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Fetal Nuchal Cystic Hygromata: Associated Malformations and Chromosomal Defects

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Key Words. Fetal cystic hygromata · Prenatal diagnosis · Ultrasonography · Fetal karyotype · Cordocentesis

Abstract. During a 6-year period (1985–1990), blood karyotyping was performed in 44 fetuses with septated, bilateral, dorsal, cervical cystic hygromata. This condition constitutes a different entity from nuchal oedema. There were 33 (75%) chromosomal abnormalities, including Turner's syndrome (n = 31), trisomy 18 (n = 1) and trisomy 21 (n = 1). Congenital heart defects (CHD), mainly coarctation of the aorta, were present in 15 of the fetuses with Turner's and in 1 of the chromosomally normal fetuses. The incidence of CHD was higher in the fetuses with ultrasonographic evidence of moderate/severe hydrops (41%; 13 of 32 cases) than in those with mild or no hydrops (25%; 3 of 12 cases). Although both the biparietal diameter (BPD) and femur length (FL) were reduced in all fetuses, the FL to BPD ratio was below the 5th percentile in 29 of the 33 (88%) chromosomally abnormal fetuses, but in only 4 of the 11 (36%) chromosomally normal ones. In the chromosomally normal group, 3 of the fetuses had multiple pterygium syndromes, and in such cases the risk of recurrence may be high. In contrast, in the group of mutant chromosomal disorders with monosomy or trisomy, the risk of recurrence is in the order of 1%.

Introduction

Nuchal cystic hygromata are developmental abnormalities of the lymphatic system. Although they are rarely seen postnatally [1], they are found in 0.5% of spontaneously aborted fetuses [2]. Prenatal diagnosis by ultrasonography is based on the demonstration of a bilateral, septated, cystic structure, located in the occipitocervical region. This condition should be distinguished from nuchal oedema, which has a high association with trisomies, or unilateral cervical cysts, which are usually detected in the 3rd trimester and have a good prognosis after postnatal surgery.

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Reports on antenatally diagnosed cystic hygromata (tables 1–3) [3–22] have established an association with hydrops fetalis (40–100%), congenital heart defects (CHD; 0–92%) and chromosomal defects (46–90%); the commonest being Turner's syndrome (44–100% of the chromosomal defects). This study extends knowledge on antenatally diagnosed cystic hygromata and reports the findings of associated malformations and chromosomal defects in 44 cases.

Patients and Methods

During a 6-year period (1985–1990), fetal blood karyotyping was performed in 44 patients with fetal dorsal, cervical, septated cystic hygromata (fig. 1). All

Table 1. Summary of reported series on antenatally diagnosed cystic hygromata providing data on the presence of associated chromosomal defects

Author	Gestation weeks	Total n	Abnormal karyotype								
			total		Turner		trisomy 21		trisomy 18		other
			n	%	n	%	n	%	n	%	
Chervenak et al. 1983 [3]	18–29	15	11	73	11	100					
Newman and Cooperberg 1984 [4]	16–26	3	2	67	1	50	1	50			
Redford et al. 1984 [5]	17–26	5	4	80	2	50	1	25	1	25	
Marchese et al. 1985 [6]	16–20	6	5	83	4	80			1	20	
Nicolaides et al. 1985 [7]	16–22	8	6	75	5	83	1	17			
Pearce et al. 1985 [8]	16–26	22	17	77	14	82	2	12	1	6	
Carr et al. 1986 [9]	17–28	5	3	60	2	67	1	33			
Garden et al. 1986 [10]	14–26	16	13	81	11	85			1	8	47XXY
Palmer et al. 1987 [11]	16–26	8	6	63	4	67	1	17			47XX+5p
Gembruch et al. 1988 [12]	13–26	29	17	48	10	59	6	35	1	6	
Hegge et al. 1988 [13]	15–17	4	3	75	2	50	1	25			
Pijpers et al. 1988 [14]	12–25	15	9	60	8	89			1	11	
Abramowicz et al. 1989 [15]	12–31	17	10	59	6	60	3	30	1	10	
Cohen et al. 1990 [16]	10–30	15	10	67	5	50	4	40	1	10	
Eydoux et al. 1989 [17]	12–32	41	19	46	14	74	4	21	1	5	
Miyabara et al. 1989 [18]	12–23	10	9	90	4	44			3	33	47XX+13; 46XX,del4p
Holzgreve et al. 1990 [19]		15	10	67	7	70	2	20	1	10	
Langer et al. 1990 [20]	12–29	17	8	47	7	88	1	12			
Rizzo et al. 1990 [21]	15–27	13	10	77	8	80	1	10	1	10	
Tannirandorn et al. 1990 [22]	16–23	11	7	64	5	71			1	14	47XX+13
Total	12–32	275	179	65	130	73	29	16	15	18	5 3%
Present series	16–26	44	33	75	31	94	1	3	1	3	

