Single foetal death in twin pregnancies: review of the maternal and neonatal outcomes and management

HHN Woo, SY Sin, LCH Tang

Objective. To review the maternal and neonatal outcomes, and management of single foetal death in twin pregnancies.

Data sources. Medline literature search (1950 to 1999) and hospital audit of single antepartum foetal deaths in twin pregnancy from 1993 through 1997.

Data selection. Key words for literature search: twin pregnancy/pregnancies; single fetal death/demise.

Data extraction. Data were extracted and reviewed independently by the authors.

Data synthesis. During the study period, 182 (0.76%) of 23,804 deliveries involved twin pregnancies. Seven (3.8%) of the twin pregnancies were complicated by the death of one foetus. Single foetal death in a twin pregnancy in the late second and third trimesters is associated with significant morbidity and mortality in the surviving co-twin, especially in a pregnancy involving monochorionic twins. Management should be individualised; conservative management is preferred by most obstetricians.

Conclusion. Single foetal death in twin pregnancies should be managed in a tertiary referral centre, where intensive foetal surveillance and adequate neonatal support are available. A multidisciplinary approach should be adopted.

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Key words: Fetal death/etiology; Pregnancy, multiple; Pregnancy outcome; Twins

Introduction

Single foetal death in twin pregnancies is not rare; the reported incidence ranges from 0.5% to 6.8%.1 The risk of mortality and morbidity in the surviving twin is considerable.1 The death of one twin is also a shock to the parents and the attending obstetrician, who need to face the substantial foetal and maternal risks. A multidisciplinary approach, counselling, emotional support, and intensive foetal surveillance are mandatory.

We performed a 5-year hospital audit of twin pregnancies and a literature review to investigate the maternal and neonatal outcomes, and management of single foetal death in twin pregnancies.

Case series

From 1993 through 1997, there were 23,804 deliveries at the Kwong Wah Hospital, among which 182 (0.76%) were twin pregnancies. Seven (3.8%) of these were complicated by the death of one foetus, and six co-twins survived. The seven cases are summarised in Table 1.

The causes of foetal death varied and included twin-twin transfusion, placental insufficiency, intrauterine growth retardation related to pre-eclampsia, velamentous insertion of the cord, cord structure, cord around the neck, and congenital abnormalities. All of the six surviving foetuses were delivered after 34 weeks. Five of them had normal development on regular follow-up, whereas one had multiple congenital abnormalities, which were known about before the death of the co-twin.

Placentas were sent for pathological examination in six cases. The results showed that four were monochorionic diamniotic, one was monoamniotic, and one was dichorionic. One placenta showed evidence of
### Table 1. Summary of seven cases of antepartum death of one twin

<table>
<thead>
<tr>
<th>No.</th>
<th>Diagnosis of IUD* (weeks)</th>
<th>Antepartum complications</th>
<th>Delivery (weeks)</th>
<th>Mode of delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>19*</td>
<td>IUD of twin II at 19 wk; IUD of twin I at 30† wk</td>
<td>30+6</td>
<td>Vaginal delivery after induction of labour</td>
</tr>
<tr>
<td>2</td>
<td>21†</td>
<td>Twin-twin transfusion detected at 20 wk; IUD of donor at 21+2 wk; maternal digoxin therapy started at 25 wk; prompt improvement of hydrops foetalis; PPROM† at 35+5 wk</td>
<td>35+5</td>
<td>Emergency LSCS† (obstruction by co-twin)</td>
</tr>
<tr>
<td>3</td>
<td>35</td>
<td>1+ proteinuria at 34 wk; pre-eclampsia at 35 wk; USG§ at 35 wk confirmed IUD of twin I, oligohydramnios in twin II, and IU.Gr‡</td>
<td>35</td>
<td>Normal spontaneous delivery</td>
</tr>
<tr>
<td>4</td>
<td>35†</td>
<td>Twin I: gross ascites, absent right kidney, pocket bottom feet, cortiatriatum; twin II: no gross anomaly; PPROM at 35+6 wk; USG confirmed IUD of twin II; paracentesis performed for twin I yielded 100 mL straw-coloured fluid</td>
<td>35+5</td>
<td>Induction of labour; emergency for LSCS foetal distress</td>
</tr>
<tr>
<td>5</td>
<td>35†</td>
<td>Twin II: poorly defined kidneys and bladder, oligohydramnios, flattened growth curve; twin I: absent left kidney; antepartum haemorrhage at 35+6 wk; USG confirmed IUD of twin II and retroplacental clot</td>
<td>35+6</td>
<td>Emergency LSCS for abruptio placentae</td>
</tr>
<tr>
<td>6</td>
<td>37+1</td>
<td>Uneventful antenatal course IUD of twin II and non-reactive cardiotography tracing for twin I at 37+1 wk</td>
<td>37+1</td>
<td>Emergency LSCS for foetal distress</td>
</tr>
<tr>
<td>7</td>
<td>38</td>
<td>Single IUD at 38 wk; conservatively managed</td>
<td>40</td>
<td>Normal spontaneous delivery</td>
</tr>
</tbody>
</table>

