Single fetal demise in monochorionic twins: a case report and literature review

Choi Wah KONG MSc in Medical Genetics (CUHK), MRCOG, FHKAM, Cert HKCOG (Maternal Fetal Medicine)
William Wing Kee TO MPH, M Phil, FRCOG, FHKAM, Cert HKCOG (Maternal Fetal Medicine)
Department of Obstetrics and Gynaecology, United Christian Hospital, Hong Kong

We report a case of single fetal demise in an apparently uncomplicated monochorionic twin pregnancy at 29 weeks of gestation. The surviving co-twin was delivered within 2 days based on ultrasound features of acute fetal anaemia. The baby had neurological damage and renal failure and progressively deteriorated to death. We review the literature on management of single fetal demise in monochorionic twin pregnancy and discuss the controversies in management.

Keywords: Fetal death; Fetofetal transfusion; Pregnancy, twin

Case presentation

A 31-year-old woman, para 3, naturally conceived a twin pregnancy. Ultrasound at 12 weeks of gestation showed monochorionic diamniotic twins. The nuchal translucency of both fetuses was normal and the first trimester combined biochemical screening showed low risk for Down syndrome. Morphology scan at 20 weeks was unremarkable. Serial ultrasound scans at 16, 20, 23, and 26 weeks of gestation showed normal growth and liquor volume of both fetuses (Figure 1). There were no growth discrepancies between the two fetuses and there was no evidence of twin-twin transfusion syndrome (TTTS).

In August 2018, she was admitted to our hospital at 29+1 weeks of gestation for decreased fetal movement of one day. Ultrasound showed that the first twin had died while the other was viable. Parameters of both fetuses were within normal range with no significant growth discrepancy (Figure 1). The liquor volume of both fetuses was normal with the deepest pocket 2.8 cm in first twin and 3.6 cm in second twin. There were no hydropic changes in the demised fetus. The umbilical artery and ductus venosus Doppler waveforms of the surviving fetus were normal, and peak systolic velocity of the middle cerebral artery Doppler was 53 cm/s, which was just below 1.5 MoM for gestation (Figure 2). Cardiotocogram tracing was unremarkable. The patient was afebrile with normal blood pressure and urine analysis. She did not have any symptoms and signs of labour. There was no evidence of pre-eclampsia or placental abruption. The maternal blood test showed no coagulopathy. With the presence of single fetal demise in a monochorionic twin pair, the risks of intrauterine death and neurological damage of the co-twin were explained to the patient. Balancing these risks with the risks of prematurity
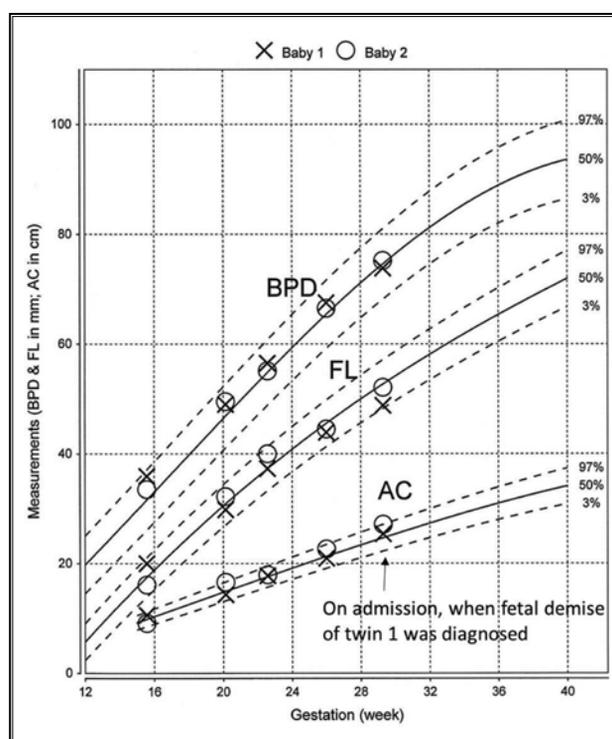

Figure 1. Ultrasonographic chart showing no significant growth discrepancies between the two fetuses

to deliver the surviving co-twin at 29 weeks of gestation, it was decided to adopt conservative management with close surveillance of the co-twin. Antenatal steroid therapy was started to enhance fetal lung maturity.

