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Prognosis for the co-twin following intrauterine single-twin death

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Title figure:
source: www.wikipedia.org; William Adolphe Bouguereau (1825 – 1905): twins

Twins are two offspring produced by the same pregnancy. Twins can be either monozygotic («identical»), meaning that they develop from one zygote, which splits and forms two embryos, or dizygotic («fraternal»), meaning that they develop from two different eggs. In fraternal twins, each twin is fertilized by its own sperm cell. Dizygotic twins (7 to 11 in 1000 deliveries) implant themselves separately and develop membranes that are independent of each other. Each twin has its own placenta, its own chorion and its own amniotic cavity. In monozygotic twins (3 to 4 in 1000 deliveries), choronicity and amnionicity depend on the timing of zygote splitting (Fig. 1). Assisted reproductive technology (ART) has markedly increased the number of multiple pregnancies with the vast majority (about 95%) being dichorionic (DC). However, ART also increases fivefold the frequency of monozygotic twinning (1). Monochorionic diamnotic (MC/DC) pregnancies can be complicated by twin-twin transfusion syndrome (TTTS); interestingly, this complication is rarer in monochorionic monoamniotic (MC/MA) twin pregnancies; however, MC/MA twin pregnancies can be complicated by cord entanglement.

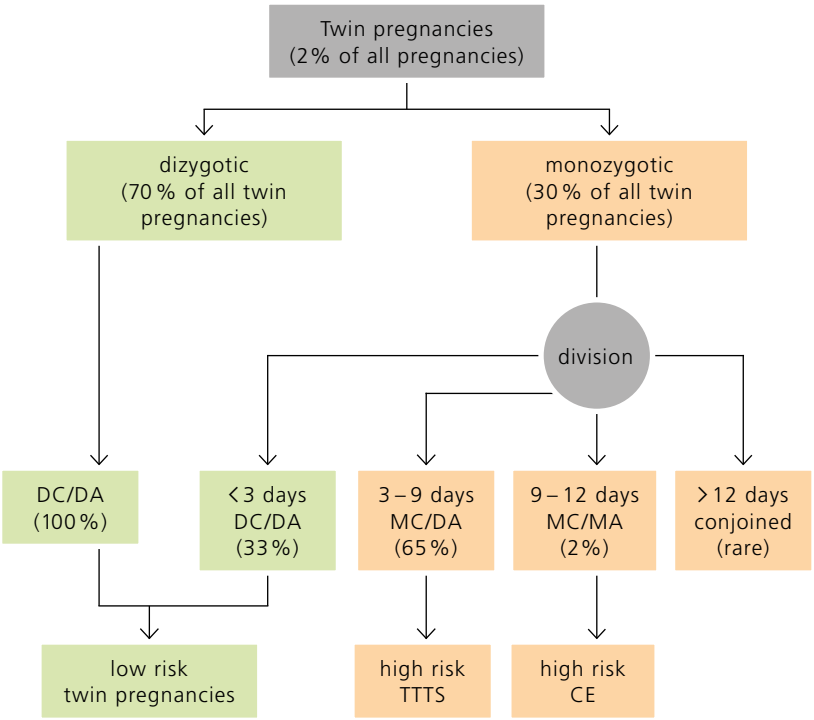

Fig. 1

Overview of different types of twin pregnancies (CE, cord entanglement; DC, dichorionic; DA, diamniotic; MC, monochorionic; MA, monoamniotic; TTTS, twin-twin transfusion syndrome)
(Source: www.neonet.ch – COTM 09 2009).

The mother was a 23-year-old G2/P2+3 who had spontaneously conceived MC/DA twins. Pregnancy had been uncomplicated with no evidence of TTTS until 31 6/7 weeks of pregnancy. At that time, the mother was hospitalized when intrauterine fetal demise (IUFD) of twin B was noted during a routine antenatal care visit. On admission, the cardiotocogram (CTG) of the surviving twin A was mildly restricted with no decelerations and fetal ultrasound revealed a small pericardial effusion, mild tricuspid regurgitation as well as a slightly elevated v_{max} in the middle cerebral artery and moderate polyhydramnios. Because the estimated fetal weight of the dead twin B was significantly lower than that of twin A and because twin B appeared to be deformed, it was felt that the IUFD had occurred at least several days ago.

Antenatal corticosteroids were administered to enhance fetal lung maturation. Two days later (i.e., at 32 1/7 weeks of pregnancy), a Cesarean section was performed because of worsening CTG, abnormal fetal Doppler signals of twin A and evidence of dilated fetal cardiomyopathy.

