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Intrauterine Fetal Demise in Multiple Gestation

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Abstract. Fifteen cases were reviewed over a five-year period at a perinatal centre with intrauterine demise of one member of a multiple gestation. Nine cases were monozygotic twin pairs, two were dizygotic, and two were triples. Gestational age ranged from 27 to 39 weeks. The management protocol consisted of delivery in all cases after confirmation of the diagnosis. In 4 cases delivery was immediate because of spontaneous labor. In the other cases elective delivery was performed if the gestational age was 37 weeks or greater or there was evidence of preeclampsia or if amniocentesis revealed a mature lecithin-sphingomyelin (L/S) ratio. Steroids were given if the L/S was immature or the attempt at amniocentesis was unsuccessful and delivery was performed 48 hours after initiation of steroid therapy. Cesarean section was the mode of delivery in 14 of the 15 cases. All of the cotwins and cotriplets survived. One survivor of a monozygous twin pair has multicystic encephalomalacia possibly implicating perinatal arterial occlusion or in utero disseminated intravascular coagulation (DIC). The intrauterine deaths are categorized into possibly avoidable deaths (2/15), unavoidable due to congenital anomalies (3/15), and unknown or unavoidable deaths (8/15).

Key words: Intrauterine fetal demise, Multiple gestation, Placental anastomoses, Perinatal arterial occlusion, Multicystic encephalomalacia, Intrauterine disseminated intravascular coagulation

INTRODUCTION

The management of intrauterine demise in a multiple gestation is a difficult clinical problem. There is understandable maternal anxiety about the well being of her surviving fetus. From available literature it is difficult to estimate the risk to the cosurvivor and develop a reasonable management protocol. The question posed is: how many survivors are normal after an in utero death of a cotwin or a cotriplet? The purpose of this paper is

to report our experience with intrauterine fetal demise in multiple gestation over a five-year period.

CASE REPORTS

Fifteen cases were identified over a five-year period (January 1977 - March 1983) with intrauterine fetal demise (IUFD) of a member of a multiple gestation. Nine cases were monozygotic (MZ) twin pairs, four were dizygotic (DZ) and two were triplets. The number of multiple gestations during the study period was 325. The incidence of IUFD in multiple gestation was 4.4% at our center. Nine of the cases were referred to our center, three cases were managed by private physicians and three were clinic patients covered by the perinatal service. Antenatal diagnosis of the IUFD was made in fourteen of the cases by ultrasound. One case was diagnosed at the time of delivery.

The management protocol consisted of delivery in all cases after repeat ultrasonic confirmation of the diagnosis in our own unit. In four cases delivery was immediate because of spontaneous labor (Table 1). Elective delivery was undertaken in four cases because the gestational age was 37 weeks or greater (see Table 2). Elective delivery was performed in Case 9 because of chronic hypertension and growth retardation and in Case 10 because of severe preeclampsia (see Table 3). The remaining five cases were electively delivered prior to thirty-seven weeks (Table 4). In four of the five cases amniocentesis was performed. If pulmonary maturity was confirmed, delivery was carried out. Steroids were given if the lecithin sphingomyelin (L/S) ratio was immature or attempt at amniocentesis was unsuccessful. Delivery was performed 48 hours after initiation of steroid therapy. Cesarean section was the mode of delivery in all cases except for Case 8. The reasons for Cesarean section are presented in Table 5.

The placenta was examined in all cases by a perinatal pathologist. Seven of the nine monochorionic placentas had demonstrable anastomoses present. Autopsy was carried out in 10 of the 15 cases by the same pathologist.

Follow-up was ascertained by reviewing charts at our developmental clinic and for those babies, who are not followed at our own institution, by consultation with the pediatrician involved. Follow-up was normal in all cases except 1 and 15. The survivor in Case 1 had a stormy neonatal course with severe respiratory distress, intraventricular hemorrhage (IVH), and asymmetric hydrocephalus.

