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Antenatal diagnosis of cystic hygroma or nuchal pad – report of 92 cases with follow up of survivors

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Abstract

Information on the outcome of pregnancy was collected on 92 fetuses with cystic hygroma or nuchal pad, identified prenatally. Forty three (47% of the total) were associated with abnormal karyotype. Twenty five (27%) had normal karyotype but an additional abnormality was identified on ultrasound scan. There were 10 liveborn babies in this group of whom seven had significant problems postnatally. In twenty four (26%) cases the cystic hygroma or nuchal pad was an isolated finding. Seventeen (89% of those in which the pregnancy was electively continued) were liveborn and reported to be normal.

Those with a normal karyotype, no other anomaly identified on antenatal scan, and smaller non-septate lesions have a good prognosis.

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Keywords: cystic hygroma, antenatal diagnosis, nuchal thickening.

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It is now well established that an increase in thickness at the back of the fetal neck identified on ultrasound scan from early pregnancy onwards is a marker for karyotypic abnormality. It may also be an early manifestation of fetal hydrops with diverse aetiology, or a true isolated cystic hygroma.[1–5] This study was initiated to provide more information for parents on prognosis for those identified with a nuchal thickening or cystic hygroma on antenatal scan, and in particular for those subsequently found to have a normal fetal karyotype.

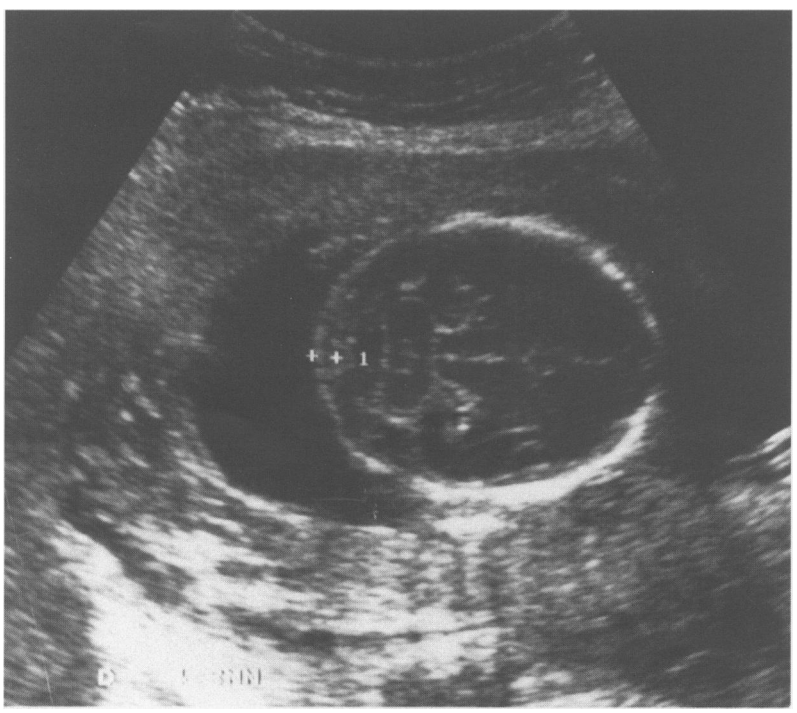

Figure 1 Ultrasound scan of fetal head at 20 weeks of gestation. Nuchal thickness measurement of 4 mm (within normal range).

Methods

All fetuses recorded as having an increased thickness at the back of the fetal neck (defined as a nuchal thickness of 6 mm or greater), described on the antenatal ultrasound report as nuchal pad, thickening, or fetal cystic hygroma between April 1989 and April 1994 at the John Radcliffe Maternity Hospital, Oxford, were identified. Gestational age at diagnosis was between 12 and 24 weeks in all but one case (33 weeks). The nature of the lesion was recorded; whether it was described as septate or non-septate and whether it was considered to be a large lesion (greater than 10 mm) or not ($\leq$10 mm). Cases were ascertained both from routine scans on local women and from those referred for a second opinion from the Oxford Region. Post mortem reports were obtained for cases in which the pregnancy was terminated or where there was an intrauterine or neonatal death. In all those cases resulting in the birth of a living child birth neonatal records were examined. For those children now aged over 1 year (21 children), a report from the general practitioner was obtained, recording information about health and development.

Results

A total of 92 cases were identified. Figure 1 demonstrates a nuchal measurement of 4 mm at 20 weeks of gestation – a normal scan. Figures 2 and 3 show scans of the fetal nuchal area with an 8 mm non-septate thickening at 20 weeks and 14 mm septate lesion at 17 weeks, respectively.

