

Prenatal management of cystic hygroma and long term outcomes

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Abstract

Cystic hygroma is a benign congenital malformation of the lymphatic system. The rate of incidence is 1-4/1000 and it can be inherited as an autosomal recessive. There is a 35-50 % chance of chromosomal abnormalities with cystic hygroma. Also euploid fetuses have 50 % structural malformation risk. The most common malformations are cardiac malformations. There's a 15 % chance of live births for affected fetuses. If there are neither chromosomal abnormalities nor structural malformations, a 95 % normal short-term pediatric outcome can be estimated. However, the overall prognosis in fetuses with cystic hygroma is poor, and a healthy survival rate is less than 5 %. There are prenatal, natal and postnatal treatment methods.

Keywords: Cystic hygroma, prenatal management, long term outcomes

Introduction

Abnormal accumulation of fluid behind the fetal neck can be classified as nuchal cystic hygroma or nuchal edema. In the case of cystic hygromas, prenatal diagnosis by sonography is based on the demonstration of a bilateral, septated, cystic structure, located in the occipitocervical region [1,2]. Cystic hygroma refers to the finding of marked and thickening skin extending along the entirety of the fetus. This finding is to be differentiated from increased nuchal edema in which skin thickening is noted at the posterior of the fetal neck only. These are currently considered a form of vascular malformation of the lymphatic system characterized by localized or diffused malformations of lymphatic channels that can be characterized as microcystic, macrocystic, or both [3].

Determined in the second trimester screening, the finding of cystic hygroma will likely become more common. Approximately 35-50% of cases have an abnormal karyotype [4]. Amongst euploid pregnancies there is almost a 50% chance of cardiac malformation or other structural abnormalities. Additionally, 25 % of pregnancies with cystic hygroma result in spontaneous intrauterine fetal demise. There's a 5% or less chance of a healthy neonate at full term with a fetus affected by cystic hygroma [5].

Incidence

Recent studies evaluated more than 38.000 unselected pregnancies from throughout the United States with first trimester sonography. The prevalence of cystic hygroma was 1 in 285 in first trimester pregnancies [5]. Fisher et al. confirmed 52 cystic hygromas, about 52.000 cases, which included terminations, intrauterine fetal deaths, still births and postnatal deaths [6].

Sonographic findings

Cystic hygroma typically develops late in the first trimester and is characterized by markedly enlarged nuchal translucency measurement that extends along the entire length of the fetal back, and in which septations are clearly visible in transverse section through the fetal neck [Figure 1]. An axial view of the fetal neck is required in order to make diagnosis [Figure 2]. In axial, view the fluid-filled cavities are commonly partitioned by a thick fibrous band corresponding to the nuchal ligament [7,8].

Differential diagnosis and prognostic indicators

The main differential diagnosis of cystic hygroma includes enlarged nuchal translucency, occipital cephalosel, and cervical teratoma. Occipital cephalosel is a calvarial bone defect. Cervical teratoma frequently appears in the anterior neck and the fetal neck is often hyperextended. Calcifications are the diagnostic for teratoma. Additionally, a fetal MRI may be helpful for diagnosis [9]. In enlarged nuchal translucency, if the nuchal thickening does not extend along the entire length of the fetal back, and if transverse septations are not visible, then the term nuchal translucency should be used. If an enlarged nuchal

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translucency identified, second trimester screen test should be apply [10]. On the other hand if nuchal translucency measurement of 3mm or greater, it is reasonable to immediately offer the patient chorionic villus sampling (CVS), [11].

Several studies show that there is a prognostic significance between septated and non-septated cystic hygroma. Some studies suggest that the presence of septations increase the risk of aneuploidy [12].



Figure 1: 12 +6 weeks fetus with cystic hygroma view.



Figure 2: 15 weeks fetus with cystic hygroma demonstrating axial view.

The overall prognosis in fetuses with cystic hygroma is poor, and the health survival rate is less than 5% [2]. In an evaluation of 132 fetuses with cystic hygroma 50% of fetuses were found to have aneuploidy. Of these aneuploidies, 40% were trisomy 21, 30% Turner syndrome, 20% trisomy 18, and 10% trisomy 13 or triploidy. 50% fetuses are found to be euploid [5]. Recently another study found that of the 40% with aneuploidy, 50% were Turner syndrome, 32% trisomy 21, 10% trisomy 18, 3.6% trisomy 13, and 36% of fetuses detected euploid [13]. On the other hand one-third of fetuses with cystic hygroma have structural malformations. The most common cardiac malformations include hypoplastic left heart, tetralogy of Fallot and a ventricular septal defect. Also the most common skeletal abnormalities include Robert's syndrome

and Cornelia de Lange syndrome [5]. The other abnormalities are diaphragmatic hernia, and central nervous system anomalies. There are some non-chromosomal syndromes associated with cystic hygroma. Amongst these syndromes, Noonan and multiple pterygium [14].

