic hygroma **Table 1** Pregnancy outcomes according to maternal age

Age	Number of patients	Abnormal Karyotype	Normal	Structural Abnormality
>35	7	6	1	0
<35	21	9	7	5

Table 2 Chromosomal abnormality distribution in different gestational weeks

Abnormal Karyotype	<14th gestational week	>14th gestational week
45, XO	3	3
Trisomy 21	3	2
Trisomy 18	1	2
Translocation	0	1
TOTAL	7	8

The remaining 8 fetuses were diagnosed after 14th gestational week, and their NT thickness were found to be within normal ranges at the first trimester screening.

Twenty-six pregnancies among the CH cases were singleton (92.8%). The remaining two were dichorionic diamniotic twin pregnancies, and both reduced to singleton pregnancies. Chromosomal abnormalities (trisomy 21 in one and trisomy 18 in the other) were detected only in one of the fetuses in these twin pregnancies. Healthy co-twins were delivered at term after selective feticide of the affected fetuses. These two cases were included in the pregnancy termination group.

Karyotype results were available for all individuals, and 15 out of the 28 had an abnormal karyotype, as shown in Table 2. CVS was performed in 18 patients (64.3%), and the remaining 10 patients underwent AC (35.7%).

Monosomy X was the most common chromosome anomaly ($n = 6$, 40%). The other aneuploidies were trisomy 21 (five cases), trisomy 18 (three cases) and translocation (one case). Turner syndrome was found to present more frequently than other aneuploidies in both (i.e., early and late onset) trimesters. Among the individuals within the early CH diagnosis group; trisomy 21 was detected in three cases and trisomy 18 was detected in one. Furthermore, two trisomy 21 cases, two trisomy 18 cases

and one case of translocation were seen in fetuses within the late onset CH group.

All observed structural abnormalities were also evaluated. There were five congenital fetal abnormalities in 28 fetuses, and the structural anomaly rate was found to be 17.8%. Specifically, prenatally diagnosed structural abnormalities in the fetuses were nuchal teratoma in one, skeletal dysplasia in one, congenital heart defect (tetralogy of Fallot) in one, congenital diaphragmatic hernia concurrent with dextrocardia in one, and multiple anomaly (i.e., hydrocephalus, single umbilical artery, rocker bottom foot, cleft lip) in one. Hydrops fetalis developed at the 20th gestational week in the fetus with nuchal teratoma, and the pregnancy was ultimately terminated following counseling with the parents. The remaining eight fetuses without any coexisting problems (chromosomal abnormalities and/or congenital malformations) were delivered without any perinatal complications. CH was regressed before the 20th gestational week in these eight cases.

Only a small number of patients (seven out of 28 mothers) were ≥ 35 years of age. However, a majority of the cases were in the young mother group (Table 1). There was only one healthy neonate in the AMA group, and the remaining six fetuses had chromosomal abnormalities. On the other hand, seven neonates (7 out of 21) were normal in

the other group of mothers under 35 years of age. Normal obstetric outcome rate was 14.3% within AMA pregnancies, and 33.3% in the young mothers group.

Discussion

Pregnancies with CH diagnosis are related with poor obstetric outcomes, and prenatal screening is obligatory (especially) for aneuploidies and structural abnormalities. However, resolution of the lesion due to recanalization of lymphatic vessels is possible, and favorable pregnancy outcomes do occur in the absence of these comorbid risk factors. The resultant healthy newborn rate was found to be 15–20% of pregnancies with CH diagnosis in prior studies [3, 10]. In our study, 28.6% of pregnancies (8 out of 28) resulted in a healthy neonate, which is in accordance with these previous studies.

Invasive prenatal procedures should be performed in all pregnancies after CH diagnosis because of the high concordance between CH and aneuploidy. Our results showed that 53% of patients with CH had an abnormal chromosome, and this was nearly the same as in the previous studies [10–12]. In our whole study group, 15 of 28 CH cases had abnormal karyotype results as follows: six monosomy X, five trisomy 21, three trisomy 18 and one translocation, respectively. We have demonstrated that 45, XO and trisomy 21 are the most frequent chromosome aneuploidies among fetuses with CH.

We also investigated if there was a relationship between aneuploidy type and gestational week at the first CH diagnosis. First trimester CH was reported to be commonly associated with trisomy 21 in a previous study [6]. In the second trimester CH diagnosis, trisomy 21 was found to be the most frequent aneuploidy in non-septated cases, and Turner syndrome was reported to be more common in septated cystic hygromas [13]. Our results were in agreement with the previous studies, in that trisomy 21 and monosomy X are the two most common chromosome abnormalities in fetuses with CH during the first and second trimesters.

More than one million women give birth every year in our country. Pregnancies ≥ 35 years of age comprise about 14% of the total number of pregnancies, according to data provided by the National Statistical Institute of Turkey [14]. It has been reported that, there is a relationship between the prenatal diagnosis of CH in elderly women and poor pregnancy outcome [15]. In our series, we have shown that one-quarter of CH cases were observed in the AMA group, and that aneuploidy rate was 85.7% in these pregnancies. These findings showed that women with AMA and CH had a higher risk of having a baby with a chromosomal abnormality, as compared with younger women.

Whereas cell-free DNA has begun to be an alternative and popular testing method for aneuploidy screening, invasive testing remains obligatory to avoid the delay in definitive diagnosis for CH [16, 17]. Detailed ultrasonography and fetal echocardiography are the other important tools in the further evaluation of these cases [7, 18]. In conclusion, patients (especially older mothers) should be well informed about poor perinatal outcome, and all interventions must be carried out at comprehensive centers.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

Ethical approval Non-interventional Clinical Researches Ethics Board of Hacettepe University had approved this retrospective study with the number of GO 16/690-04.

Informed consent Informed consent was obtained from all individual participants included in the study.

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