* IUD, intrauterine death  † LSCS, lower-segment caesarean section  ‡ PPROM, preterm prelabour rupture of membranes  § USG, ultrasonography  • IU.Gr, intrauterine growth retardation  • PDA, patent ductus arteriosus  • CT, computed tomography

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**twin-twin transfusion. Velamentous insertion of the cord was noted in the dichorionic diamniotic placenta.**

### Discussion

Enbom¹ has reported that the incidence of twin pregnancy with a single intrauterine death ranges from 0.5% to 6.8%. An incidence of 3.7% was reported in a prospective study of 188 monzygotic twins in the National Collaborative Perinatal Project.² These figures, however, are overestimates owing to biases in case selection and reported gestation. In this 5-year case series from an unselected population, there were seven pregnancies in which one of the twins died in utero. The incidence of twin pregnancy with a single intrauterine death was 3.8%.

‘Vanishing twin syndrome’ is described as a twin pregnancy that was diagnosed at one time, but with just one baby being eventually delivered. Even when there are two viable foetuses identified in the first trimester, the disappearance rate for one of them can reach 29%.³ Vaginal bleeding has been found to be the presenting symptom in 25% of cases, whereas vaginal bleeding occurs in only 7% of pregnant women in the general population.⁴ Thus, the reported incidence rates of twin pregnancy with a single foetal loss, including the figure found in this study, are likely to be underestimates. Foetus papyraceous occurs in 1 (0.54%) of 184 of twin pregnancies.⁵ Unlike vanishing twin syndrome, foetus papyraceous occurs when the foetus dies later in pregnancy, which continues thereafter. The amniotic fluid and the fluid content of the dead twin’s tissues and the placental tissue may be reabsorbed, thereby leaving the dead foetus compressed between the amniotic sac of its co-twin and the uterine wall. The degree of compression depends on the time span between foetal death and delivery; the larger the foetus, the more difficult it is to become a foetus papyraceous.⁶

Intrauterine death can occur during any gestation. However, a reliable estimate of the incidence with reference to the timing of the postconceptional loss is difficult, as large prospective studies are scarce. Among
Single foetal death in twin pregnancies

