Early 2nd trimester fetal demise in a monochorionic twin pregnancy: a cautionary tale

Abstract
It is well established that the death of one fetus in a monochorionic twin pregnancy places the surviving twin at significant risk for neuro-developmental delay or death. Although the early 1st trimester “vanishing twin” has not traditionally been considered a major risk, the precise gestational threshold beyond which a surviving twin is at risk remains uncertain. Most experts recommend serial ultrasounds and fetal MRI in the survivor, to look for evidence of ischaemic brain injury. We present a case of early monochorionic twin demise at 14–16 weeks, with evolving ventriculomegaly and ischaemic changes on fetal MRI in the co-twin, leading to termination of pregnancy at 28 weeks.

Keywords: fetal demise, monochorionic, MRI, twin.

Case
A healthy 40-year old P0+0 Caucasian woman conceived following intracytoplasmic sperm injection (ICSI) treatment. Antenatal ultrasound at 7 weeks demonstrated monochorionic-diamniotic (MCDA) twins. She had normal ultrasound scans at 9, 12 and 14 weeks and a low risk result on combined 1st trimester screening (nuchal translucency 2.4 mm for both twins). She was referred to our unit at 16 weeks to commence ultrasound surveillance for twin-twin transfusion syndrome (TTTS).

Ultrasound at 16+2 weeks revealed fetal demise in twin 1. Twin 2 appeared healthy with normal intracranial anatomy. Biometry for both twins was consistent with 16 weeks gestation and amniotic fluid volume was normal in both sacs, with no evidence of TTTS. The patient reported slight vaginal bleeding 2 weeks previously. In view of the demise of twin 1 between 14 and 16 weeks, the risk of death or neurological disability in the surviving twin and the need for close ongoing surveillance, including possible fetal MRI, was discussed. Serology for CMV, toxoplasmosis...
and parvovirus and an anti-phospholipid antibody screen were negative. An amniocentesis was declined.

At 18+3 weeks, a follow-up ultrasound demonstrated normal fetal anatomy for twin 2. There was no evidence of ventriculomegaly (posterior horn of the lateral ventricle [Vp] 8mm) or fetal anaemia (middle cerebral artery peak systolic velocity [MCA-PSV] 30cm/s). At 20+5 weeks, the Vp (8 mm) and MCA-PSV (27 cm/s) were again normal. An MRI scan of the fetal brain was recommended, to identify ischaemic injury in the surviving twin. The patient did not attend for the MRI due to safety concerns regarding MRI scanning during pregnancy.

At 22+5 weeks, examination of twin 2 revealed borderline ventriculomegaly (Vp 10mm) without fetal anaemia and the possible significance of this was discussed with the couple. The safety of fetal MRI was underscored and the patient agreed to proceed with this investigation.

MRI brain for twin 2 was performed at 26 weeks and reviewed by a Paediatric Neuro-radiologist. There was evidence of volume loss in the left parietal region, consistent with a previous ischaemic insult, and an irregular cortex suggesting polymicrogyria (Figure 1). In addition, there was mild ventriculomegaly on the right side (Vp 13 mm) and borderline ventriculomegaly on the left (Vp 10 mm). Worsening right-sided ventriculomegaly was confirmed on ultrasound scan (Figures 2 and 3) and the couple were counselled extensively by a multi-disciplinary team, comprising a fetal medicine specialist, neonatologist and social worker. The high chance of neuro-developmental delay was discussed and, in view of this, the couple requested termination of pregnancy. Labour was induced at 28 weeks following feticide with intracardiac potassium chloride and the patient had an uncomplicated vaginal delivery. Post-mortem examination was declined.