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patients were referred from other centres for further assessment of ultrasonographically detectable fetal malformations (cystic hygromata, n = 27; hydrops fetalis, n = 11; encephalocele or cervical spina bifida, n = 5; cervical teratoma, n = 1). The mean gestational age at referral was 19 (range 16–25) weeks.

Detailed ultrasound examination was performed, and the cystic hygromata as well as generalised skin edema, ascites and pleural effusions, if present, were subjectively classified as mild, moderate or severe (table 4). In addition, a systematic search was made for the detection of any other malformations (Aloka SSD-650 or Hitachi EUB 340, 3.5- or 5-MHz curvilinear transducer). Subsequently, the parents gave informed consent for rapid fetal karyotyping, which was performed by cytogenetic analysis of fetal blood obtained by cordocentesis.

The results of the ultrasound examinations and fetal karyotype were given to the referring obstetricians who undertook the further management of the patients. Details on the outcomes of pregnancies were obtained from the referring hospitals.

Results

The maternal age, gestation at referral, fetal karyotype, ultrasound findings and outcome of the 44 fetuses with nuchal cystic

Table 2. Summary of reported series on antenatally diagnosed cystic hygromata providing data on the relation between fetal karyotype and the presence of CHD

Author	Karyotype		
	normal	Turner	other
Chervenak et al. 1983 [3]	?	?	?
Newman and Cooperberg 1984 [4]	1/1	1/1	0/1
Redford et al. 1984 [5]	0/1	1/2	2/2
Marchese et al. 1985 [6]	0/1	0/4	0/1
Nicolaides et al. 1985 [7]	0/2	2/5	0/1
Pearce et al. 1985 [8]	?	?	?
Carr et al. 1986 [9]	0/2	0/2	0/1
Garden et al. 1986 [10]	0/1	0/4	?
Palmer et al. 1987 [11]	?	?	?
Gembruch et al. 1988 [12]	2/12	0/10	3/7
Hegge et al. 1988 [13]	0/1	0/2	0/1
Pijpers et al. 1988 [14]	0/6	0/8	0/1
Abramowicz et al. 1989 [15]	0/7	0/6	0/4
Cohen et al. 1990 [16]	1/5	0/5	0/5
Eydoux et al. 1989 [17]	?	?	?
Miyabara et al. 1989 [18]	1/1	4/4	4/5
Holzgreve et al. 1990 [19]	?	?	?
Langer et al. 1990 [20]	?	?	?
Rizzo et al. 1990 [21]	0/3	0/8	0/2
Tannirandorn et al. 1990 [22]	?	?	?
Total range	0–100%	0–100%	0–100%
Total mean	5/43 (12%)	8/61 (13%)	9/31 (29%)
Present series	1/11 (9%)	14/32 (44%)	0/2 (0%)

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hygromata are shown in table 4. Four of the 31 (13%) mothers whose fetuses had Turner's syndrome were asthmatic and were treated by β-sympathomimetic inhalers. In contrast, the incidence of asthma in 1,688 patients undergoing cordocentesis in our unit for fetal malformations was only 1.5% (26 cases). Another mother with fetal Turner's syndrome was taking warfarin because she had mitral valve replacement. There were no cases of consanguinity or previous pregnancies complicated by fetal hydrops or cystic hygromata.