On the next day, the maternal condition was stable and the cardiotocogram of the surviving fetus showed

Correspondence to: Dr Choi Wah KONG
Email: melizakong@gmail.com

reactive pattern. However, 1 day later, ultrasound scan showed the peak systolic velocity of the middle cerebral artery in the surviving fetus was 65 cm/s, exceeding 1.5 MoM signifying significant fetal anaemia (Figure 2). The umbilical artery Doppler and ductus venous Doppler
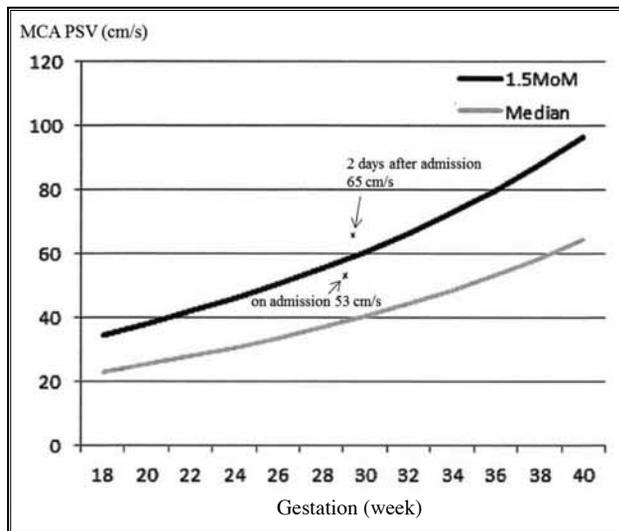

Figure 2. Peak systolic velocity (PSV) of the middle cerebral artery (MCA) of the surviving twin on admission and on day 2
The median and 1.5 MoM values were adopted from: Mari G, Deter RL, Carpenter RL, et al. Noninvasive diagnosis by Doppler ultrasonography of fetal anemia due to maternal red-cell alloimmunisation. Collaborative Group for Doppler Assessment of the Blood Velocity in Anemic Fetuses. N Engl J Med 2000;342:9-14.

remained normal, and cardiotocogram continued to show a reactive fetal heart rate pattern (Figure 3). The course of steroids was completed. The risks of progressive fetal anaemia of the surviving fetus and possible deterioration with sudden intrauterine death were explained to the patient and her family. They strongly requested delivery instead of conservative management. Maternal magnesium sulphate was given for neuroprotection before delivery. Emergency caesarean section was performed. Twin 1 was stillbirth with birthweight of 1376 g. Twin 2 was delivered with birthweight of 1690 g. The Apgar score was 5 at 1 minute and 9 at 5 minutes of life. The cord arterial pH was 7.34 with base excess -0.2.

Twin 2 was born with weak crying. He was put on continuous positive airway pressure but was subsequently intubated at 1 hour of life due to respiratory distress. Blood test showed his haemoglobin level was 5.8 g/dL, and blood transfusion was performed. He developed seizure at 3 hours of life. Anti-convulsant therapy was started. Computed tomography of the brain showed diffuse cerebral oedema with generalised hypo-attenuation of brain parenchyma, intraventricular haemorrhage, and petechial haemorrhages in both frontal lobes (Figure 4), suggestive of significant hypoxic ischemic encephalopathy. The baby developed renal failure with no urine output since birth despite trial of diuretics. The creatinine level rose from 59 (on the day of birth) to 143 (on day 2 of life) and to 326 μmol/L (on day 7 of life). The baby was deemed not suitable for haemodialysis due to his low birthweight. In
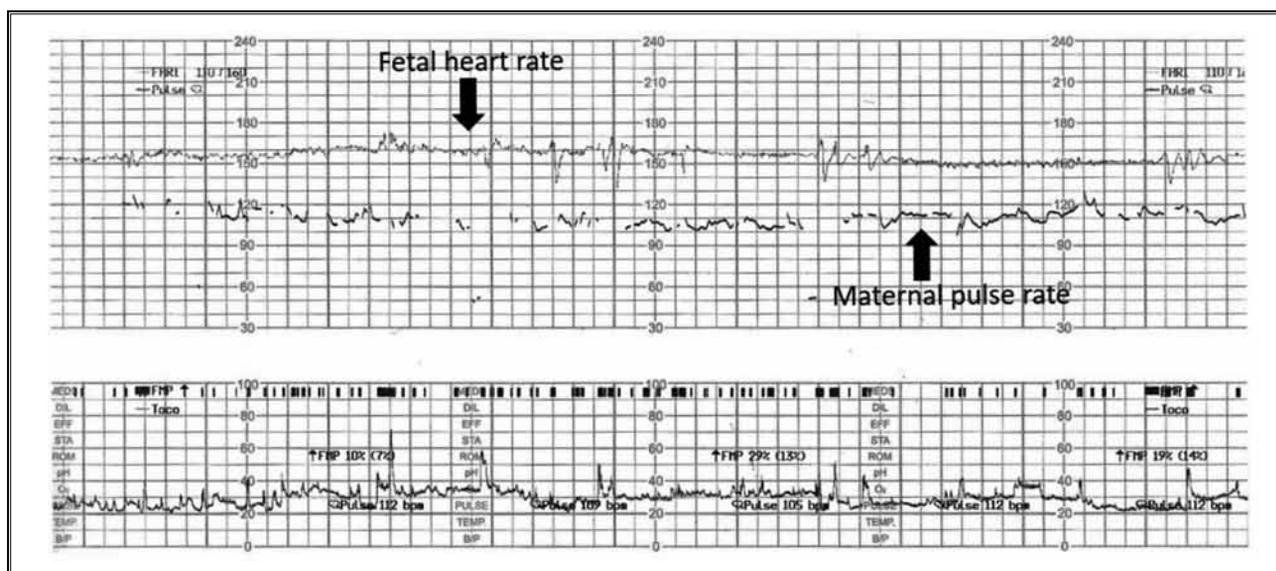