The girl adapted well with Apgar scores of 7, 8, and 9 at 1, 5 and 10 minutes, respectively. Arterial and venous umbilical cord pH values were 7.34 and 7.40, respectively. Following insertion of an umbilical venous catheter, the infant was transferred to the NICU on nasal CPAP and an FiO_2 of 0.35. The infant had a birth

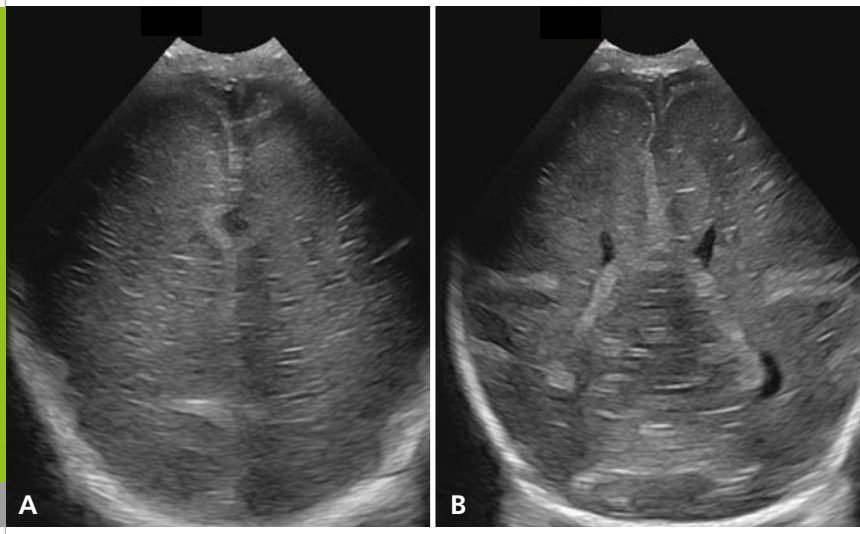

Fig. 2

Cerebral ultrasound examination (DOL 2, transverse views): hyperechogenicity of cerebral hemispheres (A) and abnormalities in the insular region (B).

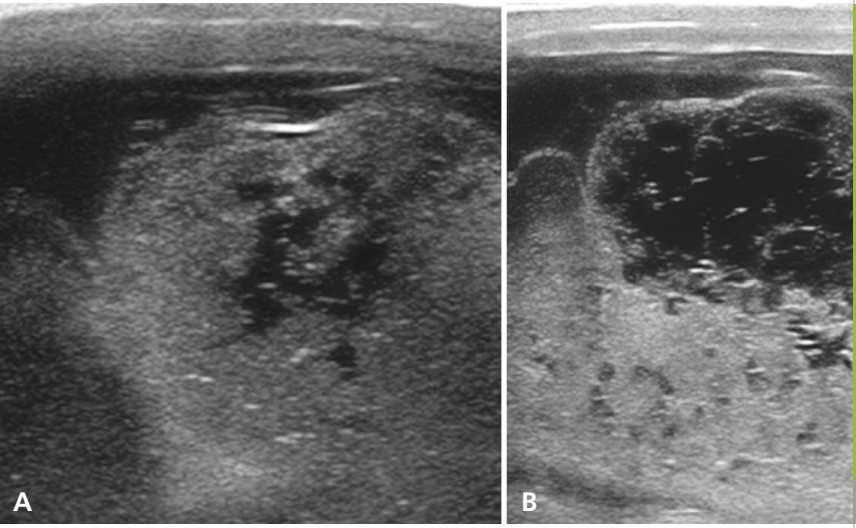

Fig. 3

Cerebral ultrasound examination (coronal view): progression of cystic lesions in the left paramedian cortex (A) DOL 2, B) DOL 6).

weight of 1870 g (P50-75), a length of 44 cm (P50-75) and a head circumference of 29 cm (P25-50). Apart from mild respiratory distress while on CPAP, her physical examination was unremarkable.

Initial laboratory results were remarkable for moderate respiratory acidosis (pH 7.23, pCO_2 8.7 kPa, BE -2.0 mmol/l), a normal lactate concentration (0.8 mmol/l) and mild anemia (hemoglobin concentration 124 g/l). Coagulation studies were normal. On echocardiography, mild to moderate persistent pulmonary hypertension of the newborn and hypertrophy of both ventricles (right > left) were noted; these abnormalities resolved completely over a period of three weeks.

