CYSTIC HYGROMA: PRENATAL DIAGNOSIS AND ANTENATAL MANAGEMENT BEFORE FETAL VIABILITY

Kistik higroma: Fetal viabiliteden önce prenatal teşhis ve antenatal yönetim

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Summary: *Cystic hygroma is a congenital malformation of the lymphatic system most often located in the neck region. In this report, four cases with cystic hygroma diagnosed by transvaginal or transabdominal ultrasonography were presented. In all cases, fetal karyotyping with amniocentesis was studied before fetal viability was reached and this revealed an abnormal karyotype (trisomy 18) in one fetus. All pregnancies were decided to be terminated owing to fetal hydrops in two, to abnormal karyotype in one and to parent's request in one fetus. Once the diagnosis of cystic hygroma has been established by ultrasonography, a meticulous ultrasonografic examination and a fetal karyotyping study should be performed and if necessary termination of pregnancy should be considered before fetal viability.*

Key Words: *Amniocentesis, Cystic hygroma, Fetal hydrops, Fetal karyotype*

Özet: *Kistik higroma sıklıkla boyun bölgesinde yerleşen, lenfatik sistemin konjenital malformasyonudur. Bu raporda transvajinal veya transabdominal ultrasonografi ile teşhis edilen kistik higromalı dört vaka sunuldu. Vakaların tümünde amniosentez ile fetal karyotipleme fetal viabilite gelişmeden önce çalışıldı ve bir vakada anormal karyotip (trisomi 18) görüldü. İki fetusda hidrops nedeniyle, bir fetusda anormal karyotip ve bir fetusda anne-babanın isteği ile gebeliklerin sonlandırılmasına karar verildi. Kistik higroma ultrasonografi ile teşhis edilirse, dikkatli bir karyotipleme çalışması yapılmalıdır ve gebeliğin sonlandırılması gerekirse bu fetal viabiliteden önce düşünülmelidir.*

Anahtar Kelimeler: *Amniosentez, Fetal hidrops, Fetal karyotip, Kistik higroma*

Cystic hygroma is a congenital malformation of the lymphatic system appearing as single or multiloculated fluid filled cavities, most often about the neck (1-3).

Ultrasonographic features of fetal cystic hygroma are far more subtle in the first trimester (4). First trimester hygromas differ in that the degree of cystic changes are not as well established, septations are less likely seen, and early sign of their development are most likely recognized as an elevated simple membrane like thickening distinctly seperated from the posterior angles of the fetal necks (5). The diagnosis of cystic hygroma in the first trimester can be well-established by transvaginal ultrasonography (6). Fetuses with first trimester cystic hygromas are at high risk for aneuploidy (5,7,8). Such fetuses with normal karyotypes will likely resolve their hygromas by 18 weeks' gestation, and most will be phenotypically normal at birth (5, 7, 8).

Prenatal diagnosis of cystic hygromas in the second trimester is not particularly difficult and is reliably done by transabdominal ultrasonography (1-3, 9-14). The single or multiple cysts are found located in the occipitocervical region. Because of the presence of multiple septa, they have a typical honeycomb appearance (2). Cystic hygromas are associated with an increased risk (59-73 %) for fetal chromosome abnormality, in particular mosaic or non-mosaic 45 X in the second trimester

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(9, 15). Furthermore in the second trimester, cystic hygromas often progress to hydrops and cause fetal death (9). The prognosis for fetuses with cystic hygroma, particularly in the presence of hydrops, is poor (9, 11).

In our article, we presented four cases with fetal cystic hygroma who were diagnosed by transvaginal or transabdominal ultrasonography, performed fetal karyotyping with amniocentesis, and terminated before fetal viability.

Case Reports

Four cases of cystic hygromas were diagnosed during antepartum period between September 1, 1995 and November 15, 1996 in Erciyes University, School of Medicine, Department of Obstetrics and Gynecology, Prenatal Diagnosis Unit. The patients were referred to our unit either from our outpatient antenatal clinic or from other clinics.

Gestational age was determined by ultrasonographic fetal diameters, in conjunction with menstrual history. The criterion for the diagnosis of cystic hygroma was a mass in the posterolateral region of the neck that was frequently asymmetrical, multiseptate, and cystic, and was not contiguous with the central nervous system (Fig. 1). A careful sonographic search for other anatomic abnormalities was conducted in each case.