Figure 3. Cardiotocogram of the surviving twin showing reactive fetal heart rate pattern even when Doppler ultrasonography of the middle cerebral artery showed fetal anaemia
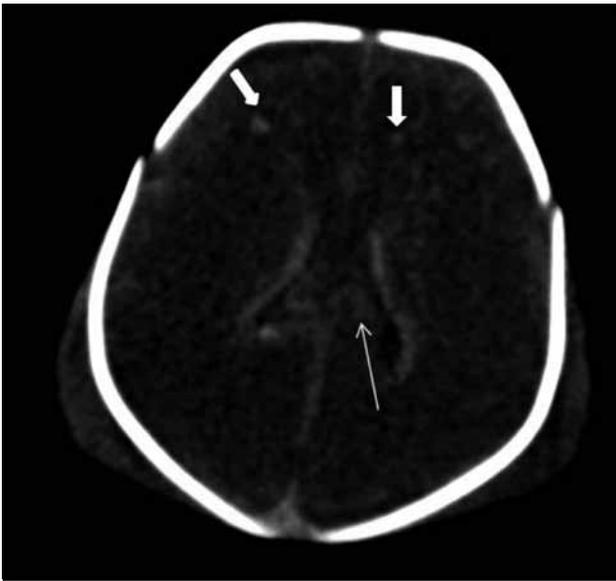
Figure 4. Computed tomography of the brain of the surviving twin 2 days after birth showing diffuse cerebral oedema with generalised hypo-attenuation of brain parenchyma, intraventricular haemorrhage (thin arrow), and petechial haemorrhages in both frontal lobes (bold arrows)

view of the poor prognosis, the couple opted for extubation on day 18 and the baby succumbed. The histology of the placenta showed monochorionic placenta with mild acute subchorionitis. The placenta karyotype was normal. The postmortem examination of twin 1 was unremarkable. The parents refused postmortem examination of twin 2.

Discussion

The incidence of single fetal demise in twin pregnancy is around 0.5% to 6.8% in all twin pregnancies during the second and third trimesters[1]. The incidence of single fetal demise in a regional unit in Hong Kong is 3.8%[2]. The causes of single fetal demise in twin pregnancy can be similar to singleton pregnancy including fetal causes such as chromosomal or genetic abnormalities, structural abnormalities, fetal infection, and placental causes such as placental insufficiency, placental abruption, and maternal causes such as pre-eclampsia. In addition, there are other specific causes for twin pregnancy with single fetal demise such as TTTS in monochorionic twins and cord entanglement in monochorionic monoamniotic twins. However, no specific cause for the intrauterine death of twin 1 was identified. The karyotype and postmortem examination were normal. There was no evidence of placental abruption and maternal pre-eclampsia. Serial ultrasound did not find any evidence of TTTS or selective intrauterine growth restriction of the demised

fetus. In a systematic review and meta-analysis of 1747 pairs of monochorionic twin pregnancies who were not complicated with TTTS, intrauterine growth restriction, or major anomalies[3], the rate of stillbirth was consistently higher in monochorionic twins than dichorionic twins at all gestations. The rate of stillbirth in uncomplicated monochorionic twins was 3.1 per 1000 pregnancies at 28-29 weeks of gestation and the prospective risk of any fetal death per uncomplicated monochorionic twin pregnancy at 28-29 week of gestation was 2.1%[3]. Therefore, single fetal demise in uncomplicated monochorionic twins is not rare.

