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Isolated single umbilical artery and fetal karyotype

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KEYWORDS: chromosomal abnormalities; karyotype; single umbilical artery; ultrasound

ABSTRACT

Objective *To determine the need for fetal karyotyping in cases of an isolated single umbilical artery (SUA) identified during the second-trimester routine anomaly scan.*

Methods *All patients booked for antenatal care and delivery in our hospital are offered two ultrasound scans in pregnancy, one at 11–13 weeks' gestation as part of screening for chromosomal defects and another at 20–23 weeks for detailed fetal examination. In addition we examine patients referred from other hospitals because of suspected fetal abnormalities during their routine second-trimester scan. We performed a search of the database to retrieve all cases with an SUA and reviewed the ultrasound findings, fetal karyotype and pregnancy outcome.*

Results *There were 643 cases with SUA, including 424 (65.9%) where the condition was isolated, 133 (20.7%) with one major fetal defect and 86 (13.4%) with multiple defects. The incidence of chromosomal abnormalities was 0% in the isolated SUA group, 3.7% in those with one defect and 50.7% in those with multiple defects. The commonest chromosomal abnormalities were trisomy 18, trisomy 13 and triploidy, which together accounted for 82.9% of cases.*

Conclusion *The finding of an SUA should prompt the sonographer to search for fetal defects and if these are found the risk for chromosomal abnormalities is increased. In cases of apparently isolated SUA there is no evidence of increased risk of chromosomal abnormalities.*

INTRODUCTION

A single umbilical artery (SUA) is found in about 1 in 200 deliveries[1]. Ultrasonographic studies in the second and third trimesters of pregnancy have reported chromosomal abnormalities in about 10% of fetuses with SUA, most commonly trisomy 18 (Table 1)[2–19]. It has therefore been recommended that such pregnancies should be offered fetal karyotyping. However, in most chromosomally abnormal fetuses there were fetal defects in addition to the SUA and it is not certain whether karyotyping is necessary in cases with isolated SUA.

The aim of this study was to examine the association between isolated SUA diagnosed during the routine second-trimester scan and chromosomal abnormalities.

METHODS

In our fetal medicine unit we examine two groups of patients. Firstly, women referred from other hospitals because of suspected fetal abnormalities during their routine second-trimester scan. Secondly, all patients booked for antenatal care and delivery in our hospital. In the second group, we offer two ultrasound scans in pregnancy, one at 11–13 weeks' gestation as part of screening for chromosomal defects[20,21] and another at 20–23 weeks for detailed fetal examination according to a standard protocol.

All scans are carried out by sonographers who have obtained The Fetal Medicine Foundation Certificate of Competence in the 20–23-week scan (http://www.fetalmedicine.com). The standard examination includes the use of color-flow mapping in the fetal pelvis to visualize the two umbilical arteries and the diagnosis of SUA. Patients with SUA and additional defects are counseled that the risk for a chromosomal abnormality is increased and they are offered fetal karyotyping. If the condition is isolated the parents are informed that it is unlikely that the fetus is chromosomally abnormal. Demographic characteristics and ultrasound findings are recorded in a fetal database at the time of the examination, and data on pregnancy outcome are obtained from the hospital records.

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Table 1 Prenatal ultrasonographic studies on single umbilical artery (SUA) reporting on the incidence of chromosomal defects both in the total group and in those with isolated SUA

Reference	*Gestational age at ultrasound scan (weeks)*	*Abnormal karyotype (n)*						
		Total n *(%)*	*Trisomy 18*	*Trisomy 13*	*Trisomy 21*	*Triploidy*	*Other*	*Isolated*
Abuhamad *et al.* (1995)[2]	25 (10–40)	6/77 (7.8)	4			1	1	0/55
Catanzarite *et al.* (1995)[3]	16–39	10/82 (12.2)	4	2	1	1	2	0/45
Parilla *et al.* (1995)[4]	25 (15–35)	0/50 (0.0)						0/50
Sepulveda *et al.* (1996)[5]	20 (15–36)	5/55 (9.1)	3	1			1	0/55
Blazer *et al.* (1997)[6]	14–16	0/46 (0.0)						0/40
Sener *et al.* (1997)[7]	20–37	1/15 (6.7)	1					1/10
Ulm *et al.* (1997)[8]	21 (16–41)	9/103 (8.7)	3	2		2	2	0/74
Chow *et al.* (1998)[9]	29 (16–41)	5/118 (4.2)	2	2			1	0/81
Lee *et al.* (1998)[10]	15–26	10/61 (16.4)	4	1	2		3	2/24
Farrell *et al.* (2000)[11]	18–22	0/22 (0.0)						0/22
Geipel *et al.* (2000)[12]	21 (13–39)	10/102 (9.8)	5	2			3	0/59
Rinehart *et al.* (2000)[13]	22 (10–34)	7/27 (25.9)	1	1	2	1	2	0/9
Budorick *et al.* (2001)[14]	2nd trimester	11/57 (19.3)	4	3	1		3	0/31
Gornall *et al.* (2003)[15]	19 (19–20)	5/107 (4.7)	1	1	1	1	1	1/87
Martinez-Payo *et al.* (2005)[16]	20 (≥ 13)	2/40 (5.0)	1	1				0/33
Volpe *et al.* (2005)[17]	17–22	6/40 (15.0)	3				3	1/24
Granese *et al.* (2007)[18]	16–23	6/61 (9.8)	1	1	2	1	1	1/39
Lubusky *et al.* (2007)[19]	16–22	19/102 (18.6)	8	1	5	1	4	0/77
Total		112/1165 (9.6)	45	18	14	8	27	6/809*

*Three cases of trisomy 18 and three cases of trisomy 21.