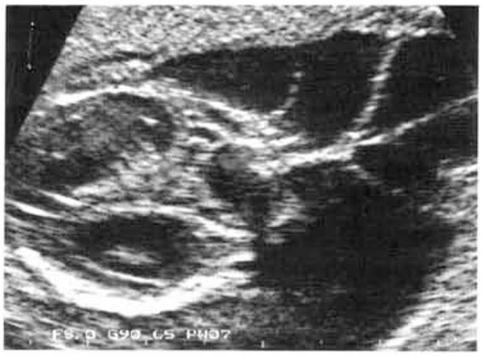

Fig. 1. Ultrasound picture of fetal nuchal cystic hygromata.

Table 3. Summary of reported series on antenatally diagnosed cystic hygromata providing data on the relation between fetal karyotype and the presence of hydrops fetalis

Author	Karyotype		
	normal	Turner	other
Chervenak et al. 1983 [3]	?	?	?
Newman and Cooperberg 1984 [4]	1/1	1/1	0/1
Redford et al. 1984 [5]	0/1	1/2	2/2
Marchese et al. 1985 [6]	0/1	0/4	0/1
Nicolaides et al. 1985 [7]	2/2	5/5	1/1
Pearce et al. 1985 [8]	?	?	?
Carr et al. 1986 [9]	0/2	0/2	0/1
Garden et al. 1986 [10]	0/1	0/4	?
Palmer et al. 1987 [11]	?	?	?
Gembruch et al. 1988 [12]	2/12	0/10	3/7
Hegge et al. 1988 [13]	0/1	2/2	1/1
Pijpers et al. 1988 [14]	0/6	0/8	0/1
Abramowicz et al. 1989 [15]	0/7	0/6	0/4
Cohen et al. 1990 [16]	1/5	0/5	0/5
Eydoux et al. 1989 [17]	?	?	?
Miyabara et al. 1989 [18]	1/1	4/4	4/5
Holzgreve et al. 1990 [19]	?	?	?
Langer et al. 1990 [20]	?	?	?
Rizzo et al. 1990 [21]	2/3	2/8	2/2
Tannirandorn et al. 1990 [22]	?	?	?
Total range	0–100%	0–100%	0–100%
Total mean	9/43 (21%)	15/61 (25%)	12/31 (39%)
Present series	9/11 (82%)	21/32 (67%)	2/2 (100%)

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Table 4. Maternal age (MA), gestation at diagnosis (GA), ultrasound findings, karyotype and outcome (O/C) of fetuses with cystic hygromata (CH)