Management of pregnancy

The detection of cystic hygroma in the first trimester patients should be counseled of a one in two risk of aneuploidy. They should be offered the definitive diagnostic testing by means of CVS. There is no need to wait until the second trimester screening test. If the CVS results confirm normal karyotype, patients should be counseled of one in two risk of structural malformations. A detailed sonography evaluation of fetal anatomy should be provided at 16-20 weeks gestation.

If detailed sonography confirms a normal fetus there is 95% normal short term pediatric outcome [15].

There is no specific intervention method for cystic hygroma. However large cystic hygroma in fetuses reaching term of gestation can complicate obstetric management. Because of the risks of airway obstruction, ex utero intrapartum treatment should be considered (EXIT), [16,17]. Pregnancies with cystic hygroma should be followed closely because cervical mass can obstruct pharynx and larynx and lead to polyhydramnios. Amnioreduction may be required to treat preterm labor. There are reports of successful vaginal delivery after intrauterine cyst decompression [8].

Fetal intervention

In the first trimester there is no specific fetal intervention for cystic hygroma. However in the second and third trimester large cystic hygromas or lymphangiomas may compress and displace the larynx, trachea and esophagus causing serious respiratory and feeding problems in neonates. Chen et al. reported multiple cyst aspirations on two fetuses [18]. Each fetus' karyotype analysis and detailed sonography was normal. They aimed to prevent polyhydramnios and progression to hydrops but they didn't find an effect on the outcome.

Ogita et al. found OK-432 (picibanil) a new and promising form of sclerotherapy. An intracystic injection of OK-432 produces a local inflammatory reaction, which leads to resolution of the lesion [19].

Candidates for OK-432 included cases with normal chromosomes and no associated malformations with lymphatic vascular disorders and/or hydrops [19]. In 2006 Ogita et al. used a rabbit experiment to determine a safe dosage of OK-432 [20].

In 2009 Mikovic et al. used that agent prenatally intrauterine intralesional on two cases of large multicystic

lymphangiomas. They noticed a progressive decrease in tumor volume. They didn't experience any complications and there were no respiratory or feeding problems in neonates. Both children were normal at the age of 2 years and 6 months [21].

The EXIT procedure is done in cases where difficulty is anticipated in neonatal airway establishment at delivery and it involves placement of an endotracheal tube before the fetus is separated from placental support [16]. This allows for management of the obstructed fetal airway via direct laryngoscopy, bronchoscopy, tracheostomy, or surgical intervention.

Postnatal therapy

Complete excision remains the treatment of choice for cystic hygroma. Complete resection is possible in only 75% of patients [22]. Partial resection leads to 50% recurrence. Cyst aspiration method is except a large cyst as a means emergency decompression. However, the cysts rapidly re-accumulate.

Recently sclerosing agents have also been used to threaten cystic hygroma (Bleomycin, OK-432), [23-25].

Prognosis

In a study of 132 fetuses with first trimester cystic hygroma, once fetal aneuploidy and structural malformations are excluded, 23 cases followed 12 to 50 months. Only 1 of 23 cases had pediatric abnormality, which is spastic diplegia [5].

In late pregnancy, before the 30 weeks of gestation associated with hydrops fetal mortality rate is approximately 100%. On the other hand, there is high risk for lethal chromosomal abnormalities as trisomy 18 and 13 [15].

Graesslin et al. found that the 18 live-born infants who had cystic hygroma with normal chromosomes were followed up for 17-98 months. Sixteen infants developed normally, while 1 developed Noonan's syndrome and 1 had a urinary tract abnormality [26].

Discussion

As a result of second trimester screening, cystic hygroma will likely become more common. Incidence is 1-4/1000. About 35-50% of cases have an abnormal karyotype. Most common aneuploidies are Turner syndrome, Trisomy 21-18 and 13. The pattern of inheritance for these syndromes varies depends upon the specific syndrome. There are reports of familial cystic hygroma. Isolated cystic hygroma can be inherited as an autosomal recessive disorder for which parents are "silent" carriers [27-28]. Euploid pregnancies have 50 % chance of structural abnormality. If karyotype is normal with no abnormalities found, medical

treatment pre or post natal can be applied. Then 5 % cases will result with a healthy baby.

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