All ultrasonographic examinations were performed with a Hitachi EUB-450 electronic ultrasound scanner (Hitachi Medical Corporation, Tokyo, Japan). Transvaginal and transabdominal ultrasonographic examinations were performed with a 6.5 MHz endovaginal convex and 3.5 MHz convex probes, respectively.

Women were provided counselling concerning diagnostic testing (i.e., serial ultrasonography, amniocentesis) and pregnancy management alternatives. The invasive procedures were done under local anesthesia, by one of the two doctors of the units as an out patient procedure (M.B., M.T.). All procedures were done under ultrasound guidance with free hand technique. Twenty gauge, 9 cm spinal needles were used for amniocentesis. Prenatal karyotyping was performed by amniocentesis. All genetic counselling and fetal karyotyping were done in the Division of Medical Biology and Genetics, Erciyes University. The diagnoses of cystic hygromas were confirmed by autopsy or detailed external physical examination.

Features of patients and fetuses are shown in Table I. Gestational trimester in the four affected fetuses were first trimester in two, second trimester in other two cases (from 12 to 20 weeks). In two cases, there was evidence of fetal hydrops, including massive skin edema, ascites, and pleural or pericardial effusions (Fig. 1). Abnormal karyotype (trisomy 18) was found in one fetus. In all cases, the pregnancies were terminated because of fetal hydrops in two cases, chromosomal abnormality in one case, and parent's request in one case. Fetal photography after termination of case no 3 who had trisomy 18 are shown in Figure 2.

Table I. Features of patients and fetuses in four cases of cystic hygroma

Case No	Patient's age (year)	Gestational age at diagnosis (week)	Fetal karyotype	Indication of fetal termination
1	14	20	46, XX	Fetal hydrops
2	22	18	46, XY	Fetal hydrops
3	25	12	47, XY, + 18	Abnormal karyotype
4	20	13	46, XX	Parent's request

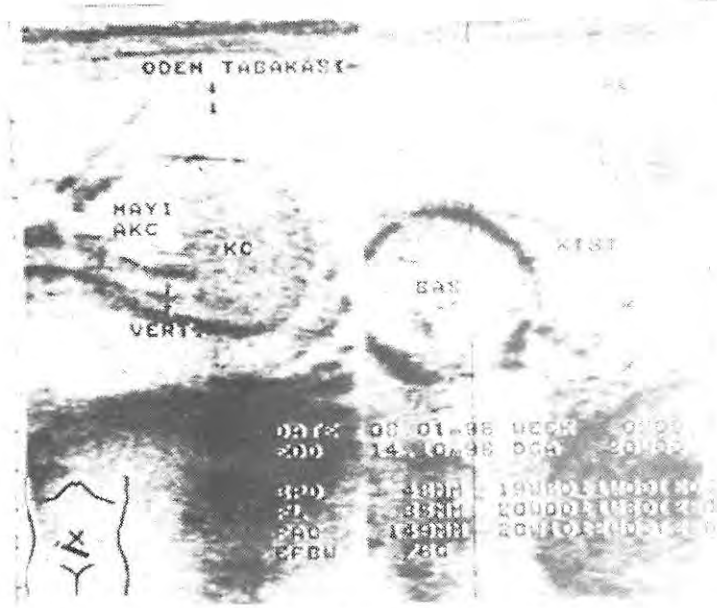

Figure 1. Abdominal Ultrasonograms Demonstrating Cystic Hygroma and Fetal Hydrops (case no 1).
Right: The transverse sonogram to right shows a cystic hygroma with a thin-walled multiseptate, fluid-filled mass. (Baş: Fetal head, K and Kist: Cystic hygroma, PL: Placenta).
Left : The longitudinal sonogram to left shows a hydropic fetus with massive skin edema, pleural effusion (Ödem tabakası: Edema, Mayi: Pleural effusion).

Figure 2. Fetus with cystic hygroma (case no 3).