Case No.	MA	GA	AFV	Hydrops				CHD	Other defects	Karyotype	O/C
				CH	OE	A	P				
1	28	19	N	+++						45,X	TOP
2	31	24	N	++						45,X	TOP
3	31	16	N	+++	++	++				45,X	TOP
4	28	16	N	++	++					45,X	TOP
5	32	17	N	+++	+	+	+			45,X	TOP
6	32	17	N	+++		+				45,X	TOP
7	30	17	N	+++	+		+			45,X	TOP
8	26	20	N	++			+			45,X	TOP
9	30	20	N	+++	+++					45,X	TOP
10	25	18	R	+++	+++					45,X	TOP
11	26	18	R	+	+++					45,X	TOP
12	40	18	R	+++	+	+	+			45,X	TOP
13	35	16	O	+++	++	++				45,X	TOP
14	31	19	O	+++	+++	+	+			45,X	TOP
15	30	18	R	+++	+++	+	+	(COA)		45,X	TOP
16	21	19	O	+++	+++		++	(COA)		45,X	TOP
17	26	20	O	+++	+++	+		(COA)		45,X	TOP
18	19	21	O	+++		++	++	COA		45,X	TOP
19	15	22	N	+++				COA		45,X	TOP
20	39	19	N	+++	+	+	++	COA		45,X	TOP
21	22	20	N	++		++		COA		45,X	TOP
22	26	20	R	+++	+++	++	+	COA		45,X	TOP
23	31	22	R	+++	++	++		COA		45,X	TOP
24	18	21	O	+++	+++	++		COA		45,X	TOP
25	28	22	O	+++	+++	++	+	COA		45,X	TOP
26	27	18	N	++		+	+	COA	H1 (horseshoe kidney)	45,X	TOP
27	37	18	O	+++	++			UVH	H2	45,X	TOP
28	20	21	O	+++	+	+		COA	H1 (horseshoe kidney)	45,X	TOP
29	26	20	O	+++	+++	++	++	COA	Multicystic Kidney	45,X	TOP
30	26	20	O	+++	+++				(Horseshoe kidney)	45,X	TOP
31	30	17	O	+++	+++		+		H2	45,X	TOP
32	37	18	N	+++	++	+			Overlapping fingers	47,XX+18	TOP
33	37	17	R	+++	+++					47,XX+21	TOP
34	37	21	N	+++	++	+			Talipes	46,XX	TOP
35	26	17	N	++	+	+	+			46,XX	TOP
36	40	18	N	+++	+++		+			46,XY	TOP
37	27	19	O	+++	+++					46,XX	TOP
38	31	16	R	+++	+++	+	+			46,XX	TOP
39	24	16	O	+++	+++		+	(COA)	Talipes	46,XX	TOP
40	37	20	N	+++	++		++		H1	46,XX	IUD
41	28	21	N	+++	++	+++	+		H1	46,XY	TOP
42	33	20	N	++					(Multiple pterygium)	46,XY	NND
43	28	20	N	+++	++	++			(Multiple pterygium)	46,XY	TOP
44	28	25	O	+++	+++	+	+		(Multiple pterygium)	46,XY	IUD

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The fetal karyotype was normal in 25% (46XX, n = 6; 46XY, n = 5) and abnormal in 75% (45X, n = 31; 47XX+18, n = 1; 47XX+21, n = 1) of the cases. The relation of maternal age and incidence of chromosomal defects is illustrated in figure 2.

In both the chromosomally normal (CN) and abnormal (CA) fetuses, the mean femur length (FL), the mean biparietal diameter (BPD) and the mean FL to BPD ratio were significantly lower than the appropriate normal mean for gestation (mean difference BPD-CN = −1.993 SD, $t = -3.15$, $p < 0.05$; mean difference BPD-CA = −2.965 SD, $t = -8.85$, $p < 0.0001$; mean difference FL-CN = −1.881 SD, $t = -3.53$, $p < 0.01$; mean difference FL-CA = −3.454 SD, $t = -12.18$, $p < 0.0001$; mean difference FL/BPD-CN = −1.288 SD, $t = -3.89$, $p < 0.01$; mean difference FL/BPD-CA = −3.014 SD, $t = -14.41$, $p < 0.0001$). Furthermore, in the chromosomally abnormal fetuses both the FL and the FL to BPD ratio were significantly lower, but the BPD was not significantly different from the mean values of the chromosomally normal fetuses (fig. 3,4; mean difference FL = −1.573 SD, $t = -2.72$, $p < 0.001$; mean difference FL/BPD = −1.726 SD, $t = -4.21$, $p < 0.0001$; mean difference BPD = −0.972 SD, $t = -1.42$, $p = 0.16$).