For single fetal demise in twin pregnancy, the outcome of the co-twin is poorer in monochorionic twins than dichorionic twins. In the 2011 systematic review and meta-analysis of 20 studies on co-twin prognosis after single fetal demise[4], the rate of co-twin death after single fetal demise was 15% in monochorionic twins, compared with 3% in dichorionic twins. The rate of neurodevelopmental impairment in the co-twin after single fetal demise was 26% in monochorionic twins, compared with 2% in dichorionic twins[4]. There are two theories for the poorer prognosis for monochorionic twins. The first theory is haemodynamic fluctuations in monochorionic twins. The death of one fetus results in low pressure in that fetal vascular tree, leading to transfer of blood from the surviving fetus 'back-bleed' through placental anastomoses to the demised fetus. This leads to hypoperfusion, hypotension, and fetal anaemia in the surviving fetus. If the hypotension is severe, this can result in tissue hypoxia, acidosis, and damage in fetal systems, particularly in the central nervous system, and possibly death of the co-twin[5-7]. The second theory is that the demised fetus produces thromboplastic material that passes from the demised fetus to the co-twin via placental vascular anastomoses, which then induces disseminated intravascular coagulopathy in the co-twin. However, there is doubt as to whether these thrombi arise from the dead twin or as a result of haemodynamic changes in the co-twin. As intracranial ultrasound anomalies had been detected in the surviving co-twin as early as 7 days, it is unclear whether disseminated intravascular coagulopathy can arise so quickly. The second theory is not supported by recent studies[5-7].

There are three patterns of brain pathology in surviving co-twins. The first is hypoxic ischaemic lesions of white matter, especially over areas supplied by the middle cerebral artery. The second is haemorrhagic lesions which may lead to post-haemorrhagic hydrocephalus. The third is anomalies secondary to a vascular disturbance including neural tube defects and optic nerve hypoplasia[6]. A study

reported that single fetal demise before 28 weeks of gestation was significantly less likely to lead to neurological damage in the co-twin than after 28 weeks of gestation (3.6% vs 20.0%, p=0.02)[8]. However, a case of single fetal demise as early as 13 weeks leading to neurological injury of the co-twin has been reported[9]. Therefore, there is no definite cut-off value as to the gestation at which the co-twin is safe from neurological damage. Our surviving co-twin was found to have neurological damage, which manifested as seizures in the early neonatal period, and lesions were discernable from computed tomography of the brain within the first week of life. The cause of neonatal death of the co-twin was due to renal failure, which was likely caused by hypoperfusion to the co-twin's kidneys after the fetal demise. When counselling patients on the prognosis of the co-twin after single fetal demise in monochorionic twin pregnancy, we usually focus on the incidence of intrauterine death and the risk of neurological damage of the surviving co-twin, and seldom refer to complications in other organ systems. Renal cortical necrosis, small bowel atresia, gastroschisis, aplasia cutis, and terminal limb infarction have all been reported in the surviving co-twin as a result from fetal anaemia[7]. Therefore, we should provide more comprehensive counselling on these possible complications, in addition to neurological damage.

There are no guidelines or gold standard for management of single fetal demise in monochorionic twin pregnancy. Recommendations are mainly based on case reports, case series, or expert opinions. In a local case series of six cases of single fetal demise in monochorionic twins, four had immediate delivery of the co-twin when the fetal demise occurred after 35 weeks of gestation, whereas two had conservative management when the fetal demise occurred at 19 and 21 weeks of gestation[2]. Management remains controversial when the fetal demise occurs in late second trimester or early third trimester, as in our patient. Some proposed a more aggressive management to deliver the surviving co-twin instead of conservative management, as there are major potential risks of leaving the co-twin in the hostile intrauterine environment that have already led to the death of one fetus[10]. In a case series of immediate delivery of the co-twin in 13 cases of twins with single fetal demise, two were found to have subsequent neurological damage, one being the results from prematurity[11]. In a retrospective study of 38 cases of twins with single fetal demise (79% were monozygotic pairs), those co-twin survivors with abnormal neurological outcomes had fetal demise at later gestations than those co-twins with normal neurological outcomes (31 vs 16.5 weeks). The former also had a shorter interval between the fetal demise and delivery

