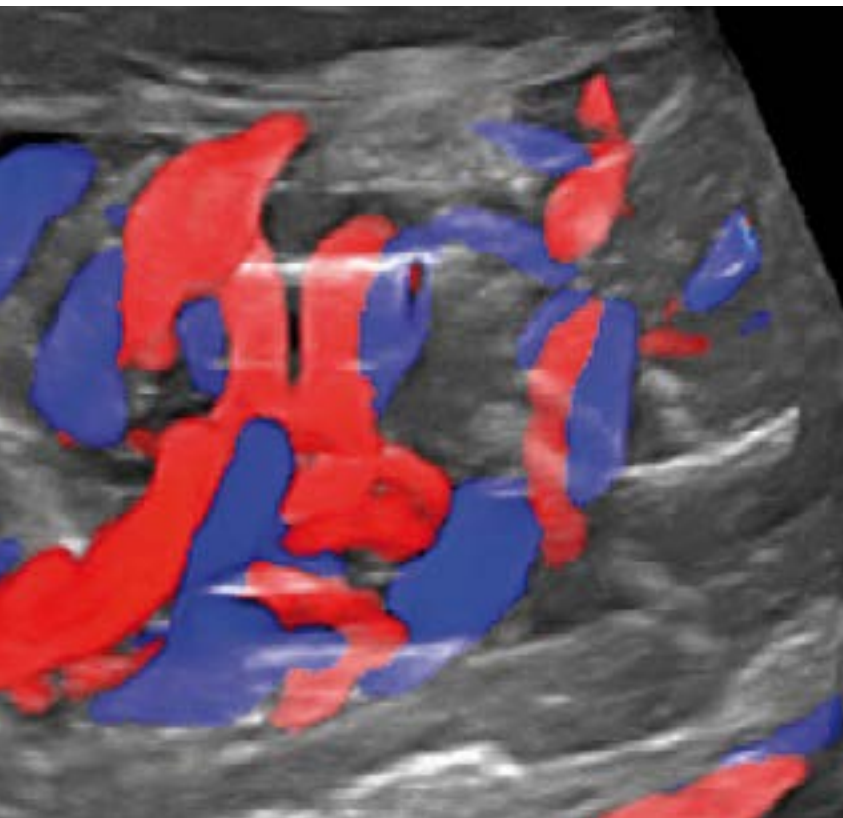


SWISS SOCIETY OF NEONATOLOGY

Twinning: When it happens  
between day 7 and 13

June 2009





The risk of complications and adverse outcome is greater in twin pregnancies compared to singletons, mainly due to the increased risk of prematurity. Complications that are unique to twins are twin-twin transfusion syndrome (TTTS), cord entanglement (CE) and cord knotting (CK). Depending on the timing of twinning, different constellations of chorionicity and amnionicity will develop which in turn are associated with TTTS or CE/CK (Fig. 1).

This monochorial monoamniotic (MC/MA) twin pregnancy in a 30-year-old G1/P1+2 was followed by serial prenatal ultrasound examinations every two weeks in an outpatient setting. In the 30th week of gestation, intrauterine fetal demise (IUFD) of one twin was detected and the mother was transferred to our institution.

Because of pathological umbilical cord Doppler examination in the surviving twin a caesarean section was performed at 29 2/7 weeks of gestation. A baby boy was born and adapted well with Apgar scores of 6, 7, 7 at 1, 5 and 10 minutes, respectively. Umbilical cord pH could not be obtained. He developed respiratory distress, was intubated in the delivery room and surfactant was administered. The umbilical cords showed extensive entanglement with a true knot (Fig. 2). The infant had mild generalized edema consistent with a early hydrops. His birth weight was 1285 g (P 25-50). The laboratory studies revealed a pancytopenia with a hemoglobin of 98 g/l, a platelet count of 138 G/l and leucocytes of 2.7 G/l.

The hydrops and the pancytopenia were thought to have resulted from feto-fetal transfusion from the surviving twin into the dead co-twin. The initial lactate level was 2.5 mmol/l indicating no acute asphyxial event.

The first cranial ultrasound on the second day of life (DOL) was normal (Fig. 3). But on DOL 8, multiple cysts in the white matrix and the cortex of the parieto-occipital region bilaterally were noted (Fig. 4). The time course suggested an intrauterine event most likely linked to the demise of the co-twin. On DOL 23, both parietal lobes were replaced by confluent cystic lesions (Fig. 5 and 6).