In the 31 fetuses with Turner's syndrome, the incidence of CHD was 48% (n = 15); furthermore, 21 (68%) fetuses had moderate/severe generalised skin edema and/or ascites or pleural effusions (table 4). In contrast, CHD and hydrops were found in 9% (n = 1) and 82% (n = 9), respectively, of the 11 chromosomally normal fetuses. Both fetuses with trisomy 18 or 21 were hydropic, but had no CHD. Oligohydramnios or decreased amniotic fluid volume were found in 21 of the 32 (66%) hydropic fetuses and in 2 of the 12 (17%) non-hydropic ones.

The diagnosis of CHD was made antenatally in only 12 of the 16 affected cases. Postmortem examination revealed multiple pte-

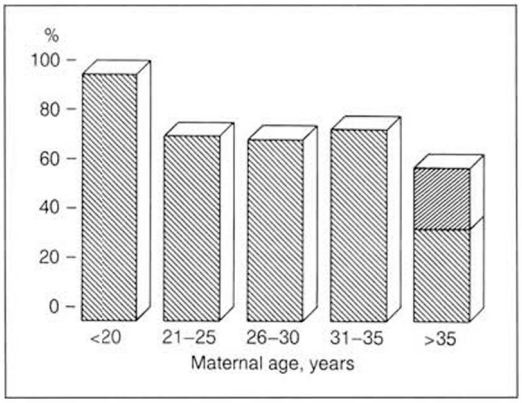

Fig. 2. Relation of maternal age and incidence of chromosomal abnormalities (▨ = Turner syndrome; ▨ = other) in fetuses with nuchal cystic hygromata.

(Footnote to table 4.)

TOP = Termination of pregnancy; NND = neonatal death; IUD = intra-uterine death.

Associated abnormalities included: hydrops with mild (+), moderate (++) or severe (+++) generalised skin oedema (OE), ascites (A) and pericardial or pleural effusions (P); CHD, mainly coarctation of the aorta (COA) and 1 case of univentricular heart (UVH); mild (H1) and moderate hydronephrosis (H2), multicystic or horseshoe kidney; talipes, overlapping fingers and multiple pterygia. The defects detected at post-mortem examination are given in brackets. The amniotic fluid (AFV) was subjectively assessed by ultrasonography as being normal (N), reduced (R) or oligohydramnios (O).

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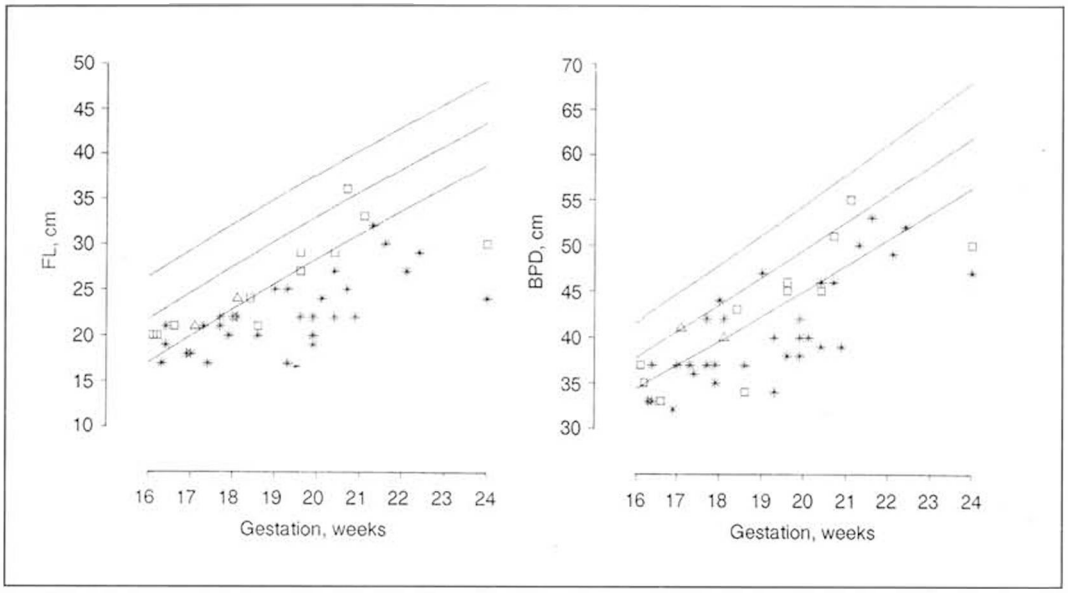