Case 15 was delivered electively at 34 weeks after steroid administration. Amniocentesis revealed dark brown fluid and it was felt that pulmonary maturity studies would not be valid. Since no dividing membrane was seen on ultrasound, the diagnosis of monoamniotic twinning was considered. The fetal heart was monitored continuously during the 48 hours of steroid administration and was reactive. The baby's condition at birth was excellent. Apgar scores were 5 at 1 minute and 8 at 5 minutes. It was noted during delivery that the fluid surrounding both infants was dark brown and that there was a cord entanglement. The cord of the macerated stillbirth was wrapped around its surviving cotwin creating a true knot. Placental examination revealed a diamniotic monochorionic placenta with rupture of the diamniotic dividing membrane which gave the false clinical impression of monoamniotic placentation. Arterio-venous anastomoses were present. The infant became jittery at 20 hours of life. Ultrasound demonstrated bilateral hydrocephalus with no evidence of IVH. Computed Tomography (CT) demonstrated multiple cystic areas in both frontal temporal and occipital lobes compatible with multicystic

TABLE 1- Spontaneous Delivery

| Case number | Gestational age (weeks) | Birth weight (g) | Placenta | Autopsy | Neonatal course of survivor | Follow-up |
|-------------|-------------------------|------------------------------|---|--|---|-------------------------|
| 1 | 27 | I* 300 II 990 | Diamniotic monochorionic no anastomoses | None, maceration present | Severe RDS; IVH; asymmetric hydrocephalus | Severe handicap at 2 yr |
| 2 | 37 | I 2452 II* 1300 | Diamniotic monochorionic, anastomoses present | Maceration, no anomalies, cord stenosis at insertion | Normal | Normal at 2 yr |
| 3 | 30 | I* 900 II 1580 III* 38 | Diamniotic dichorionic, II; Monoamniotic monochorionic, I and III | Maceration, fetus papyraceous, no anomalies | RDS | Normal at 1 yr |
| 4 | 31 | I* 960 II 840 III 910 | Diamniotic monochorionic, I and III; Diamniotic dichorionic, II | None, maceration present | RDS } Triplet IVH } II RDS } Triplet III | Normal at 6 months |

* Denotes intrauterine fetal demise (IUFD).

TABLE 2- Elective Delivery at Gestational Age 37 Weeks or Greater

| Case number | Gestational age (weeks) | Birth weight (g) | Placenta | Autopsy | Follow-up |
|-------------|-------------------------|--------------------|---|---|--------------------|
| 5 | 39 | I* 1672 II 2126 | Diamniotic dichorionic | No maceration, meconium aspiration, IUGR | Normal at 3 yr |
| 6 | 39 | I 2500 II* 1380 | Diamniotic dichorionic | No maceration, meconium aspiration | Normal at 4 yr |
| 7 | 38 | I 3770 II* 3060 | Diamniotic dichorionic | Maceration, no anomalies | Normal at 5 yr |
| 8 | 38 | I 2330 II* 640 | Diamniotic monochorionic, anastomoses present | Maceration, stenosis of cord at insertion | Normal at 3 months |

* Denotes IUFD.

TABLE 3- Elective Delivery Because of Maternal Hypertensive Disease

| Case number | Gestational age (weeks) | Birth weight (g) | Placenta | Autopsy | Neonatal course of survivor | Follow-up |
|-------------|-------------------------|-------------------|---|---|---|--|
| 9 | 34 | I 780 II* 500 | Diamniotic monochorionic, anastomoses present | Maceration, no anomalies, stenosis of cord at insertion | NICY 90 days; No RDS; No IVH | Normal at 2 yr |
| 10 | 28 | I* 452 II 1020 | Diamniotic dichorionic | No maceration, no anomalies | NICU 81 days; RDS; patent ductus arteriosus | Mild motor retardation, normal mental development at 16 months |

* Denotes IUFD.