We searched the fetal database to identify all patients with an SUA among those singleton pregnancies undergoing second-trimester scan between January 2002 and December 2008.

RESULTS

Search of the fetal database identified 686 cases with SUA but in 43 (6.3%) of these there was no pregnancy follow-up and they were excluded from further analysis. In 397 (61.7%) of the 643 cases the patients were referred from other hospitals because of the diagnosis of either SUA or other abnormalities. In 246 cases the women booked for antenatal care and delivery in our hospital and 185 (75.2%) of these had previously had an 11–13 weeks' scan as part of screening for chromosomal defects.

The median maternal age of the 643 cases was 33 (range, 15–45) years and the median gestational age at the ultrasound scan was 22 (range, 18–25) weeks. Detailed ultrasound examination demonstrated that in 424 (65.9%) cases SUA was isolated, in 133 cases (20.7%) there was one major defect and in 86 (13.4%) there were multiple defects.

Fetal karyotyping was carried out by amniocentesis at the request of the parents in 214 of the 643 (33.3%) cases with SUA. There were also six cases with multiple defects where postnatal karyotyping was performed. The 423 pregnancies with no karyotyping included 367 that resulted in the live birth of babies with no phenotypic features of a major chromosomal defect, and these babies were assumed to be euploid. There were also 56 cases of SUA where the pregnancies resulted in intrauterine fetal death or termination with no fetal karyotyping, and these cases were not considered in the further analysis of the data (Table 2).

In the 424 pregnancies with isolated SUA there were 406 cases with either prenatal karyotyping or live birth and they were all considered to be euploid. There were also 18 pregnancies resulting in fetal death with no karyotyping. In 15 of these the death occurred at a median gestation of 28 (range, 21–40) weeks and the likely cause of death was severe fetal growth restriction, with birth weight below the 5th centile. There was also one fetal death due to placental abruption at 29 weeks' gestation and two unexplained deaths at 27 and 40 weeks, respectively. None of these 18 dead fetuses had any dysmorphic features suggestive of an aneuploidy.

In 133 cases of SUA with one major fetal defect there were 77 cases that had prenatal karyotyping and in four there were chromosomal abnormalities (one case each of inversion 8p, deletion 14q, deletion 2q and unbalanced translocation resulting in derivative 13q). There were also 31 live births that were considered to be euploid and 25 terminations of pregnancy with unknown karyotype (Table 3). Therefore the incidence of chromosomal abnormalities in this group (omitting the terminations with unknown karyotype) was 3.7% (4 of 108).

In 86 cases of SUA and multiple fetal defects there were 73 (84.9%) cases with karyotyping and in 37 there were chromosomal abnormalities (trisomy 18, $n = 20$; trisomy 13, $n = 9$; triploidy, $n = 5$; Turner syndrome, $n = 2$; deletion 4p, $n = 1$). In 12 cases the pregnancies were terminated at the request of the parents and in one pregnancy there was a fetal death; in these 13 cases no karyotyping was performed. Therefore, the incidence of

Table 2 Karyotype results in fetuses or neonates with single umbilical artery in the presence and absence of other defects, and outcome of cases without karyotyping

	Karyotyping		*No karyotyping*			
Single umbilical artery	*Total*	*Abnormal*	*Total*	*Liveborn*	*IUD*	*TOP*
Isolated ($n = 424$)	70	0	354	336	18	0
One major defect ($n = 133$)	77	4 (5.2%)	56	31	0	25
Multiple defects ($n = 86$)	73	37 (50.7%)	13	0	1	12
Total ($n = 643$)	220	41 (18.6%)	423	367	19	37

Data are given as *n* or *n* (%). IUD, intrauterine death; TOP, termination of pregnancy.