Fig. 3. Fetal FL and BPD in fetuses with cystic hygromata and normal karyotype (□), Turner's syndrome (*), trisomy 21 or trisomy 18 (△) plotted on the appropriate reference range (mean, 95th and 5th percentiles) for gestation.

rygia in 3 of the 5 fetuses with normal male karyotype. Some fetuses with Turner's syndrome also had abnormalities that are not amenable to prenatal diagnosis by ultrasonography, such as horseshoe kidney (n = 3), clitoromegaly (n = 3) or bicornuate uterus (n = 1).

In the 44 cases with cystic hygromata, there were 41 elective terminations of pregnancy, 2 intra-uterine and 1 neonatal death. During the same period, an additional 2 patients were referred with the suspected diagnosis of cystic hygromata at 28 and 35 weeks gestation. In these cases, the nuchal cysts were unilateral, and there was no other malformation; the fetal karyotype was normal 46XX and 46XY, respectively. Both babies were delivered at term and survived after surgical excision of the cysts.

Discussion

Fetal nuchal cystic hygromata, diagnosed in the second trimester of pregnancy, carry a poor prognosis, and 75% are associated with Turner's syndrome. Furthermore, there is a strong association between this chromosomal abnormality and decreased FL to BPD ratio (90%) and CHD (48%). Additionally, fetuses with Turner's syndrome often have renal abnormalities (19%), but the commonest is horseshoe kidney, which may not always be amenable to prenatal diagnosis by ultrasonography. Nevertheless, in 2 of the 3 affected cases, the diagnosis was suspected by the sonographic appearance of the associated bilateral mild hydronephrosis.

The wide range in the reported incidence of hydrops fetalis, cardiac defects and both

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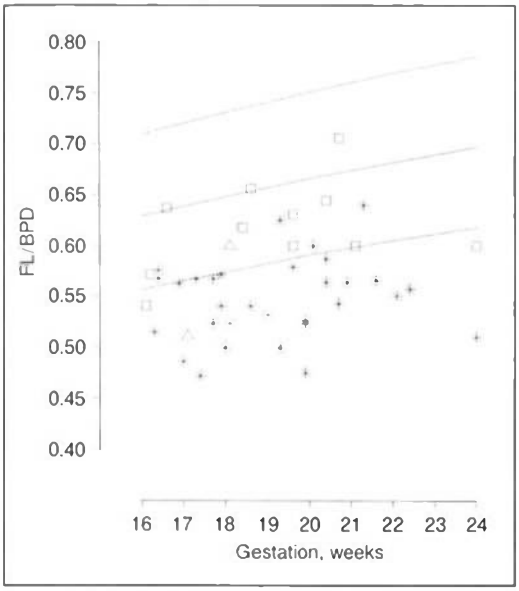

Fig. 4. Fetal FL to BPD ratio in fetuses with cystic hygromata and normal karyotype (□), Turner's syndrome (*), trisomy 21 or trisomy 18 (△) plotted on our reference range (mean, 95th and 5th percentiles) for gestation.

the presence and types of chromosomal abnormalities (tables 1–3) [3–22] may be a consequence of differences in the diagnostic criteria for cystic hygromata used in the previous reports. In the present study, only fetuses with septated, cervical, dorsal hygromata were included, and 75% had chromosomal defects; the commonest being Turner's syndrome (94%). In contrast, in our series of 114 fetuses with nuchal oedema, the incidence of chromosomal defects was 41%, and only 3 (6%) of these had Turner's syndrome [23].