<table>
<thead>
<tr>
<th>Chorioamnionicity and post-mortem results</th>
<th>Survivor characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monochorionic, monoamniotic; no significant pathology (cord stricture of twin I); macerated stillbirths: twin I, maturity 28-29 wk, no abnormality detected; twin II, grossly autolysed and necrotic, maturity 15-16 wk</td>
<td>Nil</td>
</tr>
<tr>
<td>Monochorionic, diamniotic; evidence of twin-twin transfusion; foetus papyraceous</td>
<td>Birthweight, 2540 g; well</td>
</tr>
<tr>
<td>Monochorionic, diamniotic; macerated stillbirth of twin I</td>
<td>Birthweight, 1840 g; well</td>
</tr>
<tr>
<td>Monochorionic, monoamniotic; fresh stillbirth of twin II (cord twice-wrapped around neck), polydactyly of right hand, abnormal vasculature in umbilical cord (only two vessels)</td>
<td>Birthweight, 2210 g; prune-belly syndrome, atrial septal aneurysm, PDA, dysplastic tricuspid valve, incomplete lissencephaly, malrotation of gut</td>
</tr>
<tr>
<td>Gross examination of placentas: infarction on the side of twin II with multiple calcified spots; retroplacental clot occupied one quarter of placenta on the side of twin I; macerated stillbirth of twin II, bilateral renal agenesis, pulmonary hypoplasia</td>
<td>Birthweight, 2160 g; well</td>
</tr>
<tr>
<td>Monochorionic, diamniotic; no significant pathology detected (only 20% supplied to twin II); fresh stillbirth of twin II, no congenital abnormalities, cyanosis and petechial haemorrhage on surface of thoracic organs, suggestive of asphyxia</td>
<td>Birthweight, 2260 g; generalised seizure on day 3; brain CT scan showed left frontoparietal infarct; no neurological deficit; discharged on day 14 with antiepileptic drugs; normal growth and development</td>
</tr>
<tr>
<td>Dichorionic, diamniotic; twin II: velamentous insertion of cord</td>
<td>Birthweight, 3480 g; well</td>
</tr>
</tbody>
</table>

the seven cases in this series, the gestation time varied from 19 to 38 weeks, with no apparent clustering. The timing is crucial because of its implications for the remaining course of the pregnancy. The vanishing twin phenomenon is relatively common, and the prognosis for the surviving foetus is good. In contrast, single foetal death in the second or third trimester is uncommon and has been shown to be associated with increased risk of mortality and morbidity for the surviving twin.8

In general, chorioicity rather than zygosity determines the risk of mortality and the morbidity. Hence, it is important to determine the type of placentation by ultrasonography. The perinatal mortality of monochorionic twin pregnancies is double that of dichorionic twin pregnancies.9 The prevalence of monochorionicity in single intrauterine death in twins is 50% to 70%.10,11 Eighty-three percent (5/6) of the cases in this series were monochorionic and one had definite evidence of twin-twin transfusion.

Aetiologies of intrauterine death
Factors that lead to one foetal death may affect the well-being of the co-twin. Attributable causes that have been cited include twin-twin transfusion syndrome, velamentous insertion of the cord, true cord knot, congenital anomalies, and intrauterine growth retardation.11,12 These factors are similar to the aetiologies found in this study.

Maternal complications
The association between retention of the dead foetus in utero and maternal disseminated intravascular coagulation (DIC) was first noted by Weiner et al13 in 1950, and substantiated by Pritchard and Ratnoff14 in 1955 for singleton pregnancies. They described the principal defect as a gradual reduction in the maternal fibrinogen level, especially if the time interval from the intrauterine death to delivery exceeded 5 weeks. The DIC may progress in a slow and chronic manner without being fulminant. The fibrinogen level returns to normal in all cases within 48 hours of delivery.

The underlying mechanism of DIC is not known; there may be a breach between the maternal and foetal circulations, which allows the passage of tissue thromboplastins from the dead foetus and its placenta into the maternal circulation. The transferred thromboplastins activate the extrinsic coagulation pathway and
thereby consume platelets and coagulation factors. There is widespread intravascular coagulation and generation of fibrin. The presence of fibrin activates the fibrinolytic system, whereby plasminogen is converted to plasmin, which lyases fibrin into fibrin degradation products. The inhibition of fibrin polymerisation may contribute to the defective haemostasis. Depending on the intensity of the stimulus, haemostasis impairment may occur in a varying degree of severity. Landy and Weingord have cited an incidence of maternal DIC of 25%, which is similar to the figure reported by Pritchard and Ratnoff.

Romero et al have described a case of maternal coagulopathy that led to gingival haemorrhage at 29 weeks’ gestation. The pregnancy was successfully prolonged to 36 weeks by the administration of heparin.

Although the time span from the diagnosis of intrauterine death to delivery in this study was more than 5 weeks in two of the seven mothers, none of them had clinical features of maternal DIC. The clotting profiles of the two were cross-checked and found to be normal.

Pregnancy-induced hypertension and pre-eclampsia have also been found to be associated with the intrauterine death of one twin. These conditions, however, may have been the causes of intrauterine death rather than complications.