Table 3 Findings in the group with single umbilical artery and one major fetal defect

	Karyotyping		*No karyotyping*		
Defect	*Total*	*Abnormal*	*Total*	*Liveborn*	*Termination*
Anencephaly ($n = 1$)	1	0	0	0	0
Holoprosencephaly ($n = 1$)	0	0	1	0	1
Ventriculomegaly ($n = 11$)	5	1*	6	1	5
Dandy–Walker syndrome ($n = 7$)	3	0	4	0	4
Spina bifida ($n = 4$)	3	0	1	0	1
Facial cleft ($n = 2$)	1	0	1	1	0
Cardiac abnormality ($n = 53$)	33	2†‡	20	14	6
Diaphragmatic hernia ($n = 3$)	2	0	1	1	0
Unilateral lung agenesis ($n = 1$)	1	0	0	0	0
Esophageal atresia ($n = 1$)	1	1§	0	0	0
Renal abnormality ($n = 25$)¶	9	0	16	10	6
Exomphalos ($n = 7$)	7	0	0	0	0
Limb or skeletal abnormality ($n = 12$)	7	0	5	3	2
Hydrops ($n = 5$)	4	0	1	1	0
Total ($n = 133$)	77	4	56	31	25

*Inversion 8p. †Deletion 2q. ‡Unbalanced translocation der 13. §Deletion 14q. ¶Including renal agenesis, dysplasia, hydronephrosis, duplex and pelvic kidneys.

chromosomal abnormalities in this group was 50.7% (37 of 73).

In the 246 cases booked for antenatal care and delivery in our hospital the incidence of single or multiple defects in the second-trimester scan was 4.3% (8 of 185) in those with prior first-trimester screening and 24.6% (15 of 61) in those without (chi-squared $P < 0.001$). All the chromosomal abnormalities were from the group that had not undergone first-trimester screening. In the 397 women referred from other hospitals the incidence of single or multiple fetal defects found in the second-trimester scan was 49.4% (196 of 397), which was significantly higher than the incidence in women booked for antenatal care and delivery in our hospital both in the total population (9.3% (23 of 246), chi-squared $P < 0.001$) and in the subgroups with prior first-trimester screening (4.3%, $P < 0.001$) and without such prior screening (24.6%, $P < 0.001$).

DISCUSSION

The findings of this study confirm the results of previous reports of a high association between an SUA and chromosomal abnormalities, most commonly trisomy 18[2–19]. However, in all chromosomally abnormal fetuses there were one or more fetal defects. The risk for chromosomal abnormalities can increase from about 4% for a single defect to 50% for multiple defects.

The overall prevalence of one or more defects in our population of fetuses with SUA is not applicable to all populations because we had a mixture of patients referred to a specialist center and those booked for routine care in our hospital. This is well illustrated by our finding that the incidence of such defects was about 50% in the referred patients and about 10% in those examined routinely. An additional finding is that in the era of first-trimester screening the incidence of major defects diagnosed in the second-trimester is substantially reduced. In the second-trimester scan the SUA is isolated in more than 95% of cases with prior first-trimester screening compared to about 75% in those without such prior screening.

A study of pregnancies undergoing chorionic villus sampling at 11–14 weeks' gestation reported that the incidence of chromosomal abnormalities in cases with SUA was 50%, and that two-thirds of these had trisomy 18[22]. First-trimester screening and diagnosis of aneuploidies and other major defects often results in termination of pregnancy and consequently a substantial

reduction in the incidence of such abnormalities in the second trimester. First-trimester screening by a combination of fetal nuchal translucency, fetal heart rate and maternal serum free β-human chorionic gonadotropin (β-hCG) and pregnancy-associated plasma protein-A (PAPP-A) can identify about 90% of fetuses with trisomy 21 and about 95% of those with trisomies 18 and 13 at a false-positive rate of 3.1%[23]. Additionally, in the first-trimester scan it is easy to detect Turner syndrome because about 90% of cases present with a substantially increased nuchal translucency thickness[24] and also triploidy, which presents with severe asymmetrical fetal growth restriction and major reduction in free β-hCG and PAPP-A (digynic type) or partially molar placenta and substantially increased serum free β-hCG (diandric type)[25].

The finding of an SUA in the second trimester should prompt the sonographer to undertake a systematic search for fetal defects. As shown in our study the risk for chromosomal abnormalities can increase from about 4% for a single defect to 50% for multiple defects. Indeed it is possible that this high incidence of aneuploidies in such cases may have been underestimated, because in about 15% of our cases the pregnancies were terminated without fetal karyotyping.

In fetuses with SUA where after careful examination no other associated anomalies are found there is no indication for fetal karyotyping because in such fetuses we found no evidence of increased risk for aneuploidies. In 18 of the 424 cases in this group, including 15 with severe growth restriction, there were fetal deaths and the karyotype was not known. Although the risk of both fetal growth restriction and death in chromosomally abnormal fetuses is increased it is unlikely that our cases had chromosomal defects because they were phenotypically normal. In a previous study before the introduction of first-trimester screening for aneuploidies we examined 458 growth-restricted fetuses at 17–39 weeks' gestation and reported that the incidence of chromosomal defects was 19%, but in 96% of aneuploid fetuses there were easily recognizable multisystem defects[26].

The finding of an SUA should prompt the sonographer to search for fetal defects, and if these are found the risk for chromosomal abnormalities is increased. In cases of apparently isolated SUA there is no evidence of increased risk for chromosomal abnormalities.

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