Elejalde et al. [24] in a post-mortem study proposed that cysts of the nuchal area are signs of four causally and pathogenetically different entities: those due to post-mortem subdermic changes, those related to fetal Turner's syndrome, those where the nuchal cyst is associated with a chromosomal, inherited or congenital syndrome, and fourthly those related to an autosomal recessive or sporadic syndrome.

Nuchal cystic hygromata are thought to represent overdistention of the jugular lymphatic sacs as a consequence of failure of communication with the internal jugular vein [25]. Secondary dilatation of the lymphatic channels draining the chest and limbs results in peripheral lymphoedema and development of non-immune hydrops. Clark [26] suggested that the associated cardiovascular malformations, primarily coarctation of the aorta and other defects in the spectrum of left heart obstruction, are the consequence of altered intracardiac blood flow due to compression of the ascending aorta by the distended intrathoracic lymphatic channels. Miyabara et al. [18] noted that these fetuses have, in addition to the cystic hygromata and cardiac defects, generalised lymphatic and thymic hypoplasia. They hypothesised that the underlying mechanism for all these malformations is decreased or delayed migration of neural crest cells and abnormal interaction with the extracellular matrix. Although in our study the incidence of CHD was higher in fetuses with Turner's syndrome (48%) than in those with normal karyotype (9%) and in fetuses with moderate/severe hydrops (41%) than in those with mild or no hydrops (25%), the majority of fetuses with cystic hygromata had no cardiac defect. Nevertheless, since the commonest cardiovascular defect is coarctation of the aorta, this may not be readily identified, even at post-mortem examination, offering a possible explanation for the wide range in the reported incidence in previous studies (table 2).

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Byrne et al. [2] and Carr et al. [9] examined spontaneously aborted fetuses with cystic hygromata and suggested that generalised edema represents strong phenotypic evidence of Turner's syndrome. Thus, all 6 of their fetuses with edema had Turner's syndrome; in contrast 3 of the non-hydropic fetuses had normal karyotype and 1 had trisomy 21. However, in our series the presence of hydrops was not a useful predictor of karyotype because moderate to severe hydrops was present in 21 of the 31 (68%) fetuses with Turner's syndrome and in 9 of the 11 (82%) with normal karyotypes. Similarly, in the previous reports of antenatally diganosed cystic hygromata, hydrops was observed in 21% of chromosomally normal fetuses and in 25% of those with Turner's syndrome (table 3).

Although chromosomally abnormal fetuses are often growth retarded, in fetuses with cystic hygromata, measurement of the abdominal circumference is not a useful predictor of karyotype because this measurement is greatly affected by the presence or absence of ascites and generalised edema. In contrast, measurements of FL and BPD are useful predictors of the fetal karyotype because although both measurements are decreased in fetuses with cystic hygromata, the degree of femur shortening in the chromosomally abnormal fetuses is greater. Furthermore, the deviation from normality in FL increases with advancing gestation (fig. 3).

The incidence of Turner's syndrome, in contrast to that of trisomies, is inversely related to maternal age [27]. In this series, the highest proportion of fetuses with Turner's syndrome was in mothers under 20 years old; in contrast, both fetuses with autosomal trisomies were in mothers over 35 years old (fig. 2). One possible explanation for these findings is that the frequency of monosomy X conceptions in younger mothers is increased. Since over 60% of Turner syndrome fetuses have lost the paternal X chromosome, which signals a very significant paternal contribution to the origin of this syndrome, and since maternal and paternal ages are correlated, this would also imply that there is also an increased risk of younger fathers producing sperm nullisomic for a sex chromosome. An alternative explanation for the inverse maternal age relationship with fetal Turner's syndrome is that there is a relatively high frequency of conception of 45,X embryos in mothers of all ages, but a younger uterus is better able to sustain an abnormal pregnancy, particularly one with a 95% lethality rate [27], than that of an older woman.