Effects of foetal death on the surviving twin

To date, a first-trimester intrauterine death has not been found to have adverse effects on the surviving twin. A loss in the second or third trimester, however, is more complex. In dichorionic twins, the prognosis for the surviving twin is relatively good and immaturity is the main risk factor. In the case of monochorionic twins, the prognosis is poor and associated with neurological damage in the survivor. Antenatal ultrasonographic evaluation of chorionicity is thus important in assessing the potential risk.

The observed survival difference between dichorionic and monochorionic twins has been attributed to placental vascular anastomoses, which is rarely seen in dichorionic placentas. The reported frequency of vascular connections in monochorionic placentas ranges from 85% to 98%. Furthermore, Spellacy found anastomoses between monochorionic placentas in almost all cases in which placental circulations were injected after delivery. The presence of placental vascular anastomosis might lead to vascular disruption injury. If this injury were to occur in early pregnancy, it would typically result in atresia or selective tissue loss. If it were to occur in later gestation, it might result in tissue infarction and cystic changes.

Two mechanisms of injury have been proposed: haemodynamic fluctuation, and transchorionic embolisation and coagulopathy. In monochorionic twin pregnancies, the co-twin may exsanguinate into the dead twin through placental vascular anastomoses when the blood pressure falls at the time of intrauterine death. By sampling foetal blood, Okamura et al have demonstrated that this event could cause acute anaemia in a previously polycythaemic recipient following the death of the donor twin, especially when intrauterine death had occurred within 24 hours of sampling. The degree of twin-twin transfusion depends on the number, size, and type of placental vascular anastomoses. Such abrupt and severe haemodynamic changes at the time of one intrauterine death may result in ischaemic damage to the brain and lead to cyst formation in the surviving twin. In mono-amniotic twins, umbilical cord entanglement may reduce the umbilical cord circulation in both twins for a considerable period of time. Additional abrupt hypotension would lead to further hypoxic damage to the surviving foetus. Rupture of the thin dividing septum in diamniotic twins can also lead to the same complication.

Benirschke proposed that injuries found in a surviving monochorionic twin when the co-twin was macerated at birth were due to DIC, which was induced by the passage of thromboplastin and thrombin from the macerated twin and its placenta through vascular anastomoses. Furthermore, Moore et al and Yoshioka et al have provided autopsy and radiographic evidence of vascular aetiology secondary to embolisation from the deceased twin. These theories, however, have been dismissed by the general medical community. Patten et al have demonstrated ultrasonographic evidence of intracranial abnormalities in the surviving twin as early as 7 days after the death of the co-twin, and it is unlikely that coagulopathy would have developed so rapidly. Bejar et al have shown that antenatal necrosis of the cerebral white matter is significantly associated with intrauterine death of the co-twin and multiple placental vascular connections. Fusi and Gordon have suggested that circulatory disturbances and a sudden drop in blood pressure are as important as maternal DIC in the resulting morbidity.

In view of the possibility of death or neurological damage to the remaining foetus, selective foetocide has
been suggested to be contra-indicated in monochorionic twins.\textsuperscript{30} However, selective foeticide may have a role in the management of refractory twin-twin transfusion syndrome.\textsuperscript{31} To prevent the surviving foetus from exsanguinating into the terminated foetus, foeticide should involve an occlusive technique: both the umbilical artery and vein should be simultaneously occluded. Foetoscopic and ultrasound-guided cord ligation techniques have recently been described.\textsuperscript{32,33}

