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Dilemmas in the management of twins discordant for anencephaly diagnosed at 11 + 0 to 13 + 6 weeks of gestation

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KEYWORDS: anencephaly; cord occlusion; embryo reduction; first trimester; twins

ABSTRACT

Objective *To help develop an evidence-based approach to the best management of twin pregnancies discordant for anencephaly.*

Methods *We retrospectively examined the management and outcome of 18 pregnancies discordant for anencephaly diagnosed at 11 + 0 to 13 + 6 weeks of gestation in our center. We combined these data with those from other publications. In total, there were 44 dichorionic pregnancies that were managed expectantly (*n = *35) or by selective feticide (*n = *9) and 19 monochorionic pregnancies that were managed expectantly. We also reviewed the literature to ascertain the outcome of monochorionic twin pregnancies undergoing cord occlusion.*

Results *In the 35 dichorionic pregnancies that were managed expectantly, 20 (57.1%) developed polyhydramnios at 25–31 weeks; 13 were managed expectantly, five had amniodrainage and two had selective feticide. In 34 of the 35 cases the non-anencephalic twin was liveborn at a median gestation of 36 (range, 28–39) weeks and in six (17.6%) of these it was born before 33 weeks. In the dichorionic pregnancies that had selective feticide, there was one miscarriage and eight (88.9%) live births at a median gestation of 37 (range, 30–40) weeks and in one (12.5%) of these it was born before 33 weeks. In the monochorionic pregnancies, four (21.1%) anencephalic fetuses died at 20–32 weeks and in three of these the normal co-twin also died. In the 16 (84.2%) cases resulting in the live birth of the normal twin, delivery occurred at a median gestation of 33 (range, 27–39) weeks and in six (37.5%) of these it was before 33 weeks. Ultrasound-guided bipolar cord coagulation in 92 pregnancies, mostly complicated by twin reversed arterial perfusion sequence or severe twin-to-twin transfusion syndrome, was associated with a survival rate of 77.2% and early preterm delivery rate of 31.0%.*

Conclusion *Dichorionic twins discordant for anencephaly are best managed with serial ultrasound examinations for early diagnosis of polyhydramnios, which can then be treated either by amniodrainage or selective feticide. In monochorionic twins it is uncertain whether the best management is expectant or by cord occlusion.*

INTRODUCTION

Effective screening for chromosomal abnormalities provided by the measurement of fetal nuchal translucency (NT) thickness has led to the widespread introduction of ultrasound scanning at 11 + 0 to 13 + 6 weeks of gestation[1,2]. During the first-trimester scan many major fetal abnormalities, such as anencephaly, can be reliably diagnosed[3–5]. In twin pregnancies the prevalence of anencepaly is higher than in singletons and the prevalence of discordance for anencephaly is higher in monochorionic than in dichorionic twins[6,7].

In twin pregnancies discordant for anencephaly the two main risks to the survival of the normal twin arise from the spontaneous death of the anencephalic fetus or the development of polyhydramnios[7]. The first-trimester diagnosis of such pregnancies raises a major dilemma as to which is the best management strategy to minimize the risk of death and early premature delivery of the normal twin. In dichorionic twin pregnancies discordant for anencephaly the two management options are selective feticide by intracardiac injection of potassium

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chloride (KCl) or serial ultrasound examinations for early diagnosis of polyhydramnios, which can then be treated either by amniodrainage or selective feticide[7]. In monochorionic twin pregnancies, which are characterized by the presence of communicating blood vessels between the two fetoplacental circulations, the main option is expectant management. The alternative is to consider selective feticide by cord occlusion[8–10].

The aim of this study was to review the management and outcome of twin pregnancies discordant for fetal anencephaly diagnosed in our center at 11 + 0 to 13 + 6 weeks of gestation. We also reviewed the outcome of such pregnancies reported in other series and the outcome of monochorionic twin pregnancies subjected to selective cord occlusion to help develop an evidence-based approach to the best management of twin pregnancies discordant for anencephaly.