The possible unexpected association between maternal asthma and/or β-sympathomimetic inhalation with fetal Turner's syndrome requires further investigation before any firm conclusions can be drawn.

The outcome for fetuses with isolated, usually unilocular, anterior or lateral cervical cysts, diagnosed in the third trimester of pregnancy is good as demonstrated by 2 of our fetuses and 5 previously reported fetuses [20, 28, 29]. In contrast, nuchal cystic hygromata presenting in the second trimester represent a different condition and carry an extremely poor prognosis (table 5).

The risk of recurrence in cases of a mutant chromosomal disorder with monosomy or trisomy is in the order of 1%. There is also one variant of Turner's syndrome in which the karyotype is apparently that of a normal male, but in which there is deletion of the terminal portion of the short arm of the Y chromosome. This is the equivalent region to the part of the X chromosome which

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escapes inactivation and is thus responsible for the difference between a Turner female and a normal female in whom X inactivation occurs [30]. Thus, despite the presence of a Y chromosome, these males are genetically equivalent to a Turner female, because they lack identical DNA sequences. In the group without chromosomal defects, the presence of associated malformations may lead to the diagnosis of a syndrome with a known mode of inheritance. Three of our 5 male fetuses had multiple pterygium syndrome which may have an autosomal dominant, autosomal recessive or X-linked mode of inheritance and therefore a high risk of recurrence [31]. In others, parental consanguinity or a history of affected siblings would suggest a genetic, probably autosomal recessive inheritance and the risk of recurrence might be as high as 25% [16]. In our series, there was no history of parental consanguinity or of affected siblings.

Nuchal cystic hygromata are commonly associated with Turner's syndrome, and they

Table 5. Summary of reported series on antenatally diagnosed cystic hygromata providing data on the outcome of pregnancy

Author	n	Survival		TOP		IUD		NND	
		n	%	n	%	n	%	n	%
Chervenak et al. 1983 [3]	15	0	0	6	67	7	20	2	13
Newman and Cooperberg 1984 [4]	3	0	0	2	67	1	33		
Redford et al. 1984 [5]	5	0	0	5	100				
Marchese et al. 1984 [6]	6	0	0	4	67	2	33		
Nicolaides et al. 1985 [7]	8	0	0	7	88	1	12		
Pearce et al. 1985 [8]	22	2	9	17	77	3	14		
Carr et al. 1986 [9]	5	0	0	1	20	4	80		
Garden et al. 1986 [10]	16	0	0	15	94	1	6		
Palmer et al. 1987 [11]									
Gembruch et al. 1988 [12]	29	1	3	24	83	4	14		
Hegge et al. 1988 [13]	4	0	0	4	100				
Pijpers et al. 1988 [14]	15	0	0	13	7	2	13		
Abramowicz et al. 1989 [15]	17	1	6	9	53	5	29	2	12
Cohen et al. 1989 [16]	15	0	0	12	80	3	20		
Eydoux et al. 1989 [17]									
Miyabara et al. 1989 [18]	10	0	0	10	100				
Holzgreve et al. 1990 [19]									
Langer et al. 1990 [20]	17	1	6	15	88			1	6
Rizzo et al. 1990 [21]									
Tannirandorn et al. 1990 [22]	11	1	9	8	73	2	18		
Total	198	6	3	152	77	35	18	5	2
Present series	44	0	0	41	93	2	5	1	2

TOP = Termination of pregnancy; NND = neonatal death; IUD = intra-uterine death.

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represent a different pathological entity from nuchal oedema, which is primarily associated with trisomies. In the differential diagnosis of fetuses with cystic hygromata, low maternal age, cardiac defects and decreased FL to BPD ratio are suggestive of Turner's syndrome, and the risk of recurrence is low. In the group of chromosomally normal fetuses, the parents should be warned that the risk of recurrence may be high and further investigations are necessary to elucidate a possible genetic syndrome.

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