On day of life (DOL) 2, a cerebral ultrasound revealed bilateral hyperechogenic abnormalities of the cerebral cortex and the insular region (Fig. 2); in addition, bilateral symmetric cystic lesions were demonstrated in the paramedian parietal area (Fig. 3A). These lesions progressed to extensive bilateral multicystic encephalomalacia on DOL 6 (Fig. 3B) and DOL 28 (Fig. 4, 5).

Prior do discharge, polysomnography revealed highly abnormal EEG activity and subclinical seizures. Otoacoustic emissions were normal. The infant was discharged home on DOL 43 at a corrected gestational age of 38 2/7 weeks.

At last follow-up (corrected age of 13 months),

the patient suffered from severe dystonic cerebral palsy and occasional epileptic seizures despite treatment with balclofen, chlorahydrate, diazepam and valproic acid. Her head circumference was 42.2 cm (z-score –2.6).

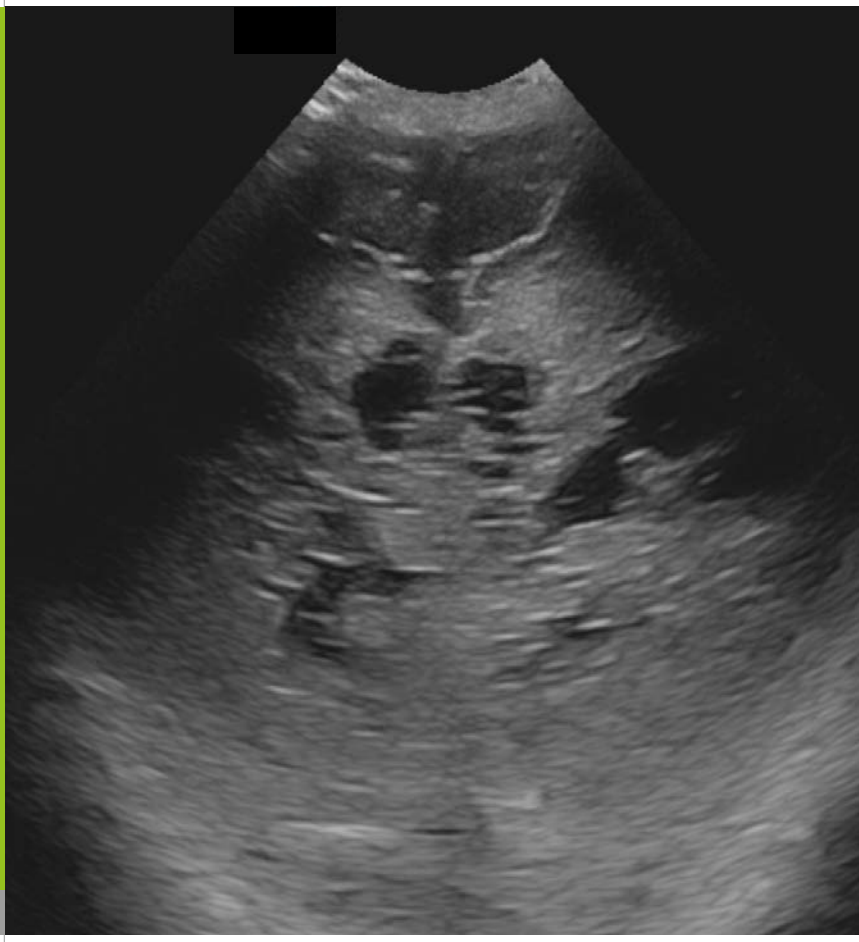

Fig. 4

Cerebral ultrasound examination (DOL 6, coronal view): extensive destruction of paramedian, insular and thalamic brain tissue.