Discussion

The lymphatic system begins to develop at the end of the fifth week of gestation, and lymphatic vessels develop in a manner analogous to blood vessel formation. The early lymph capillaries join to form a network of lymphatic channels and lymph sacs (1-3, 9). At 40 days of gestation, the communication between primitive structure and juguler vein is formed. If the lymphatic and venous system fail to connect, the jugular lymphs sacs enlarge and fluid accumulates beneath the fetal skin within and along the distribution of these tracts. Cystic hygromas of the posterior triangles of the neck, which may extend from the top of the head to the lumbar region, secondarily result. Protein concentrations in the cystic hygroma may be high, which contributes to the hypoproteinemia, resulting in the generalized edema and sequelae of nonimmune hydrops (1-3, 9). We also found fetal hydrops in two of our cases.

If the jugular lymph sacs and the jugular veins establish connection, or if an alternate route of drainage develops before intrauterine death, the

hygromas may theoretically regress and edema may resolve. Secondary webbing of the neck and neonatal peripheral lymphedema may persist as residual sequelae, as typically noted in newborns with Turner Syndrome. These phenotypic features that results from the aforementioned embryonic accidents formulate the jugular lymphatic obstruction sequence of fetal malformation (16).

The incidence of cystic hygroma is approximately 1.6 : 10000 pregnancies or 0.8 % of pregnancies at risk for a structural anomaly (3). The most common regions of cystic hygroma are the neck (75 %) followed by the axillary region (20 %), retroperitoneum and abdominal viscera (2 %), limbs, bones and mesentery (2 %), and cervicomediastinum (1 %) (3). In all of our cases, cystic hygromas are also located in the neck.

Although prenatal diagnosis of cystic hygroma in the second trimester is not particularly difficult and is reliably done by transabdominal ultrasonography, this diagnosis in the first trimester may be difficult and may require transvaginal ultrasonography (4-6). Our two cases in the first trimester were diagnosed by transvaginal ultrasonography.

Craniocervical masses such as neural tube defects, cystic teratomas, nuchal edema, or residual gestational sacs of a vanishing twin conception must be considered in the differential diagnosis (1-3).

Authors have shown an increased risk (47-100 %) for fetal chromosome abnormalities in cases of fetal cystic hygroma detected in the first trimester, specifically autosomal aneuploidy at frequencies consistently higher than those associated with second trimester cystic hygroma (5-7). The higher frequency of autosomal abnormalites in the first trimester may lead to increased first trimester spontaneous abortions, resulting in second trimester cystic hygroma cases showing higher relative frequencies of mosaic and non-mosaic monosomy X.

Second-trimester nuchal cystic hygromas have also been shown to have a high incidence of association with chromosomally abnormal fetuses (9, 15). Several reviews have shown the most common aberration to be Turner Syndrome (45, X), representing nearly 60 % of chromosomally abnormal fetuses. Cervical hygromas can also be present in trisomy 13, 18, and 21 fetuses and have been described in XXY, duplication of 11p, 6q-, 13q-, 18q-, and trisomy 22 mosaicism (1-3, 9, 15).

In Turkey, Ermiş et al. found three pathologic karyotypes in 17 fetuses with cystic hygroma (17.6 %) and all of them were 45X. These authors suggest that a reason of the low percent of chromosomal abnormalities in their cases may be consanguinity. Because, in their cases, other than having chromosomal abnormalities, there were five (45.5 %) consanguinity in 11 cases. There is also an increased risk of birth defects due to abnormal recessive genes when parents are blood-related (13). Although we found a case of trisomy 18 in our cases, we believe that the number of our cases is very low to comment.

When a normal karyotype in the second trimester is present, the cystic hygroma may signal the presence of a single gene disorder such as Noonan Syndrome (17), Robert Syndrome (18) or the autosomal recessive form of cystic hygroma (19). Regardless of the underlying cause, this abnormality is correlated with poor perinatal outcome when it occurs in the second trimester (20). In the presence of a normal karyotype fetuses with a first trimester nuchal hygroma have an excellent prognosis (5, 7, 8). Normal outcome was seen in 80 % pregnancies carried to the third trimester (8).

In conclusion, when a prenatal diagnosis of cystic hygroma by transvaginal or transabdominal ultrasonography is made, the determination of the karyotype should be recommended in all cases. Ultrasonographic examination for diagnosis of fetal hydrops should aid in the management of the pregnancy and is useful in the counselling of future pregnancies. In the fetus with associated chromosomal abnormality or hydrops, the chance of survival is small; therefore, the option of pregnancy termination should be offered before fetal viability.