METHODS

The Harris Birthright Research Centre for Fetal Medicine is a referral center for fetal diagnosis and therapy. In all pregnancies examined at 11 + 0 to 13 + 6 weeks of gestation the fetal crown–rump length and NT thickness are measured and a systematic search is made for any major structural abnormalities[1,2]. In twin pregnancies chorionicity is determined by examining the inter-twin membrane at its junction with the placenta[11]. In twin pregnancies discordant for major abnormalities the parents are counselled as to the options of continuing the pregnancy, termination of the pregnancy or selective feticide. In dichorionic twins selective feticide is performed by the ultrasound-guided fetal intracardiac injection of KCl. Demographic characteristics and ultrasound findings at each visit are recorded in a fetal database at the time of the examination. Data on pregnancy outcome are obtained from the patients themselves, their general practitioners or the maternity units in which they delivered.

A computer search was made to identify all twin pregnancies that were examined between January 1993 and September 2004. The selection criteria were that firstly, in each pregnancy both fetuses were alive at the scan performed at 11 + 0 to 13 + 6 weeks and secondly, at least one of the fetuses had anencephaly. A MEDLINE search was performed to identify English language publications on the prenatal diagnosis and management of twin pregnancies with anencephaly and those reporting on cord occlusion in monochorionic twins. A database of individual cases was made from these publications and our cases.

RESULTS

Our data

The computer search of our database identified 18 pregnancies (13 dichorionic and five monochorionic) with one normal and one anencephalic fetus diagnosed at 11 + 0 to 13 + 6 (median 12) weeks' gestation. In the dichorionic pregnancies the parents elected termination in one case, selective feticide in three and expectant management in nine. In the selective feticide group the three pregnancies resulted in delivery at 37, 38 and 40 weeks, respectively, and the normal babies survived. In the expectant management group all nine normal babies survived after delivery at 33–37 (median 36) weeks; in six cases the anencephalic baby was liveborn but died in the neonatal period, in two cases the fetus died *in utero* and in one selective feticide was carried out at 25 weeks because of the development of polyhydramnios. There were another four cases where polyhydramnios developed at 28–30 weeks. Two were managed expectantly, and in two amniodrainage was carried out. The decision in favor of amniodrainage, rather than expectant management, was based on the severity of the polyhydramnios, both in terms of the discomfort to the patient and any associated shortening of the cervical length to less than 25 mm.

In the monochorionic pregnancies, the parents elected termination in three cases and expectant management in two; these resulted in delivery at 32 and 39 weeks, respectively, and the normal babies survived while the anencephalic ones died in the neonatal period.

Combined data from previous publications

The literature search identified six papers that reported data on the management of their own series of twin pregnancies discordant for anencephaly[7,12–16]. In total, including our cases, there were 44 dichorionic pregnancies that were managed expectantly ($n = 35$) or by selective feticide ($n = 9$) and 19 monochorionic pregnancies that were managed expectantly (Tables 1–3).

In the 35 dichorionic pregnancies that were managed expectantly, 20 (57.1%) developed polyhydramnios at 25–31 weeks; 13 were managed expectantly, five had amniodrainage and two had selective feticide (Table 1). In 34 of the 35 cases the non-anencephalic twin was liveborn at a median gestation of 36 (range, 28–39) weeks and in six (17.6%) of these it was born before 33 weeks.

In the nine dichorionic pregnancies that had selective feticide, at a median gestation of 17 (range, 12–21) weeks, there was one miscarriage 3 weeks after the procedure and eight (88.9%) live births at a median gestation of 37 (range, 30–40) weeks; in one (12.5%) of these the twin was born before 33 weeks (Table 2).