Results were analysed in three groups. Table 1 gives information on maternal age, scan findings, size and nature (septate or non-septate) of the lesion and gestation at diagnosis in 43 cases with confirmed karyotypic abnormality classified according to karyotype.

Table 2 gives details of the second group of 25 cases identified with normal karyotype but with an additional abnormality identified on scan, classified according to pregnancy outcome. Mean (standard deviation) maternal age

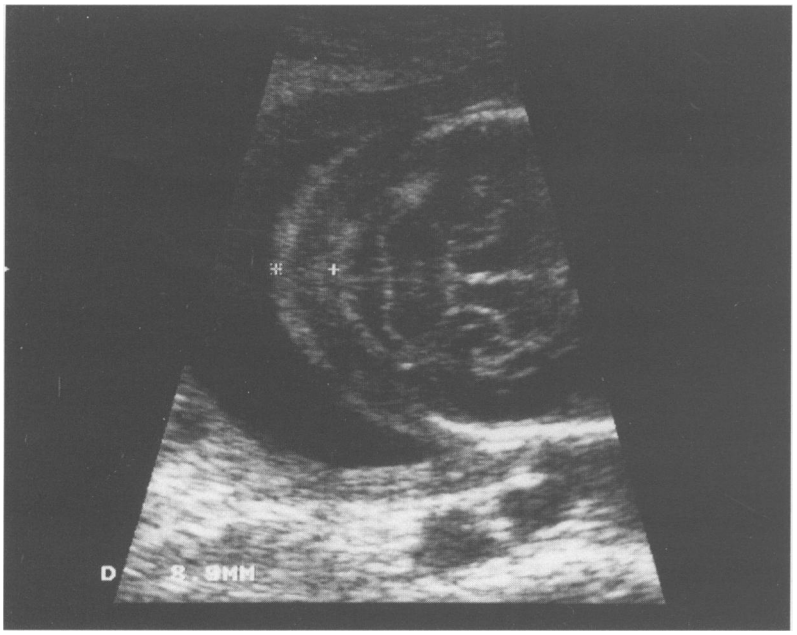

Figure 2 Ultrasound scan of fetal head at 20 weeks of gestation showing non-septate nuchal thickening of 8 mm.

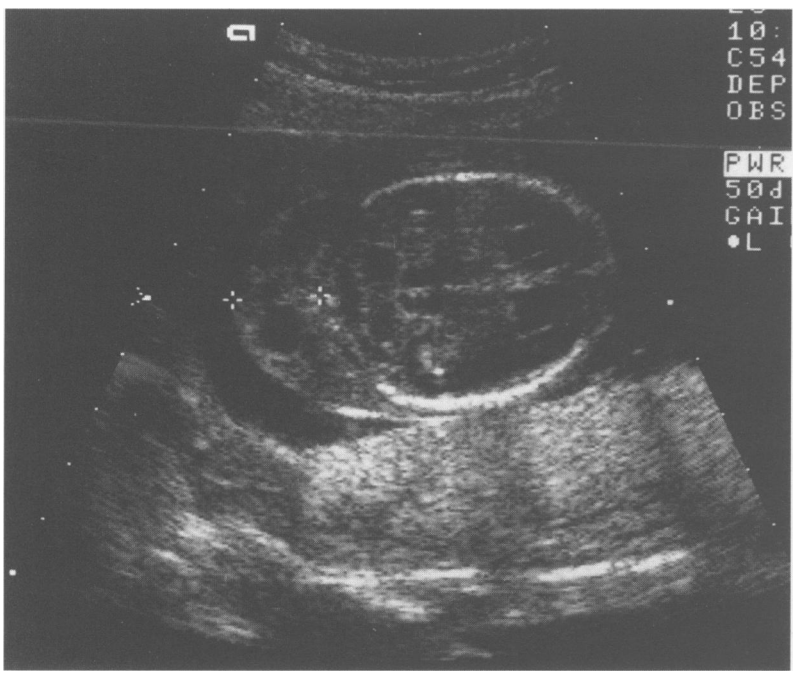

Figure 3 Ultrasound scan of fetal head at 17 weeks of gestation showing septate nuchal thickening of 14 mm.