Discussion
Chorionicity is the most important determinant of fetal outcome in twin pregnancies. The perinatal loss rate has consistently been shown to be higher in monochorionic (MC) versus dichorionic twins, likely related to haemodynamic imbalances. Within this cohort, the highest rates of MC fetal loss were found during weeks 18–22; at the 14–16 week stage the reported loss rate was just 5 per 1000 MC twins. In addition to an inherently higher rate of fetal loss, the consequences of single fetal demise in MC twins are far graver. A meta-analysis of 22 studies reported MC twin pregnancies with single fetal demise to be associated with a substantial 15% risk of co-twin death and a 26% rate of neuro-developmental impairment. These results are supported by the largest single-centre study to date, which recently reported severe cerebral injury in 26% of MC survivors. The unique placental angio-architecture of MC twins means that demise of one of a monochorionic pair can allow acute exsanguination of the surviving fetus into the demised co-twin via anastomoses in the shared placenta. This may result in hypovolaemia, hypotension and
and cerebral ischaemia and/or infarction in the surviving twin.9 This theory of intertwin haemodynamic imbalance is supported by small scale studies of prompt fetal blood sampling following twin demise, which noted high rates of fetal anaemia in surviving MC twins.9,10 Additionally, a recently reported case appeared to capture video-graphically the precise moment of fetal exsanguination at 19 weeks following a monochorionic co-twin death.11

It is widely accepted that MC twin pregnancies complicated by single twin demise warrant close fetal monitoring in an experienced fetal medicine unit. Different patterns of survivor neurological injury may evolve, which may be detectable on ultrasound, fetal MRI or both.12 Most commonly, fetal MRI is suggested three to four weeks after the presumed twin demise, to minimise the chance of a falsely-reassuring MRI performed too soon after the neurological insult.13 In the present case, MRI was recommended at 20 weeks but the patient did not attend, due to safety concerns following ‘internet-based research’. When the MRI was finally obtained at 26 weeks, abnormal ventricular dilatation (Vp 13 mm) was already evident on ultrasound. Several instances of abnormal MRI despite normal ultrasound following MC twin demise have been reported.14 Couples should be reassured that no deleterious effects on the developing fetus following MRI have been demonstrated15 and that fetal MRI is strongly recommended in these cases.

Given the high rates of consequent morbidity, attempts have been made to identify predictors of neurological sequelae in co-twin survivors.7 Aside from chorionicity itself, the variable most commonly studied is the gestational age at the time of fetal demise. The “vanishing twin syndrome” refers to a confirmed twin pregnancy complicated by loss of a twin early in the 1st trimester.13 In practice, most fetal medicine specialists recommend routine antenatal care in pregnancies complicated by an early vanishing twin.5,13 However, there is an emerging hypothesis that under-reported first trimester vanishing monochorionic twins may contribute to the antenatal origin of cerebral palsy in apparent singleton survivors.16 Furthermore, residual singletons following a vanishing twin appear to have higher rates of preterm delivery compared to true singletons following assisted reproduction.17

In cases of single fetal demise complicating MC twins, a clear gestational threshold, beyond which the survivor is at significant risk, has not been identified.15 Many experts believe that a genuine risk to the surviving MC twin only applies to cases of co-twin demise in the 2nd or 3rd trimesters (i.e. beyond 14 weeks).16 While this is consistent with the internationally-accepted commencement of TTTS surveillance at 16 weeks (a related condition also secondary to underlying placental anastomoses18), hard scientific evidence is lacking. Indeed, rare cases of ischaemic injury to survivors following co-twin demise as early as 9 and 12 weeks have been reported.22,19 In the largest reported single-centre study, the earliest co-twin death resulting in survivor neurological injury was at 19 weeks.7 The present case, with MRI-confirmed cerebral ischaemia following co-twin death at 14 to 16 weeks, is one of the earliest reported cases to date.
Conclusion
In monochorionic twin pregnancies complicated by single fetal demise, the surviving twin is known to be at risk for cerebral ischaemia and neuro-developmental delay. This risk is generally thought to be highest in cases of fetal demise in the 2nd and 3rd trimesters. The present case highlights the risk to twin survivors even at early gestational ages and underscores the critical importance of close fetal surveillance with ultrasound and MRI in such cases.

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