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———— ORIGINAL ARTICLE ————

Perinatal results following the prenatal ultrasound diagnosis of single umbilical artery

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Objective. To study the perinatal results in our population, following the prenatal ultrasound diagnosis of a single umbilical artery (SUA), as this alteration is associated with fetal malformations, chromosomal abnormality, and poor perinatal results.
Materials and methods. A retrospective review of all obstetric ultrasounds carried out between October 2000 and December 2003 in our service, obtaining the postnatal results of the fetuses diagnosed with an SUA.
Results. From a total of 5987 pregnant patients examined by ultrasound scan at 20th week, an SUA was found in 40 cases, representing an incidence of 0.7%. Of these, 84.6% were normal pregnancies at birth and 15.4% presented other malformations and/or chromosomal abnormalities. No aneuploidy was found in pregnancies where there were no other associated findings in the ultrasound scan at 20 weeks. All cases with serious congenital malformations accompanying the SUA were diagnosed prenatally. There was a 5% of perinatal mortality rate among our fetuses with SUA, which represents a mortality rate 10 times greater than the overall rate among our patients.
Conclusions. The ultrasound discovery of an SUA implies the meticulous search for other associated malformations, and in the absence of these, the risk of a chromosomal abnormality is very low, unless it is a high-risk patient. However, the growth and well-being of the fetus must be carefully monitored in the last 3 months, although the ultrasound scan does not show any other associated alterations.

Key words: chromosomal abnormality; congenital malformation; single umbilical artery; ultrasound scan; umbilical cord

Ultrasound scans are carried out as part of the normal practice for the correct monitoring of both low- and high-risk pregnancies. There are unquestionable benefits obtained from the practice of carrying out an ultrasound scan before the 24th week, among others, they enable the perinatal mortality rate to be lowered (1). The

Spanish Gynecology and Obstetrics Association (SEGO) recommends that an ultrasound scan be carried out at around the 20th week of both low- and high-risk pregnancies. This exploration is basically designed to make a prenatal diagnosis of congenital malformations and to discover markers of chromosomopathies. In this ultrasound scan, fetal measurements are made, an assessment is made of the fetal morphology, and the placenta, number of vessels in the cord, and quantity of amniotic fluid are examined (2, 3). The abnormality in the number of cord vessels is not considered a minor ultrasound marker by the SEGO (4).

As the single umbilical artery (SUA) has been associated with fetal abnormalities such as structural malformations, chromosomopathies, and growth abnormalities, we believe that the investigation of the perinatal results in fetuses diagnosed with an SUA in the normal ultrasound procedure would be of interest. In most cases, this diagnosis was made at the 20th week scan, when, as we previously mentioned, the number of cord vessels is routinely checked in our service.

The aim of this study is to determine the clinical significance of an SUA in our population, and if possible, the most appropriate plan of action, when this diagnosis is made during pregnancy.

Materials and methods

A retrospective analysis is performed including all cases with SUA diagnosed from October 2000 to December 2003. In this period, a total of 42 fetuses had a diagnosis of SUA, although two cases were not included because of the lack of data.

For some of the data obtained, case–control studies were carried out, with two controls per case ($n = 82$). To do this, we used births chosen at random, occurring within 4 consecutive days, in the same hospital where patients with SUA are handled.

In our population, all pregnant women were referred for second trimester scan to our department, being carried out by a small group of US-specialized obstetricians. This means that the ultrasound screening is carried out on a heterogeneous population that includes both low- and high-risk patients; therefore, an important bias is ruled out.

The ultrasound scans were carried out with a General Electrics Pro 500 equipment, using a sectorial probe at 3.5 mHz. In most cases, color Doppler examination was used to find the two umbilical arteries, which surround separately both sides of the vesical wall of the fetus and later leave the fetal abdominal wall joint (Fig. 1), diagnosing SUA in the absence of one of them (Fig. 2). We believe that this method is more reliable than the scanning of the number of vessels in a cross section of a free loop of umbilical cord (Fig. 3).