In the 19 monochorionic pregnancies that were managed expectantly, 10 developed polyhydramnios at 26–29 weeks and in three of these amniodrainage was carried out (Table 3). In four (21.1%) of the 19 cases the anencephalic fetus died at 20–32 weeks and in three of these the normal co-twin also died. In the 16 (84.2%) cases resulting in the live birth of the normal twin, delivery occurred at a median gestation of 33 (range, 27–39) weeks, and in six (37.5%) of these it occurred before 33 weeks.

Table 1 Expectant management of dichorionic twin pregnancies discordant for anencephaly

			Anencephalic twin		*Normal twin*	
Reference	*Diagnosis (weeks)*	*Polyhydramnios and management*	*Outcome*	*Gestation (weeks)*	*Outcome*	*Gestation (weeks)*
Present study	12	No polyhydramnios	Fetal death	32	Live birth	36
Leeker & Beinder 2004[13]	21	No polyhydramnios	Neonatal death	28	Live birth	28
Sebire *et al*. 1997[7]	19	No polyhydramnios	Neonatal death	34	Live birth	34
Sebire *et al*. 1997[7]	18	No polyhydramnios	Neonatal death	35	Live birth	35
Present study	13	No polyhydramnios	Neonatal death	36	Live birth	36
Lipitz *et al*. 1995[12]	21	No polyhydramnios	Neonatal death	36	Live birth	36
Lipitz *et al*. 1995[12]	14	No polyhydramnios	Neonatal death	36	Live birth	36
Lipitz *et al*. 1995[12]	14	No polyhydramnios	Neonatal death	36	Live birth	36
Present study	12	No polyhydramnios	Neonatal death	36	Live birth	36
Present study	13	No polyhydramnios	Neonatal death	37	Live birth	37
Lipitz *et al*. 1995[12]	20	No polyhydramnios	Neonatal death	37	Live birth	37
Sebire *et al*. 1997	20	No polyhydramnios	Neonatal death	38	Live birth	38
Lipitz *et al*. 1995[12]	21	No polyhydramnios	Neonatal death	39	Live birth	39
Lipitz *et al*. 1995[12]	16	No polyhydramnios	Neonatal death	39	Live birth	39
Lipitz *et al*. 1995[12]	20	No polyhydramnios	Neonatal death	39	Live birth	39
Gul *et al*. 2005[16]	28	Polyhydramnios. No amniodrainage	Neonatal death	29	Fetal death	29
Lipitz *et al*. 1995[12]	21	Polyhydramnios. No amniodrainage	Neonatal death	29	Live birth*	29
Lipitz *et al*. 1995[12]	15	Polyhydramnios. No amniodrainage	Neonatal death	31	Live birth	31
Gul *et al*. 2005[16]	29	Polyhydramnios. No amniodrainage	Neonatal death	32	Live birth	32
Present study	12	Polyhydramnios. No amniodrainage	Fetal death	32	Live birth	33
Lipitz *et al*. 1995[12]	14	Polyhydramnios. No amniodrainage	Neonatal death	33	Live birth	33
Present study	12	Polyhydramnios. No amniodrainage	Neonatal death	34	Live birth	34
Gul *et al*. 2005[16]	35	Polyhydramnios. No amniodrainage	Neonatal death	35	Live birth	35
Lipitz *et al*. 1995[12]	26	Polyhydramnios. No amniodrainage	Neonatal death	36	Live birth	36
Lipitz *et al*. 1995[12]	14	Polyhydramnios. No amniodrainage	Neonatal death	36	Neonatal death†	36
Gul *et al*. 2005[16]	31	Polyhydramnios. No amniodrainage	Neonatal death	37	Live birth	37
Lipitz *et al*. 1995[12]	21	Polyhydramnios. No amniodrainage	Neonatal death	37	Live birth	37
Lipitz *et al*. 1995[12]	18	Polyhydramnios. No amniodrainage	Neonatal death	37	Live birth	37
Leeker & Beinder 2004[13]	28	Polyhydramnios. Amniodrainage at 31 weeks	Neonatal death	32	Live birth	32
Gul *et al*. 2005[16]	31	Polyhydramnios. Amniodrainage at 31 weeks	Neonatal death	32	Live birth	32
Present study	14	Polyhydramnios. Amniodrainage at 28 and 31 weeks	Neonatal death	34	Live birth	34
Present study	12	Polyhydramnios. Amniodrainage at 31 weeks	Neonatal death	34	Live birth	34
Sebire *et al*. 1997[7]	18	Polyhydramnios. Amniodrainage at 30, 32 and 34 weeks	Neonatal death	35	Live birth	35
Present study	11	Polyhydramnios. Feticide	Feticide	25	Live birth	36
Sebire *et al*. 1997[7]	17	Polyhydramnios. Feticide	Feticide	30	Live birth	36