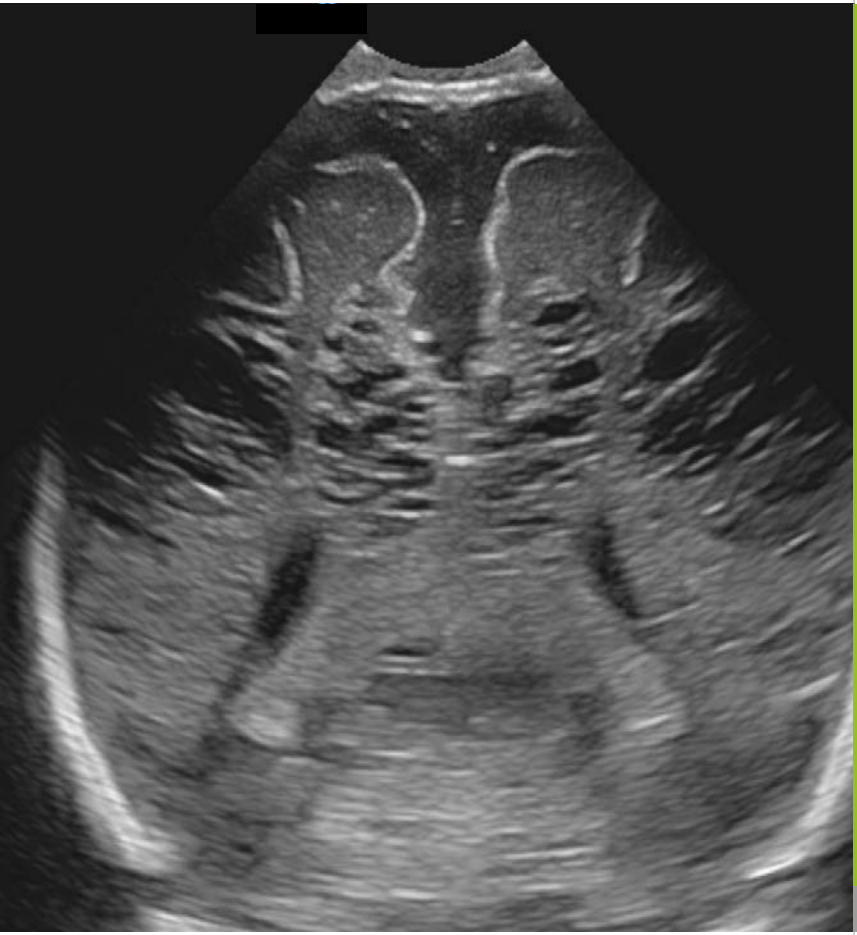

Fig. 5

Cerebral ultrasound examination (DOL 28, coronal view): progression of wide-spread multicystic encephalomalacia.

DISCUSSION

Single intrauterine fetal demise (sIUFD) occurs in 3.7 – 6.8 % of all twin pregnancies and considerably increases the complication rate in the co-twin including fetal loss, premature delivery, and end-organ damage (1). The etiology of sIUFD in twin pregnancy can either be similar to that in singletons (e.g., genetic or anatomical abnormalities, placental insufficiency, placental abruption, cord abnormalities, maternal disease) or unique to the twinning process. In MC pregnancies, sIUFD may result from TTTS; however, often the etiology remains elusive.

The prevalence of MC twinning among cases of sIUFD in twins is 50 – 70% (2) and therefore higher than expected given an MC incidence of only 30% among all twin pregnancies (Fig. 1). Poor prognosis of the surviving twin in MC twin pregnancies is a well-known phenomenon. A 2006 meta-analysis assessed the risk of co-twin mortality and neurological morbidity (3). The risk of MC and DC twin death following sIUFD was 12% and 4% respectively. The risk of neurological abnormality in the surviving MC and DC co-twin was 18% and 1%, respectively (Table).

When sIUFD occurs between the first trimester and the limit of viability, risk of damage to the survivor is significant with a variety of injury patterns: neural tube defects, optic nerve hypoplasia, multicystic encephalomalacia, hydrancephaly, porencephaly,

Table

Co-twin complications Following sIUFD	MC twin pregnancy	DC twin pregnancy	OR (95% CI)
Mortality	12%	4%	6.04 (1.84 – 19.87)
Neurologic abnormality	18%	4%	4.07 (1.32 –12.51)
Preterm delivery	68%	57%	1.91 (0.70 – 5.21)

Comparison of complication rates in surviving twins following sIUFD between MC and DC twin pregnancies adapted from a meta-analysis by Ong et al. (3).

posthemorrhagic hydrocephalus, bilateral renal cortical necrosis, unilateral absence of a kidney, gastrointestinal tract atresia, gastroschisis, hemifacial macrosomia, and aplasia cutis of the scalp, trunk or limbs (4). When sIUFD occurs in the late second and early third trimester, clinicians and parents are faced with the dilemma of either delivering a premature twin or ongoing expectant management potentially putting the surviving twin at risk for morbidity or mortality. Recent insights into the mechanisms that are involved in potentially harming the surviving twin are helpful in this context (Fig. 6).