in this group at date of diagnosis was 30 (6) years. There were 10 liveborn babies in this group, seven of whom have or have had a major problem. Two have undiagnosed syndromes with dysmorphism and developmental delay – one of these babies has features similar to those seen in his mother and it is thought that these may represent a Mendelian dominant disorder. One girl has congenital hydrocephalus, as was suspected on prenatal scan. There were two diaphragmatic herniae, one suspected prenatally and successfully repaired at birth. The other occurred in a child considered normal at birth but who, on investigation of poor feeding and vomiting at 6 months of age, was found to have a small left sided diaphragmatic defect with herniation of some small and large bowel into the chest. Surgery was successful and the child is now a normal 3 year old. One case was identified as having pleural effusions in addition to a septate cystic hygroma at 32 weeks gestation and had pleuro-amniotic shunts inserted. Following delivery at 37 weeks the baby girl had a persistent chylothorax and severe respiratory problems. She was discharged from hospital still oxygen dependent at the age of 7 months. Now aged 4, she has some of the features of Noonan's syndrome, although not enough to confirm the diagnosis. A fetus identified as having nuchal thickening plus mild ventriculomegaly and mild bilateral renal pelvic dilatation has been diagnosed as having the X-linked overgrowth Simpson-Golabi-Behmal syndrome. A previous pregnancy had been terminated following similar findings plus cleft palate and cystic kidneys. The mother's brother has subsequently been diagnosed with this syndrome. This child, now aged 4, has the features of the syndrome and is slightly developmentally delayed. Three babies in this group seem to be normal and have had no clinically relevant problems. One had a large septate lesion diagnosed at 12 weeks of gestation. Transient pleural effusions and ascites developed during the second trimester. The neck lesion was visible on scan until 34 weeks and a normal baby boy was delivered at term with slightly loose skin at the back of the neck. The additional scan findings in the other two normal children in this group, now aged 1 and 3 years, were choroid plexus cysts with amniotic band, and bilateral renal pelvic dilatation, respectively.

Table 3 gives information on the 24 cases with an isolated neck lesion – normal karyotype

Table 1 Forty three cases with cystic hygroma or nuchal pad plus abnormal karyotype

	Trisomy 21 (n=16)	*Trisomy 18 (n=11)*	*Trisomy 13 (n=1)*	*Monosomy X (n=11)*	*Triploidy (n=1)*	*Structural unbalanced (n=3)*
Maternal age, years (mean (SD))	35 (8)	33 (9)	29	29 (9)	27	37 (2)
Gestation at diagnosis (weeks)	13–20	14–18	20	13–24	17	15–19
Size of lesion <or=10 mm/>10 mm	10/6	4/7	1/0	1/10	1/0	3/0
Non-septate/septate	10/6	5/6	1/0	1/10	1/0	3/0
Additional abnormality on scan	1 A-V canal defect	10 General hydrops (3), IUD (2), structural abnormality (5)	1 Cleft lip and palate, hydronephrosis	5 Hydrops, cystic kidney (1)	1 Ascites	1 Hydronephrosis
Outcome of pregnancy	TOP 14, LB 2	TOP 9, IUD 2	TOP 1	TOP 7, IUD 2, LB 2	TOP 1	TOP 3

TOP: termination of pregnancy; IUD: intrauterine death; LB: live birth.

Table 2 Twenty five cases with cystic hygroma or nuchal pad, normal karyotype, plus additional abnormality identified on scan

Outcome of pregnancy	*TOP (n=8)*	*IUD (n=6)*	*NND (n=1)*	*Liveborn with significant problems (n=7)*	*Liveborn normal (n=3)*
Gestation (weeks at diagnosis)	13–20	12–22	20	18–33	12, 19, 20
Size of lesion ≤10 mm/ >10 mm	3/5*	1/5*	0/1	6/1*	2/1*
Non-septate/ septate	3/5*	1/5*	1/0	6/1*	2/1*
Additional abnormality on scan	*Ventriculomegaly, talipes, BRPD *Hydrops Hydrops *Hydrops, pleural effusions, hydronephrosis Diaphragmatic hernia, hyperechogenic kidneys Hypoplastic left heart Short limbs, CLP *Short limbs, hydrops	Ascites *BRPD+cardiomyopathy+ polyhydramnios Hydrops Hydrops Hydrops *Pericardial effusion, unilateral hydronephrosis	Oligohydramnios+ pleural effusions	BRPD, CPC, talipes BRPD, ventriculomegaly Ventriculomegaly L. pleural effusion – diaphragmatic hernia. BRPD *Bilateral pleural effusions. Some features of Noonan's syndrome Ventriculomegaly (mild), BRPD	*Transient pleural effusions and ascites CPC, amniotic band BRPD
Final clinical diagnosis/post mortem findings	*CH, talipes, BRPD, dysmorphic, no diagnosis *Large CH, hydrops *AR multiple pterygia syndrome *Hydrops, cleft palate, L. hydronephrosis Diaphragmatic hernia, BRPD, pulmonary hypoplasia Hypoplastic left heart SRPS, Majewski type *?SR(P)S or thanatophoric	Hydrops *IUD, 30/40 Noonan's syndrome CH, hydrops CH, hydrops CH, hydrops *IUD at 27/40, no post mortem	Premature dysmorphic features, ? due to oligohydramnios	Undiagnosed? Dominant dysmorphic/development delay syndrome Undiagnosed dysmorphic/developmental delay/epilepsy Congenital hydrocephalus Diaphragmatic hernia (repaired at birth). Developmental normal age 1 y Diaphragmatic hernia (diagnosed and repaired 6 months after birth). Developmental normal age 4 y Persistent chylothorax after delivery Simpson-Golabi-Behmal syndrome	*Slightly loose skin at back of neck; normal male baby Normal 1 y.old Normal 3 y old