(2.5 vs 21 weeks) and were delivered earlier in gestation (36.5 vs 39.5 weeks). A more conservative approach is advocated, because the ischemic brain damage in the co-twin likely occurs during or soon after the fetal demise; thus, immediate delivery would not prevent this damage but would add to the complications of prematurity[6]. Prematurity and low birthweight are the main risk factors for poor neurological outcome of the surviving co-twin[12].

As the complications of the surviving co-twin in a monochorionic twin pair are largely related to hypoperfusion and fetal anaemia, intrauterine transfusion of the surviving co-twin is suggested. In two case series on 22 pairs of twin pregnancies, fetal blood sampling was performed after single fetal demise[13,14]. Nine surviving co-twins were non-anaemic and had normal outcomes, whereas the remaining 13 were anaemic and underwent in-utero blood transfusion. Of the latter, six had normal neurological outcomes, three had abnormal brain scan on follow-up and were terminated, two had intrauterine death at 24 hours after transfusion, one was delivered at 34 weeks with neurological damage, and one was delivered at 29 weeks with subsequent neonatal death[13,14]. Intrauterine blood transfusion may prevent death of the co-twin but whether it can prevent neurological damage is controversial, as the damage may have already occurred shortly after twin fetal demise and before intrauterine transfusion. In our patient, if intrauterine blood transfusion was performed instead of delivery when Doppler parameters showed signs of fetal anaemia, the pregnancy might be prolonged to a later gestation for the baby to gain sufficient birthweight and maturity for renal dialysis after delivery. However, it is unknown whether the neurological outcome and renal failure of the surviving co-twin could be improved by intrauterine transfusion. Nevertheless, if the surviving co-twin was suspected to have anaemia on ultrasound, the option of intrauterine blood transfusion could be offered while pointing out the limited evidence supporting such treatment, and the patient could be referred to a quaternary centre where intrauterine transfusion could be arranged.

After single fetal demise in twin pregnancy, spontaneous labour may occur. However, some women may develop pre-eclampsia and placental abruption and necessitate immediate delivery of the co-twin. In the systematic review and meta-analysis of co-twin prognosis after single fetal demise, the risk of preterm delivery of the surviving co-twin was 68% in monochorionic twins, which included spontaneous labour and intragenic delivery[4]. Most reviews advocate regular surveillance of the surviving co-twin by ultrasound for fetal signs of anaemia, fetal growth

and liquor volume and by cardiotocogram for fetal well being[1,2,5,6]. In our patient, the peak systolic velocity of the middle cerebral artery can reflect the anaemic status of the surviving co-twin, but the cardiotocogram was not useful. The cardiotocogram pattern was still reactive immediately before delivery, even when the baby was found to be severely anaemic after birth. Therefore, a reactive cardiotocogram pattern alone should not be regarded as normal fetal well-being without consideration of other ultrasound parameters. For prediction of neurological damage in the surviving co-twin, apart from regular ultrasonography of the brain, magnetic resonance imaging of the brain is regarded as 'routine' imaging for such cases, and can be performed around 2-3 weeks after the fetal demise to detect any structural evidence of neurological damage. The sensitivity of such imaging remains unknown[1,5-7].

Conclusion

The prognosis of the co-twin in single fetal demise in monochorionic twin pregnancy is poorer than dichorionic twin pregnancy. Accurate determination of chorionicity in early gestation is crucial for all twin pregnancies, as the subsequent monitoring and management is different. Regular ultrasound surveillance and appropriate intervention to avoid single fetal demise in monochorionic twins such as in those with TTTS or selective intrauterine growth restriction is a more effective way to prevent adverse outcome of the co-twin, compared with close surveillance after single fetal demise, which cannot guarantee good outcome of the surviving co-twin. There is no gold standard for the optimal management of the surviving co-twin, but the current evidence favours conservative management before 34 weeks of gestation. The role of intrauterine transfusion is controversial, and treatment should be individualised.

Declaration

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