In cases of SUA, if the ultrasound scan did not present any other morphological alterations or visible markers of chromosomopathies at that time, and it was a low-risk pregnancy (maternal age < 35 years old), the patient was given a new appointment to repeat the ultrasound scan within 4–6 weeks, with the aim of confirming the diagnosis of there being no other alterations. If one of the aforementioned premises was not met, a study of the fetal karyotype was indicated.

Data on postnatal normality or pathology were obtained either by pediatric reports (if available) or by a telephonic questionnaire answered by the mothers.

To study the results, we designed a protocol of data capture. Data particularly assessed were age of the mother, stage of pregnancy at which the diagnosis was made, karyotype of the fetus or newborn (NB), the stage of gestation at which the pregnancy ended, birth via, malformations described at birth and their correlation with the ultrasound diagnosis, weight at birth, and some markers of fetal well-being (APGAR and cord pH).

The statistical analysis was carried out with the computer package spss for Windows 10.0. For qualitative variables,

Fig. 1. Color Doppler ultrasound at 20 weeks of gestation where both umbilical arteries are seen surrounding the fetal bladder.

Fig. 2. Single umbilical artery at 24 weeks of gestation.

Fig. 3. Cross section of the umbilical cord at 24 weeks of gestation where only two vessels are seen.

the summary of data was carried out using frequency and percentage distribution tables. The quantitative variables are shown as an average ± standard deviation. In order to compare quantitative variables the Student *t*-test was used, or nonparametrical tests, in the event that they were not normal (Mann–Whitney *U*-test). The chi-square test was used to evaluate the association between qualitative variables, and the exact test of Fisher was also used when necessary. The level of statistical significance was estimated at $P < 0.05$.

Results

Between October 2000 and December 2003, 42 cases of SUA were diagnosed among a total of 5987 patients, scanned at around the 20th week of pregnancy, thus representing a prevalence of 0.7%. The average stage of pregnancy at which the SUA was diagnosed was at 20 weeks and 4 days, although the earliest diagnosis was made at 13 weeks.

The average age of the mother in the case group was 30.8 ± 5.4 years and in the control group 31.2 ± 5.4 years, with no significant differences found between them ($P = 0.6$). Neither were there differences in the gestational age at birth (38 ± 3.9 vs. 38.4 ± 2.5). The number of cesarean sections tended to be greater in the SUA cases (23.8%) than in the controls (17.9%) ($P = 0.086$).

The average birth weight in the SUA cases was 2945 ± 746 g which was significantly lower than the control weights (3202 ± 475 g) ($P = 0.028$).

We found five cases with ultrasound alterations associated with the finding of SUA (12%) and four patients with ultrasound alterations among the controls (4%) (Table I). Therefore, we obtained a relative risk (RR) of associated ultrasound alterations, if there was an SUA, 2.85 times greater than in pregnancies without SUA, although we did not obtain a statistical significance ($P < 0.14$, 95% CI 0.7–0.12).

In the postnatal evaluation, six NBs, among the SUA cases, presented malformations (15%) and two among the controls (2.3%) (Table II), obtaining a risk 7.4 times greater of presenting malformations after birth if diagnosed with SUA ($P < 0.012$, 95% CI 1.4–38.8).

Malformations associated with SUA were not diagnosed prenatally in two cases, which consisted in two hypospadias.

Of the six cases of SUA with associated anomalies, five presented genitourinary malformations (83%). Thus, in our patients, we have found that, if there is an alteration associated with SUA, it is very likely that it will be genitourinary.

On studying the karyotypes of the fetuses with ultrasound alterations associated with SUA, we obtained three normal karyotypes, one trisomy 13, and one trisomy 18 (40% karyotype anomalies in fetuses with SUA and associated anomalies) (Table I).