To date, the types of structural abnormalities observed in the surviving twin have included neural tube defects, optic nerve hypoplasia, hypoxic ischaemic lesions of the white matter (eg multicystic encephalomalacia), microcephaly (cerebral atrophy), hydranencephaly, porencephaly, haemorrhagic lesions of white matter, posthaemorrhagic hydrocephalus, bilateral renal cortical necrosis, unilateral absence of a kidney, gastro-intestinal tract atresia, gastrochisis, hemifacial microsomia, and aplasia cutis affecting the scalp, trunk, or limbs.\textsuperscript{11} Two of the twins in this study had congenital anomalies, which antedated the death of the co-twin. A third had left frontoparietal infarction diagnosed by ultrasonography as well as computed tomography of the brain; however, no neurological deficit was found during regular follow-up. Multiple organ infarction may lead to severe disability in survivors and may cause intrauterine or neonatal death,\textsuperscript{34} although the risk is unknown, because no large study has been conducted. In the National Collaborative Perinatal Project, Melnick\textsuperscript{2} calculated a risk of 0.5\% for DIC and brain damage in the monozygotic surviving twin. Carlson and Towers\textsuperscript{35} have estimated that the occurrence of major morbidity and mortality in a monochorionic gestation after a foetal death is 17\%, whereas Fusi and Gordon\textsuperscript{7} have suggested a risk of 26\%.

Single intrauterine death causes unreliable biochemical screening results for both structural defects and chromosomal abnormalities.\textsuperscript{36} The surviving twin may have chronically elevated $\alpha$-fetoprotein levels, and inadvertent puncture of the collapsing sac may lead to an unreliable amniocentesis result.\textsuperscript{11} No case of infection has been reported.

Labour may be precipitated;\textsuperscript{12} approximately 90\% of twin pregnancies complicated with single intrauterine death deliver within 3 weeks of the time of diagnosis.\textsuperscript{37} The prognosis then depends on the maturity of the surviving twin. Foetus papyraceous can also cause dystocia if the dead foetus lies transversely in the pelvis below the presenting part of the surviving twin.\textsuperscript{38} In one of the cases in the present series, early foetal loss at 21 weeks was followed by delivery by emergency caesarean section after preterm rupture of the membranes because of the obstructing first twin.

### Management of twin pregnancies with one dead foetus

With the more frequent use of ultrasonography and cardiotocography for surveillance, the death of one twin is more likely to be detected antenatally. Once the diagnosis is verified, there is considerable pressure on the patient, the family, and the medical team, even moreso because it is impossible to predict all of the major foetal complications.\textsuperscript{1} Antenatal death of one foetus in the late second or third trimester of a twin pregnancy poses an important management dilemma in obstetrics. The risks of leaving the surviving twin in the hostile intrauterine environment that may have caused the death of the co-twin must be balanced against the problems associated with preterm delivery. The rarity of the condition and the absence of large-scale studies make it difficult to advise the parents on the prognosis and optimal management. In general, conservative management is advocated. A brief summary of the literature and management guidelines are shown in Table 2 and the Box, respectively.

D’Alton et al\textsuperscript{12} delivered 14 out of 15 such patients by caesarean section. The rationale was that the hostile intrauterine environment had led to the death of one twin; provided that the second twin was not grossly immature, delivery was indicated to prevent further damage. Such an aggressive approach, however, did not prove to have a better outcome, as substantiated by other studies.\textsuperscript{6,35,39} Because preterm delivery occurred in 50\% of cases, Kilby et al\textsuperscript{17} and Prompeler et al\textsuperscript{40} have suggested that the foetal outcome is mainly gestation-dependent and the goal should be to prolong pregnancy.\textsuperscript{13} Santema et al\textsuperscript{10} have suggested that prematurity and low birthweight may be attributed to increased neurological complications in the surviving twin, because cerebral abnormalities secondary to coagulopathy have not been observed.

For cases of impending single death, preventive measures such as pre-emptive delivery might be a better choice. In fact, the critical moment of shunting when one twin dies is often missed, and if much of the insult is sustained at the time of co-twin’s death, rapid diagnosis and delivery may not help. True prevention of brain damage is possible only by inducing delivery before the vulnerable twin dies in utero. Even this strategy does not guarantee that brain damage has not occurred in the presence of placental anastomoses.\textsuperscript{29}
Cattanach et al.42 favour conservative management until 37 weeks’ gestation, if foetal movements, cardiotocography, and ultrasonography show no abnormalities. Santema et al.10 have advocated treating impending preterm labour before 34 weeks with intravenous tocolytics. Carlson and Towers.35 have recommended that delivery should be considered after 32 weeks if lung maturity is documented; if the lungs are immature, steroids could be given and maturity re-evaluated afterwards. It has been suggested that after 37 weeks’ gestation, the surviving twin should be delivered once intrauterine death of the co-twin has been diagnosed.11 Before that, immediate delivery should be directed by obstetric indications. In the seven cases of this study, four had immediate delivery after the diagnosis. They included two with foetal distress, one placental abruption, and one spontaneous labour. All four pregnancies were beyond 34 weeks’ gestation. Of the remaining three cases, which were managed conservatively, one co-twin died—probably due to cord stricture—while the other two showed no abnormality.