CH: cystic hygroma; BRPD: bilateral renal pelvic dilatation; SRPS: short rib polydactyly syndrome; CPC: choroid plexus cysts; CLP: cleft lip and palate; AR: autosomal recessive. *Neck lesion >10 mm.

and no other abnormality identified on scan. Mean (SD) maternal age at time of diagnosis was 31 (6) years. Five of these pregnancies were electively terminated; three of these were large lesions (>10 mm), and four were septate. Post mortem examination confirmed isolated cystic hygroma in two cases, cystic hygroma plus cleft palate in a third, but in two fetuses no abnormality was detected. There were two intrauterine deaths: one had a large neck lesion diagnosed at 12 weeks, and the other nuchal thickening at 22 weeks. Amniocentesis and fetal blood sampling, respectively, had been performed a week before the intrauterine deaths were diagnosed. In both cases a post-mortem examination revealed no abnormality. Seventeen babies in this group were liveborn. Information on all of these was available at birth – all reported to be normal babies without major problems on discharge from the maternity hospital.

Information on 10 children, now aged more than 1 year, was obtained from the general practitioner. The age range of the five boys and five girls is 1 to 5 years. Birthweights ranged from 2970 to 5875 g. All are considered to be developmentally normal. Minor problems reported are coloboma, hydrocoele (cleared spontaneously), and tongue tie (in one child); asthma, and enlarged tonsils. One child had a small patent ductus arteriosus and had hyaline membrane disease and hypocalcaemia in the neonatal period. She is now a developmentally normal 5 year old.

Discussion

The intention of this study was to describe the outcome of pregnancy in fetuses documented as having a nuchal thickness of 6 mm or more at any gestational age. In recent years sonographic identification of a more subtle degree of nuchal abnormality has been described – nuchal translucency of >3 mm between 11 and 13 weeks gestation.[6] However, at the time of initiation of this study (1989) this had not been described and its usefulness for general population screening is still being evaluated.[7]

In this study the population studied was selected and because of the referral pattern involving other centres no inference on incidence of nuchal thickening/cystic hygroma can be made. However, it helps with some unanswered questions. Those parents relieved that chromosome analysis has given a normal result often remain worried that there is something else wrong with their child. There is little

Table 3 Twenty four cases with isolated cystic hygroma/nuchal pad

Outcome	*TOP (n=5)*	*IUD (n=2)*	*Liveborn (n=17)*
Gestation (weeks) at diagnosis	13–14	12; 22	11–23
Size of lesion ≤10 mm/>10 mm	2/3	1/1	15/2
Non-septate/septate	1/4	1/1	15/2
Postmortem information/final clinical diagnosis	CH confirmed (2), CH+cleft palate (1), NAD (2)	NAD (2), ?related to FBS, amniocentesis	Information at birth on 17, and at ages 1–5 years on 10, all developmentally normal. Minor abnormalities reported-coloboma, hydrocoele, PDA, asthma

TOP: Termination of pregnancy; IUD: Intrauterine death; NAD: Nothing abnormal detected; FBS: Fetal blood sample.

information available giving details of survivors beyond the neonatal period.

This study confirms the well documented association between abnormal karyotype and nuchal thickening.[1 2] Although as expected the mean maternal age was higher in the mothers of fetuses with autosomal trisomy, 13 out of 28 were aged under 35 years at the time of diagnosis and so on the basis of maternal age alone would not have been offered amniocentesis. Overall, in this study there were 48 cases with isolated neck lesions of whom 24 (50%) had a chromosome abnormality and of the 44 with additional anomaly on scan, 19 (43%) had abnormal karyotype (table 4) – the addition of another anomaly did not increase the risk for chromosome abnormality.