*Polyhydramnios in the sac of the non-anencephalic fetus with duodenal atresia. †Ebstein anomaly.

Table 2 Selective feticide in dichorionic twin pregnancies discordant for anencephaly

	Anencephalic twin		*Normal twin*	
Reference	*Outcome*	*Gestation (weeks)*	*Outcome*	*Gestation (weeks)*
Present study	Feticide	12	Live birth	37
Present study	Feticide	12	Live birth	38
Present study	Feticide	13	Live birth	40
Leeker & Beinder 2004[13]	Feticide	15	Live birth	39
Sebire *et al*. 1997[7]	Feticide	17	Live birth	37
Sebire *et al*. 1997[7]	Feticide	18	Live birth	30
Sebire *et al*. 1997[7]	Feticide	18	Miscarriage	21
Sebire *et al*. 1997[7]	Feticide	20	Live birth	37
Sebire *et al*. 1997[7]	Feticide	21	Live birth	37

Table 3 Expectant management of monochorionic twin pregnancies discordant for anencephaly

				Anencephalic twin		*Normal twin*	
Reference	*Diagnosis (weeks)*	*Amnionicity*	*Polyhydramnios, management*	*Outcome*	*Gestation (weeks)*	*Outcome*	*Gestation (weeks)*
Sebire *et al.* 1997[7]	16	Diamniotic	No polyhydramnios	Fetal death	20	Fetal death	20
Sebire *et al.* 1997[7]	18	Diamniotic	No polyhydramnios	Fetal death	32	Fetal death	32
Leeker & Beinder 2004[13]	15	Monoamniotic	No polyhydramnios	Fetal death	24	Live birth	33
Sebire *et al.* 1997[7]	16	Diamniotic	Polyhydramnios. No amniodrainage	Fetal death	28	Fetal death	28
Leeker & Beinder 2004[13]	27	Diamniotic	No polyhydramnios	Neonatal death	27	Live birth	29
Sebire *et al.* 1997[7]	15	Diamniotic	No polyhydramnios	Neonatal death	36	Live birth	36
Sebire *et al.* 1997[7]	20	Diamniotic	No polyhydramnios	Neonatal death	36	Live birth	36
Sebire *et al.* 1997[7]	16	Diamniotic	No polyhydramnios	Neonatal death	36	Live birth	36
Sebire *et al.* 1997[7]	17	Diamniotic	No polyhydramnios	Neonatal death	37	Live birth	37
Present study	12	Diamniotic	No polyhydramnios	Neonatal death	39	Live birth	39
Sebire *et al.* 1997[7]	20	Diamniotic	Polyhydramnios. No amniodrainage	Neonatal death	27	Live birth	27
Sebire *et al.* 1997[7]	15	Diamniotic	Polyhydramnios. No amniodrainage	Neonatal death	31	Live birth	31
Gul *et al.* 2005[16]	24	Diamniotic	Polyhydramnios. No amniodrainage	Neonatal death	33	Live birth	33
Lim *et al.* 2005[14]	18	Monoamniotic	Polyhydramnios. No amniodrainage	Neonatal death	31	Live birth	31
Lim *et al.* 2005[14]	18	Monoamniotic	Polyhydramnios. No amniodrainage	Neonatal death	33	Live birth	33
Kriplani *et al.* 1998[15]	11	Monoamniotic	Polyhydramnios. No amniodrainage	Neonatal death	38	Live birth	38
Sebire *et al.* 1997[7]	21	Diamniotic	Polyhydramnios. Amniodrainage at 29 weeks	Neonatal death	30	Live birth	30
Present study	13	Diamniotic	Polyhydramnios. Amniodrainage at 27 weeks	Neonatal death	32	Live birth	32
Sebire *et al.* 1997[7]	15	Diamniotic	Polyhydramnios. Amniodrainage at 26 and 28 weeks	Neonatal death	33	Live birth	33