REFERENCES

1. Chervenak FA, Isaacson GC, Campbell S. Anomalies of the neck. In Chervenak FA, Isaacson GC, Campbell S (eds), Ultrasound in Obstetrics and Gynecology. Little, Brown and Company, Boston 1993, pp 853-858.
2. Reece EA, Goldstein I, Hobbins JC. Fundamentals of Obstetrics & Gynecologic Ultrasound. Appleton & Lange, Connecticut 1994, pp 69-72.
3. Jeanty P. Neck and Chest. In Fleischer AC, Manning FA, Jeanty P, Romero R (eds), Sonography in Obstetrics and Gynecology, Principles & Practice (5th ed). Appleton & Lange, Connecticut 1996, pp 393-410.
4. Hertzberg BS, Bowie JD, Carroll BS, Killam AP, Ruiz P. Normal sonographic appearance of the fetal neck late in the first trimester: The pseudomembrane. Radiology 1989; 171: 427-429.
5. Johnson MP, Johnson A, Holz[illegible] W, et al. First-trimester simple hygro[illegible] use and outcome. Am J Obstet Gynecol 1993; 168: 156-161.
6. Bronshtein M, Rottem S, Yoffe N, Blumenfeld Z. First-trimester and early second-trimester diagnosis of nuchal cystic hygroma by transvaginal sonography: Diverse prognosis of the septated from the nonseptated lesion. Am J Obstet Gynecol 1989; 161: 78-82.
7. Shulman LP, Emerson DS, Felker RE, Phillips OP, Simpson JL, Elias S. High frequency of cytogenetic abnormalities in fetuses with cystic hygroma diagnosed in the first trimester. Obstet Gynecol 1992; 80: 80-82.
8. Trauffer PML, Anderson CE, Johnson A, Heeger S, Morgan P, Wagner RJ. The natural history of euploid pregnancies with first-trimester cystic hygromas. Am J Obstet Gynecol 1994; 170: 1279-1284.
9. Chervenak FA, Isaacson G, Blakemore KJ, et al. Fetal cystic hygroma, cause and natural history. N Eng J Med 1983; 309: 822-825.
10. Chervenak FA, Isaacson G, Tortora M. A sonographic study of fetal cystic hygromas. J Clin Ultrasound 1985; 13: 311-315.
11. Garden AS, Benzie RJ, Miskin M, Gardner HA. Fetal cystic hygroma colli: Antenatal diagnosis significance, and management. Am J Obstet Gynecol 1986; 154: 221-225.
12. Uslu T, Koç A, Ortaç F, Dündar İ. Fetal cystic hygroma. Anatolian Journal Gynecology Obstetrics 1992; 2: 109-111.
13. Ermiş H, Görk B, Kovancı E, İbrahimoğlu L, Yüksel A. Cystic Hygroma: Prenatal diagnosis and antenatal management. Medical Bulletin of İstanbul Medical Faculty 1995; 28: 32-36.
14. Taşyurt A, Leylek ÖA, Şahin M. Giant cystic hygroma (A case report) (English abstract) Journal of Gynecology and Obstetrics 1996; 10: 116-119.
15. Geembruch V, Hansmann M, Bald R, Zerres K, Schwanitz G, Fodisch HJ. Prenatal diagnosis and management in fetuses with cystic hygromato colli. Eur J Obstet Gynecol Reprod Biol 1988; 29: 241-255.
16. Jones KL. Smith's recognizable patterns of human malformation (4th ed). WB Saunders, Philadelphia 1988, pp: 560-561.
17. Kalousek DK, Seller MJ. Differential diagnosis of posterior cervical hygroma in previable fetuses. Am J Med Genet 1987; 3 (suppl): 83-92.
18. Graham JM, Stephens TD, Shepard TH. Nuchal cystic hygroma in a fetus with previable fetuses. Am J Med Genet 1983; 15: 163-167.
19. Comchock FS, Wapner RJ, Kurtz A, Chatzkel S, Barnhart JS, Lesnick DC. Not all cystic hygromas occur in the Ullrich-Turner Syndrome. Am J Med Genet 1982; 12: 327-331.
20. Abramowicz JC, Warsof SL, Doyle DL, et al. Congenital cystic hygroma of the neck diagnosed prenatally; outcome with normal and abnormal karyotype. Prenat Diagn 1989; 9: 321-327.