Historically, poor prognosis of surviving co-twins after sIUFD in MC pregnancies had been related to some form of «twin embolization syndrome» and resulting disseminated intravascular coagulation (DIC). Currently, hemodynamic imbalance is thought to be the main mechanism leading to adverse outcomes in surviving twins. A sudden fall in vascular resistance around the time of death of one twin causes shunting of blood from the surviving fetus to the dead fetus (1). There are many factors which affect the rate of acute fetofetal hemorrhage after sIUFD. These include the number, the size and the type of vascular anastomoses. If there are major placental vascular communications, the death of one twin will probably lead to immediate life-threatening hypovolemia of the co-twin. It is unlikely that any intervention would save the co-twin. With fewer and smaller vascular anastomoses, the rete

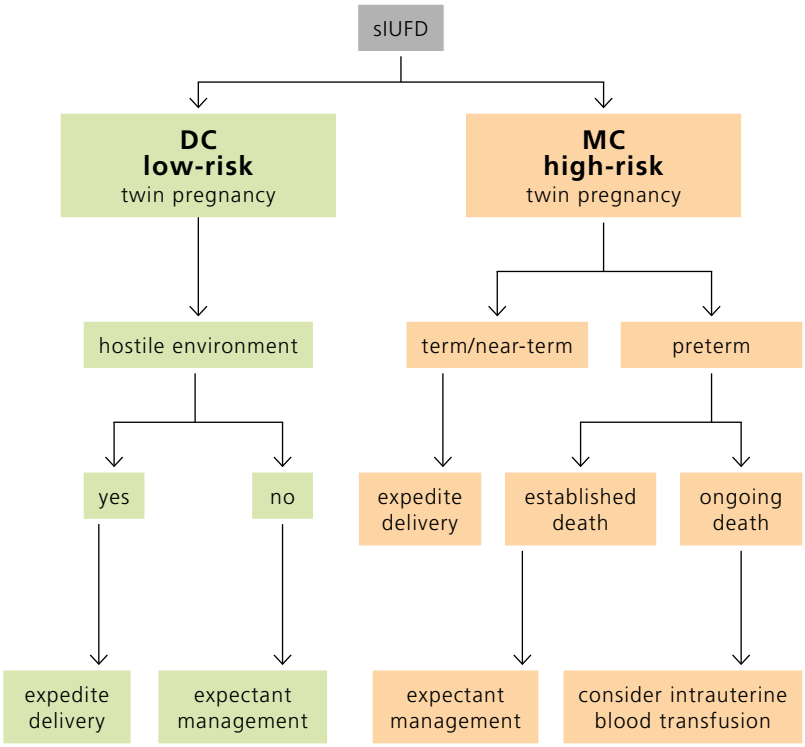

Fig. 6

Management of sIUFD in twin pregnancies adapted from Blickstein et al. (1): delivery of surviving DC co-twin only indicated if hostile intrauterine environment is threatening; delivery of surviving MC twin depends on gestational age and timing of sIUFD.

of exsanguination would likely be slower, and active interventions might have the potential to alter outcome for the surviving twin.

Acute fetofetal hemorrhage leads to intrauterine hypotension, hypoperfusion und end-organ damage. Studies of fetal blood sampling immediately before and within 24 hours of death in MC twin pregnancies complicated by sIUFD demonstrated a marked drop in hematocrit in surviving twins supporting acute TTTS after sIUFD (5, 6). Quintero et al. presented direct fetoscopic evidence of this mechanism. They also suggested that perimortem fetofetal hemorrhage may take place in less than three hours following sIUFD (7). This latter observation is important when considering management options for the surviving co-twin (Fig. 6). Obviously, the window for a potentially effective treatment by intrauterine transfusion is very narrow; reported success rates of such an intervention vary substantially (8 – 10).

Following sIUFD in this MC/DA twin pregnancy, the presented surviving co-twin sustained extensive cerebral damage and devastating long-term neurodevelopmental impairment. We speculate that sIUFD had occurred several days before presentation to the maternal fetal medicine unit and intrauterine blood transfusion or immediate delivery would have had no impact on the outcome.

See also: COTM 08/2001: Surviving twin with encephalomalacia; COTM 10/2002: Aplasia cutis congenita in a surviving twin; COTM 03/2006: Twin-twin transfusion syndrome; COTM 06/2009: Twinning: when it happens between day 7 and 13.

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