Table 4 Cord occlusion in monochorionic twins

Method of cord occlusion	n	*Gestation (weeks, mean (range))*	*Success* (n *(%))*	*Survival* (n *(%))*	*Delivery < 33* weeks (n *(%))*
Endoscopic laser coagulation[8,17,18]	6	19 (16–28)	4 (66.7)	6 (100)	2/6 (33.3)
Endoscopic cord ligation[9,19–24]	24	23 (16–27)	19 (79.2)	13 (54.2)	9/13 (69.2)
Bipolar cord coagulation[10,24–26]	92	21 (16–34)	88 (95.7)	71 (77.2)	22/71 (31.0)

Cord occlusion in monochorionic twins

The literature search on cord occlusion in monochorionic twins essentially identified three methods (Table 4)[8–10,17–26]. The first method was endoscopic laser coagulation of the umbilical cord vessels, which was attempted in six pregnancies complicated by twin reversed arterial perfusion (TRAP) sequence[8,17,18]. The procedure was successful in arresting the cord blood flow only in the cases treated before 21 weeks' gestation. All pump twins survived but 33.3% were delivered before 33 weeks. The second method was endoscopic cord ligation, which was attempted in 24 cases complicated by TRAP ($n = 14$), severe twin-to-twin-transfusion syndrome (TTTS; $n = 7$) or discordance for major fetal defects ($n = 3$)[9,19–24]. The procedure was successful in arresting the cord blood flow in 19 cases, it failed in three and it resulted in occluding the wrong cord in two. The survival rate was 54.2%, and 69.2% of the survivors were born before 33 weeks' gestation. The third method was ultrasound-guided bipolar cord coagulation, which was attempted in 92 cases complicated by TRAP ($n = 26$), severe TTTS ($n = 39$) or discordance for major defects ($n = 27$)[10,24–26]. The procedure was successful in arresting the cord blood flow in all but four cases. The overall survival rate was 77.2%, and 31.0% of the survivors were born before 33 weeks. The respective rates for the subgroup with

discordancy for major defects ($n = 27$) were 70.4% and 15.8%.

DISCUSSION

The data of this study suggest that in dichorionic twin pregnancies discordant for anencephaly, diagnosed at $11 + 0$ to $13 + 6$ weeks of gestation, the parents can be counselled that, in order to minimize the risk of miscarriage and maximize the chance of live birth beyond 33 weeks, the pregnancy is best managed expectantly with the option of amniodrainage or selective feticide should polyhydramnios develop after 24 weeks. The final decision on these two options will depend on the prevailing laws for the particular country and moral, religious, or psychological issues for each family. In contrast, in monochorionic twin pregnancies expectant management is associated with spontaneous intrauterine death of the anencephalic fetus in about 20% of cases, and can cause death or disability in the co-twin. There are no useful data on the alternative management of selective feticide but the application of ultrasound-guided bipolar coagulation in monochrionic twin pregnancies with other complications is encouraging.

Miscarriage or fetal death between 12 and 23 weeks occurs in about 1% of cases in singletons, in 2% of dichorionic and 12% of monochorionic twin pregnancies[23]. Another important complication of pregnancy is delivery before 33 weeks' gestation. Almost all babies born before 24 weeks die and almost all born after 33 weeks survive. Delivery between 24 and 33 weeks is associated with a high chance of neonatal death and disability in the survivors. The chance of spontaneous delivery between 24 and 33 weeks is about 1% in singletons, 6% in dichorionic and 9% in monochorionic twin pregnancies[27].