TABLE 4- Elective Delivery After Confirmation of Pulmonary Maturity

| Case Number | Gestational age (weeks) | Birth weight (g) | Placenta | Autopsy | Neonatal course of survivor | Follow-up |
|-------------|-------------------------|--------------------|---|---------------------------------|---|------------------------------------|
| 11 | 32 | I 1370 II* 580 | Diamniotic monochorionic, no anastomoses, intertwining of cords | None, maceration present | NICU 12 days; no RDS; no IVH; | Normal at 6 months |
| 12 | 35 | I 1985 II* 3250 | Diamniotic monochorionic, anastomoses | No maceration nonimmune hydrops | Normal | Normal at 4 yr |
| 13 | 35 | I 2020 II* 1850 | Diamniotic monochorionic, anastomoses | None, maceration present | Normal | Normal at 18 months |
| 14 | 34 | I 3170 II* 1248 | Diamniotic monochorionic, anastomoses | Maceration, Potter's syndrome | Normal | Normal at 2 yr |
| 15 | 34 | I 2450 II* 2180 | Diamniotic monochorionic, anastomoses, true knot in cord | None, maceration present | Seizure activity, CT-multicystic encephalomalacia | Responds to sound only at 5 months |

* Denotes IUFD.

TABLE 5 - Indications for Cesarean Section

| Indication | Case number |
|--|-------------------------|
| Abnormal presentation of surviving twin or triplet | 1, 3, 4, 10, 12, 13, 15 |
| Repeat Cesarean section | 5, 11 |
| Placenta previa | 9 |
| Failure to progress in labor | 2 |
| Not stated on chart | 6, 7, 14 |

encephalomalacia. The brain stem and cerebellum were intact. EEG demonstrated absence of cortical activity. The infant responds to sound only, at 5 months of age.

Duration of IUFD

The duration of the IUFD could only be calculated by crude estimation. Cases 5, 6, 10, and 13 had no maceration and this was consistent with death within 24 hours of delivery. All of the other cases had severe maceration consistent with fetal death of at least four days duration.

Cause of IUFD

The cause of the intrauterine demise was unknown in many instances. Cases 2, 8, 9, 14 had evidence of stenosis of the cord before insertion into the umbilicus. Sections of the cord in this area of stenosis revealed total obliteration of the vein in two cases. Case 11 had rupture of the diamniotic dividing membrane with intertwining of both cords and Case 15 had a true knot of one cord around the other. It is unknown if the cord complications were responsible for the demise. Two cases had autopsy-proven congenital heart disease and Case 14 had Potter's syndrome. Case 13 had prenatal evidence of hydrops with fetal ascites but permission for autopsy was not granted. Maternal hypertensive disease with placental insufficiency was presumed responsible for the fetal demise in Cases 9 and 10.

Two cases were potentially avoidable deaths. Retrospective review showed a discrepancy greater than 0.7 cm in the biparietal diameter (BPD) of the cotwins. In Case 2 a BPD discrepancy of 1.2 cm was noted 3 weeks prior to delivery and in Case 6 a BPD discrepancy of 0.8 cm was detected 2 weeks prior to delivery. These babies may have benefited from earlier delivery.

Coagulation studies were performed in all mothers that were delivered electively before 37 weeks and no evidence of DIC was found. A full coagulation profile was not carried out on the babies. The ten infants admitted to the neonatal intensive care unit (NICU) had complete blood counts and platelet counts which were all in the normal range.

DISCUSSION

In our five-year experience it is of interest to note that nine of the thirteen intrauterine deaths in twins were in MZ twins and the two deaths in triplet pregnancies also had monochorionic placentation. Monozygosity predisposes to mortality in two principal ways. The first relates to the increased incidence of cord complications and the second is due to twin-to-twin transfusion. Recent reports indicate that the survivor of a macerated MZ cotwin may be at increased risk. Structural defects have been reported in children

whose MZ cotwin died in utero [3]. In 1961 Benirschke [1] reported a monoamniotic monochorionic female twin pair in which the cotwin of a macerated stillbirth had muscle rigidity, seizures and died at 62 hours of age. Autopsy of this liveborn female revealed necrosis of brain, spleen and renal cortices. Multiple thrombi were found occluding most blood vessels. Embolization of thromboplastin rich material from the dead to its live cotwin through placental anastomoses was proposed by Benirschke as the most plausible explanation of the infant's widespread necrosis. Moore et al [5] reported three similar cases where the predominant features were renal cortical and cerebral necrosis. Each was the product of a twin pregnancy with a stillborn macerated sibling.