The rate of caesarean section has varied considerably (19%-92%) among the reported studies.7,12 and there is no specific contra-indication to vaginal delivery.11 Bell et al.43 have shown that an increased rate of caesarean section, from 3.2% to 50.8%, does not lead to a significant reduction in perinatal mortality or morbidity. Single intrauterine death per se in twin pregnancy is not an indication for caesarean section, unless there is evidence that the twins are monoamniotic with a 25% risk of cord entanglement or knotting.42

It is recommended that all twin pregnancies with one dead foetus should be managed in tertiary referral
centres with sufficient neonatal support. A management plan should be individualised. Intensive foetal surveillance is required and the determination of chorionicity, particularly in the first trimester, is crucial.\textsuperscript{44,45} Subsequent ultrasound scans serve to detect foetal anomalies and assess foetal growth and liquor volume. These measurements are complemented by regular non-stress testing, biophysical profiling, and Doppler ultrasonographic studies.\textsuperscript{11} Cranial sonography, if necessary by the transvaginal route, may provide additional information. Despite close surveillance, however, pitfalls remain: neurological damage may occur in the surviving co-twin with normal antenatal ultrasound findings, reactive cardiotocography tracings, and an intact brainstem as detected by postnatal computed tomography.\textsuperscript{12} Furthermore, in utero detection of cerebral injury depends on the time interval from the insult to the scan. Unlike haemorrhagic lesions, ischaemic lesions in the early phase may be difficult to visualise. Magnetic resonance imaging has been shown to be helpful,\textsuperscript{46} and echoencephalography can detect antenatal necrosis of cerebral white matter as brain atrophy or cavities in the white matter by day 3 of life.\textsuperscript{29} A thorough neonatal evaluation is indicated for the surviving twin to detect central nervous system, renal, circulatory, and cutaneous defects. Investigations may include high-resolution ultrasonography of the brain, computed tomography, renal function studies, and magnetic resonance imaging. Long-term follow up is mandatory.\textsuperscript{11}

After delivery, the placenta should be examined macroscopically and histologically to determine the placentation. Santema et al\textsuperscript{10} have argued that other than chorionicity, histology is not informative, because of the extensive secondary changes caused by the dead foetus. In the five monochorionic twins in this series, only one had histological evidence of vascular anastomoses. This low rate of observation could be due to the collapse of chorionic vessels of the dead foetus, thus making the recognition of vascular communications difficult. Post-mortem examination should be arranged, but in most instances, it does not reveal any cause, because the foetus is macerated and the tissues are autolysed.\textsuperscript{10}

Parental anxiety may be an important factor in persuading the obstetrician to intervene.\textsuperscript{11} Complex emotional response caused by grieving the death of one twin, while anxiously awaiting the birth of the survivor should be addressed. A multidisciplinary approach and counselling should therefore be offered in all cases. Voluntary support groups may be helpful in this regard. In the future, the surviving child may have guilty feelings towards the dead sibling, or the survivor may be blamed for the co-twin’s death. Hence, psychological back-up for the survivor is also important.

Conclusion

The sequelae of a single foetal death in a twin pregnancy depend on the gestation and placentation. Death in the late second or third trimester is associated with significant morbidity and mortality in the surviving twin. The problems are more severe in monochorionic twin pregnancies. Antenatal evaluation of chorionicity by ultrasonography is important to assess the potential risk. Conservative management is preferred. However, the risk of keeping the surviving twin in a hostile intrauterine environment must be weighed against the risk of preterm delivery. Adequate counselling, psychological support, and long-term follow-up are mandatory.

References

14. Pritchard JA, Ratnoff OD. Studies of fibrinogen and other