The data from the dichorionic twin pregnancies discordant for anencephaly that were managed expectantly demonstrate that firstly, the risk of fetal death or miscarriage between 12 and 23 weeks (none in the 13 cases that were diagnosed at 11–14 weeks) may not be higher than in dichorionic pregnancies with normal fetuses, and secondly, the rate of early preterm delivery is higher than in dichorionic twin pregnancies with normal fetuses (18% vs. 6%). In about 55% of cases polyhydramnios develops at 25–31 weeks of gestation, and although 65% of these can be managed expectantly, in the other 35% it may be necessary to carry out amniodrainage or selective feticide.

The data from the dichorionic twin pregnancies discordant for anencephaly that were managed by elective selective feticide at 12–21 (median 17) weeks are derived from only nine cases and in this respect do not allow definite conclusions to be drawn. Nevertheless, in one of the nine cases there was a miscarriage and in another there was early preterm delivery. The median gestation of the live births was similar to that in pregnancies that were managed expectantly (37 vs. 36 weeks). These data demonstrate that firstly, selective feticide can cause miscarriage of the whole pregnancy, and secondly, selective feticide may not reduce the rate of early preterm delivery. Supportive evidence for these two conclusions is provided by the data from a multicenter study of selective feticide in 345 dichorionic pregnancies discordant for chromosomal, Mendelian or structural abnormalities[28]. The rate of miscarriage or death of the normal fetus was 7.9%, and delivery at 25–32 weeks occurred in 12.4% of cases.

The data from the monochorionic twin pregnancies discordant for anencephaly that were managed expectantly demonstrate that firstly, the risk of fetal death of the anencephalic fetus is about 20% and that in the majority of cases this event is accompanied by death of the normal fetus, and secondly, the rate of early preterm delivery may be higher than in dichorionic twins discordant for anencephaly (38% vs. 18%). Consequently, the outlook for monochorionic pregnancies is worse than that for dichorionic twins. The extent to which this outcome can be improved by selective feticide remains to be determined. In monochorionic twins, unlike dichorionic twins, selective feticide by intracardiac injection of KCl is inappropriate. This is because, owing to the invariable presence of intertwin placental vascular anastomoses, the KCl may enter the circulation of the normal fetus or the normal fetus may suffer death or brain damage from exsanguination into the dead fetus[29].

Over the last 15 years a wide range of techniques for selective feticide in monochorionic twins have been described and subsequently abandoned, apart from three that aim at arresting blood flow in the umbilical cord vessels of the abnormal twin[30]. On the basis of currently available data (Table 4) it appears that cord ligation should be abandoned because of the high associated mortality and early preterm delivery rates. Endoscopic laser coagulation of the umbilical cord vessels has been performed in only a small number of cases, but appears to be successful when it is carried out before 20 weeks. However, such a procedure in patients with anencephaly would present unique challenges, the most important of which is the bloody discoloration of the amniotic fluid[31]. Ultrasound-guided bipolar cord coagulation is certainly successful in arresting the umbilical circulation. The reported survival rate of about 75% and early preterm delivery rate of about 30% may not be better than the respective rates in the monochorionic twins discordant for anencephaly that were managed expectantly (Table 3).

In conclusion, in dichorionic twins discordant for anencephaly, polyhydramnios complicates about 55% of pregnancies and this is the main risk to the co-twin. Such pregnancies are best managed with serial ultrasound examinations for early diagnosis of polyhydramnios, which can then be treated either by amniodrainage or selective feticide. In monochorionic twins, the normal fetus is threatened not only by the associated polyhydramnios but also by the hemodynamic consequences of the spontaneous death of the abnormal twin, which is common. The extent to which the outcome of such pregnancies is improved by cord occlusion remains to be determined.

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