There were two deaths among the SUA cases, the first antenatally in the 38th week of pregnancy (due to unknown causes with autopsy and karyotype being normal) and the second due to abruptio placentae in the 27th week of pregnancy, which was also a fetus with premature IUGR (the autopsy confirmed the left pyelocalyceal ectasia already diagnosed during pregnancy, with normal karyotype). This means that the perinatal mortality was 5% among SUA cases, almost 10 times higher than the rest of our population, not including the two cases with altered karyotype, as in the case of trisomy 18, termination of pregnancy (TOP) was chosen, and the NB with trisomy 13 remained alive. If we look at the perinatal mortality of fetuses with SUA, without other associated malformations, we find that it is 2.8%, five times greater than that of the Hospital where almost all of the births in our health area are attended. We did not find significant differences on studying the sex of the NB with and without malformations, the age of the mother, the birth weight or the Apgar, among the cases. Neither did we find differences between the cases and the controls in the aforementioned variables except, as we already mentioned, in the birth weight.

Discussion

Because SUA may be associated with other fetal malformations, karyotype anomalies, preterm birth, and low birth weight, the routine study of the umbilical cord is interesting.

Table I. Prenatally detected anomalies and karyotype

Cases ($n = 5$; 12%)	Controls ($n = 4$; 4%)
Fallot tetralogy (46XY) (1 case)	Vesical dilatation (1 case)
Renal agenesis and dilation of posterior horns of lateral ventricle (46XX) (1 case)	Duodenal atresia and hydramnios (1 case)
Enlarged nuchal fold (47XY+13) (1 case)	Oligohydramnios (1 case)
Pyelocalyceal dilatation (46XX) (1 case)	Intrauterine growth retardation (1 case)
Choroid plexus cyst (47XX+18) (1 case)	

Table II. Postnatally detected malformations

Cases ($n = 6$; 15%)	Controls ($n = 2$; 2.3%)
Fallot Tetralogy (46XY) with hypospadias (1 case)	Agenesis of ocular globes (1 case)
Right renal agenesis and dilation of posterior horns of lateral ventricle (4XX) (1 case)	Duodenal atresia (1 case)
Polydactyly, musculoskeletal alt., mental deficiency (47XY+13) (1 case)	
Right kidney ectasia (46XX) (1 case)	
Hypospadias (2 cases)	

The incidence of SUA varies according to the population studied. It is greater among the population with a high risk of malformation and in the prenatal studies carried out. So it varies between 3.1 per 1000 in the Gornall series (5), obtained postnatally in a general population, and 1.2–2% (6) in prenatal series. It is three or four times more frequent in twin pregnancies.

As is known, the umbilical cord normally contains one vein and two arteries. The development of the vasculature of the cord begins at the end of the third week of gestation. Apart from the two arteries and the vein, the cord also contains the vitelline duct and its vessels (vitelline artery and vein), the latter normally regressing at the end of the third month. Three mechanisms are suggested to explain the absence of one of the two arteries: primary agenesis, secondary atrophy, and persistence of the only existing artery in the early stages of the embryonic life (7). It is believed that atrophy is the most frequent mechanism. When both umbilical arteries close and the vitelline artery persists, it has been classified as an SUA type II and corresponds with approximately 1.4% of SUA cases. This type is normally associated with sirenomelia or caudal regression syndrome (8). It is thought that the cause is insufficient irrigation of the terminal portion of the embryo, and depending on the stage of development at which this occurs, it will produce different clinical symptoms, so that if it occurs later, the result may be a fetus with no malformations (9). Hypoplasia of one of the two umbilical arteries is much less frequent, affecting 0.03% of pregnancies, and is associated with IUGR, maternal diabetes, polyhydramnios, and congenital cardiopathy, described in a case of trisomy 18. This hypoplasia probably represents an incomplete form of SUA (10).

The ultrasound diagnosis is normally carried out with color Doppler imaging, seeking the intrapelvic route of the umbilical arteries of the fetus, their passage around the fetal bladder to then enter the anterior abdominal wall and form part of the umbilical cord, although it is also useful to scan the free loop of the cord in a cross section, to see the number of vessels (11). The cord should be assessed in several sections, from the fetus to the placenta because as we previously mentioned, it is possible that the number of vessels varies along the length of the cord, and in these cases, they may also be linked to fetal malformations (12).