In our series Case 15 has brain damage possibly as a result of perinatal arterial occlusion. This infant had multicystic encephalomalacia present on CT scan on the second day of life and this presumably may have occurred in utero secondary to arterial occlusion from thrombosis or embolus. Embolization through the placental anastomoses from the dead to the live cotwin is a distinct possibility. Arterial thrombosis resulting from DIC is more unlikely as the infant's CBC and platelet count were normal. There was a true knot involving the cords of the macerated stillbirth and the survivor (see Figure). It is possible that a hypotensive episode during cord entanglement could have caused multiple infarcts and encephalomalacia. We feel that both hypotension and perinatal embolization are plausible explanations for encephalomalacia in our case but we cannot make a definitive statement about its etiology. Yoshioka et al [6] reported cystic encephalomalacia in three infants with cerebral palsy. Each patient was the product of a twin pregnancy with a stillborn macerated cotwin. Angiography in two of these patients showed no filling of the posterior parietal or the angular arteries suggesting perinatal arterial occlusion as a cause of multicystic encephalomalacia. Our patient did not have angiography. Renal scan was performed in a search for other areas of embolization and infarction but was negative.

The incidence of abnormality in the cotwin of a macerated stillbirth is unknown. Durkin et al [2] in an analysis of etiologic factors in cerebral palsy with severe mental retardation proposed that DIC due to prenatal death of a twin may have been the cause of brain damage in several patients. Melnick [4] using twin data from the prospective national collaborative perinatal project identified seven MZ twin pairs with a macerated cotwin. One of the cosurvivors died at two months of age and postmortem examination demonstrated cerebellar necrosis supporting the brain damage/DIC hypothesis. Another survivor in this group had a head circumference at the third percentile from one year of age to age 7, but psychomotor development was normal. In our series two MZ survivors with a macerated cotwin now have brain damage. We can only implicate perinatal arterial occlusion as a possible cause of brain damage in Case 15. Case 1 can be explained on the basis of prematurity, severe respiratory distress and IVH with asymmetric hydrocephalus.

From a review of our series it is clear that if the gestational age is 37 weeks or greater, or if there is an underlying condition identifiable that could cause uteroplacental insufficiency, it is appropriate to electively deliver a multiple gestation with an IUID. Many cases will not present a management problem because labor has already begun when the diagnosis is made. A small group of patients with intrauterine demise in a multiple gestation less than 37 weeks remains. This group comprised 5 patients in the present series and 5/325 or 1.6% of all our multiple gestations over a five-year period. We have used a management protocol of elective delivery after confirmation of pulmonary maturity in these five cases. Four out of five infants are normal on follow up and one is severely compromised. Despite the presence of severe brain damage at birth we had no antenatal

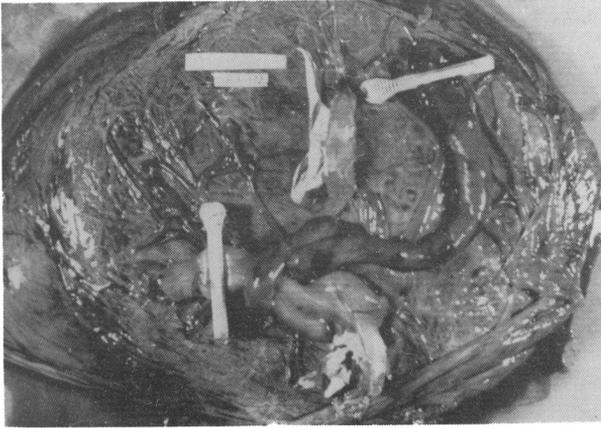


Figure. Case number 15, demonstrating cord entanglement. The dark cord is from the macerated stillbirth. The placenta is diamniotic monochorionic with a membrane defect.

evidence of any compromise on this infant. The fetal heart rate tracing was reactive and an ultrasonic assessment revealed the presence of fetal breathing, gross fetal body movements and normal fetal tone. CT scan demonstrated sparing of the brain stem which would account for the reactive antenatal nonstress test. Perinatal arterial occlusion due to thrombosis or embolus seems to be an unpredictable event. At the present time we have no accurate way of deciding whether the surviving twin would benefit from early elective delivery. Because of this we do not recommend elective delivery prior to 37 weeks for the cosurvivor of a macerated stillbirth unless antenatal surveillance is suggestive of fetal compromise.

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