Twenty five cases had normal karyotype but another abnormality identified on scan. Eight of these pregnancies were electively terminated. There were 10 survivors of whom only three have had no problems at all and only five (29% of those not terminated) are known to be developmentally normal (table 5). Two of these five had diaphragmatic herniae (one diagnosed six months after birth). Increased central venous pressure may have caused the nuchal thickening.

Of the 24 fetuses with a normal karyotype and isolated neck lesions, five pregnancies were terminated. Two pregnancies resulted in intrauterine death and 17 (89% of those pregnancies that were not electively terminated) in livebirths (table 5). None of the seventeen had major problems identified at examination shortly after birth, and information from their general practitioners on 10 children, now aged between 1 and 5 years, shows that they are developing normally.

Several single gene defects have been reported in association with nuchal pad and cystic hygroma.[2 5 8–10] In this study one boy has Simpson-Golabi-Behmel syndrome. There are two possible cases of Noonan's syndrome, one liveborn girl, now aged 4, and one which resulted in intrauterine death. Other single gene defects in this group resulted in termination of pregnancy or intrauterine death. The autosomal recessive multiple pterygia syndrome. Majewski type short ribbed polydactyly syndrome (SRPS), and possible SRPS or thanatophoric variant, were diagnosed following post mortem and *x* ray examinations.

The terminology used in describing thickening at the back of the fetal neck is confusing and the spectrum of severity is wide. The two ends of the spectrum – non-septate nuchal thickening and massive multilocular cystic hygroma – may have distinct aetiologies although they both carry an increased risk for karyotypic abnormality. The aetiology of fetal cystic hygroma is thought to be a failure in the development of the normal communication between the jugular lymphatic system with the venous system, resulting in stasis of lymph fluid.[1 3] If no communication occurs this is a lethal condition, but if a link is made the cystic hygroma collapses and there may be the stigmata well known in Turner's syndrome such as pterygium colli, peripheral lymphoedema, posteriorly rotated ears, low hairline. Whether non-septate nuchal thickening is caused by dysfunctional communication between the lymphatic and venous systems, with perhaps earlier correction, is not known. The natural history of these lesions is very variable, some large lesions being transient and others starting, when first seen, as non-septate nuchal thickenings which become fluid filled, septate, and eventually develop generalised hydrops. None of the babies in this study had a classic cystic hygroma present at birth that required surgery.

The importance of the nature and size of the neck lesions has been investigated before.[5 11] Bronshtein *et al* reported a live birth rate of 94% in a study of fetuses with non-septated cystic hygromas against only 12% in the septated group. Abnormal karyotype was present in 5·7% of the non-septate group compared with 72% of the septate group. In the present study lesions measuring less than 10 mm were, with only one exception, described as non-septate and lesions measuring over 10 mm were septate (two exceptions). There was a higher risk of chromosome abnormality in the non-septate cases than that described by others. Overall, there were 51 cases described as non-septate and 41 as septate. In the non-septate group 21 out of 51 (41%) had an abnormal karyotype. Twenty two of 41 (54%) septate cases were karyotypically abnormal. Amongst the 27 liveborn babies with normal chromosomes, 23 (85%) had non-septate lesions identified on antenatal scan. Thus although survival with good outcome following demonstration of very large septate lesions in both karyotypically normal and abnormal (Turner's syndrome) fetuses is reported here and previously,[12 13] in the absence of a chromosome abnormality a non-septate lesion carries a better prognosis.

This study confirms a high risk for adverse outcome associated with the finding of swelling behind the fetal neck at antenatal scan regardless of the size of the lesion. Recommended management includes karyotyping, detailed ultrasound scan between 18 and 22 weeks of gestation with particular reference to the heart, and, in the event of any other abnormality being identified on scan, the offer of genetic counselling. After birth, assessment by a neonatal paediatrician is indicated. There is some reassurance for a good outcome for those with a normal karyotype and no other abnormality identified on scan.

Table 4 Number (percentage) with abnormal karyotype according to whether the neck lesion was isolated or not

	(n=)	Abnormal karyotype (%)
Isolated neck lesion	48	24 (50)
Neck lesion+other scan abnormality	44	19 (43)

Table 5 Outcome data in karyotypically normal pregnancies which were not electively terminated according to whether the neck lesion was isolated or not

	(n=)	Liveborn 'normal' children (%)
Isolated neck lesion (normal karyotype)	19	17 (89)
Neck lesion+other scan abnormality (normal karyotype)	17	5 (29)

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