The false-positive rates vary between 20 (13) and 6% (14), but the most recent series are closer to the latter (15), and this decrease is related to the use of color Doppler imaging and the higher resolution of the equipment. When the study is carried out on NB, it is found that detection may be as low as 30% (5).

It is not clear why this anomaly is linked to other fetal anomalies, and although there is no unique malformative pattern, the most frequent anomalies are genitourinary, followed by cardiovascular malformations, whilst gastrointestinal malformations are the least frequent (5). We have found these same data in our cases. In the study by Gornall et al. (5), the diagnosis of congenital anomaly was almost seven times greater in the case group than in the control group. In this study, 20% of the fetuses with SUA had an added congenital anomaly. This is not always detected by ultrasound; thus, the anomalies not diagnosed may be 7% (16). Table III summarizes the studies published and the variation of the findings of malformations and chromosomal alterations between one author and another (5, 6, 14, 17). As can be seen, our data are very similar to the Gornall series, which was carried out postnatally, studying NB with SUA diagnosed immediately after birth when checked by the pediatrician. Our results show that the systematic scanning with Doppler for the number of umbilical arteries in the 20th week of pregnancy is probably a good diagnostic method. Our findings are also similar to the Blazer study, carried out on a general population, as regards the finding of malformations, except no chromosomopathy is found, this perhaps being due to the limited number of cases in both series. However, they differ greatly from the results of Geipel et al. but this study, although it assesses the low- and high-risk population, carried out a routine ultrasound scans in only 42 of 102 cases, and the rest had some associated risk factor, such as advanced age of the mother, twin pregnancy,

Table III. Comparison of findings among different authors

Author	Number of cases	Isolated SUA (Ultrasonography normal)		SUA with malformations by ultrasonography	
		With chromosomal abnormality	Without chromosomal abnormality	With chromosomal abnormality	Without chromosomal abnormality
Abuhamad*	77	57 (74%)	0	14 (18.2%)	6 (7.8%)
Blazer†	46	40 (87%)	0	6 (13%)	
Geipel†	102	59 (57.8%)	0	33 (32.4%)	10 (9.8%)
Gornall‡	107	86 (80.4%)	1 (0.6%) (Down's syndrome)	14 (13%)	6 (6%)
Ourselves†	40	33 (82.5%)	0	5 (12.5%)	2 (5%)

*High-risk population study based on prenatal findings.
†High- and low-risk population study based on prenatal data.
‡High- and low-risk population study based on postnatal data.

altered biochemical screening, or suspected associated congenital malformations in a previous ultrasound, i.e. it is probably a biased population from the outset.

The diagnostic attitude on finding an SUA may be controversial. All authors agree that if an SUA is found, a detailed ultrasound must be carried out, by an ultrasound specialist, in order to detect other associated fetal anomalies (8, 16). If a careful ultrasound scan reveals the SUA as an isolated finding, the handling of the pregnancy seems debatable. Catanzarite et al. (18) advise that, if no other associated malformations are found, the ultrasound scan should be repeated between 22 and 24 gestational weeks and that it should be monitored by ultrasound to detect possible alterations in fetal growth, reserving the invasive procedures for karyotyping only in the case of IUGR or if other associated structural anomalies appear. Other authors recommend adding a fetal echocardiography to the ultrasound exploration if an SUA is found as an isolated finding (15, 19). Abuhamad (14) also recommends the use of an echocardiography, as in 9% of the cases they found an associated cardiac malformation, but a genetic study is only carried out if associated anomalies are detected by ultrasound. Chow et al. (16), bearing in mind that they find 7% of alterations that are not detected by ultrasound, offer genetic advice and even fetal karyotyping, as the risk of genetic alterations may be high. Persutte and Hobbins (8) recommend a high-resolution ultrasound scan, fetal echocardiography, genetic study, exhaustive fetal monitoring, and careful fetal assessment after birth. As there is a 25% risk of an aneuploidy if another anomaly is detected by ultrasound (17), it appears that a fetal chromosomal study should be carried out. If other anomalies are not found, carrying out a karyotype is debatable, as an aneuploidy is found in 1% of fetuses (5) only in one article (Table III);

therefore, other factors should be borne in mind such as the age of the mother. Few authors advise a genetic study if there are no other associated alterations (5, 17, 19). However, the possibility of undetected alterations before the birth must be discussed with parents.

In view of our data, and even we have not found any chromosomal alteration in fetuses with isolated SUA, we believe that complete information should be offered to the parents in order to facilitate their decision making. The aneuploidies most frequently found are 18 and 13 (14, 15), although it is found in others such as 22 (17).

The presence of an SUA as an isolated finding, in studies on the general population, is linked to a poor perinatal result, when compared with fetuses with two arteries. They tend to be of low weight, premature and twice as much below the 10 percentile in weight; likewise, a cesarean section is more frequent. Perinatal mortality is greater, six times greater for fetuses with SUA, and three times greater for fetuses with SUA and without associated malformations (5).

It is not clear why fetuses with SUA achieve poorer perinatal results, even without associated malformations. It has been demonstrated that these cords have a lower number of spirals (20) and lesser quantity of Wharton jelly, which make them less resistant in situations of stress, such as birth or compression of the umbilical cord, and may act in synergy with other unfavorable circumstances (21). In fact, we had a fetal loss in the 38th week of pregnancy of a completely normal fetus which, 48 hr before death, had normal umbilical fetal Doppler velocimetry.

All of these data lead us to postulate that a reasonable monitoring system would be: a systematic screening for SUA at the 20th week ultrasound; in the event of an SUA diagnosis, ultrasound monitoring, with particular assessment of the fetal heart in prenatal diagnosis clinics; and
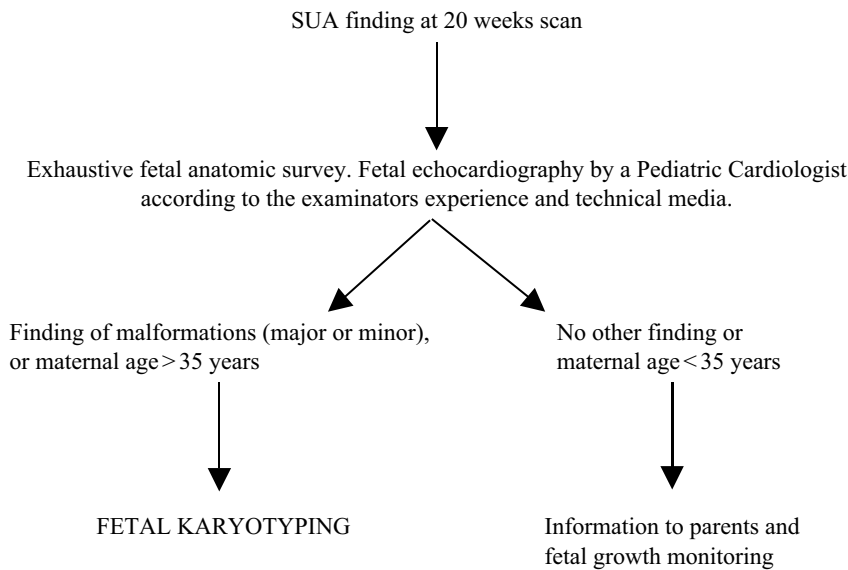
SUA finding at 20 weeks scan

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Exhaustive fetal anatomic survey. Fetal echocardiography by a Pediatric Cardiologist according to the examinators experience and technical media.

Finding of malformations (major or minor), or maternal age > 35 years

No other finding or maternal age < 35 years

↓

FETAL KARYOTYPING

Information to parents and fetal growth monitoring

Fig. 4. Diagnostic algorithm.

the study of fetal karyotype if there are other associated malformations, or ultrasound markers of chromosomopathy as well as other unfavorable factors such as the maternal age. In any case, exhaustive information should be provided to parents who shall take the final decision, bearing in mind the possible malformations not diagnosed by ultrasound, and whether they require a fetal karyotype study to be carried out. If subsequent explorations are normal, antenatal fetal growth and wellbeing controls should be carried out, considering it as a pregnancy at risk until birth (Fig. 4).

Acknowledgments

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