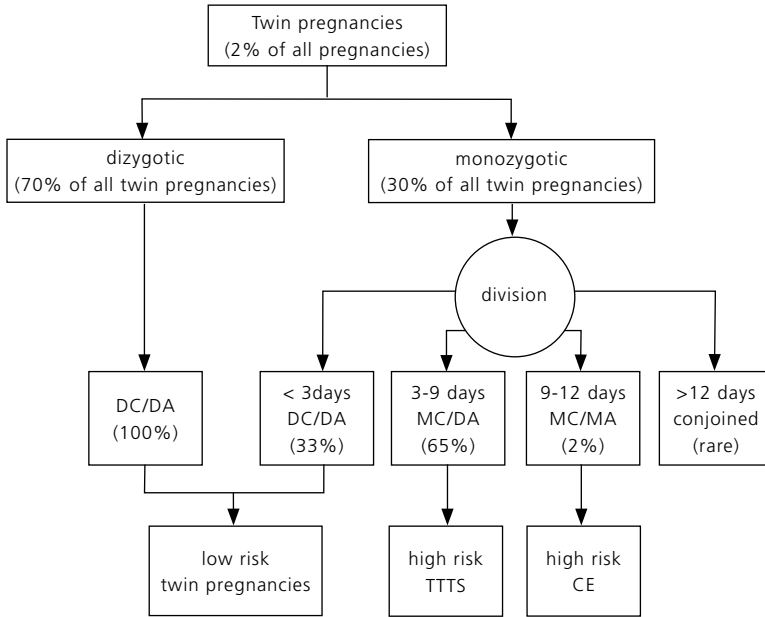


Fig. 1

*Overview of different types of twin pregnancies (CE, cord entanglement; DC, dichorionic; DA, diamniotic; MC, monochorionic; MA, monoamniotic; TTTS, twin-twin transfusion syndrome).*

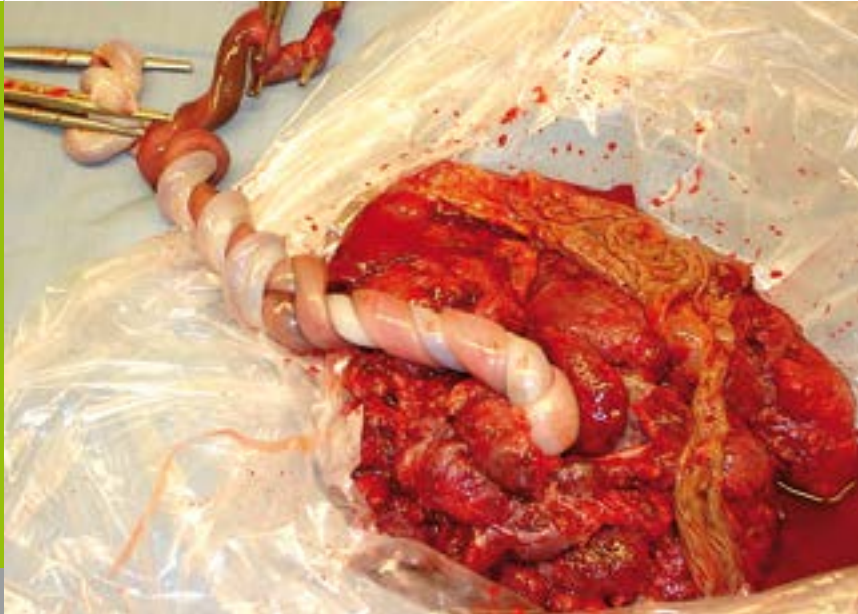


Fig. 2

*Case 1: cord entanglement with true knot.*

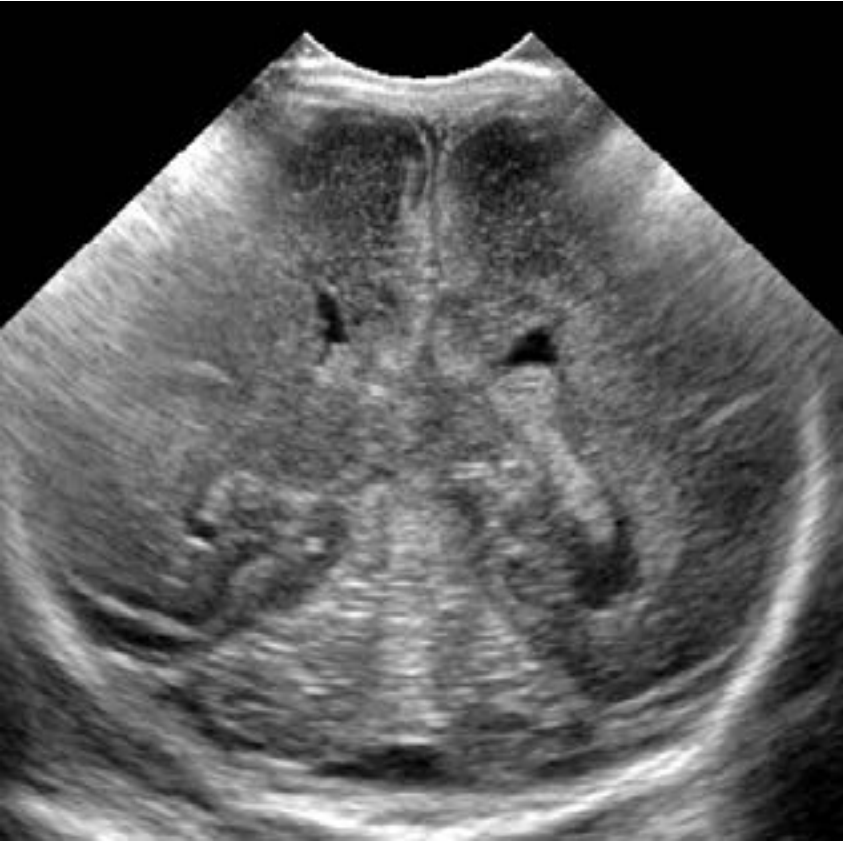


Fig. 3

*Case 1: normal cranial ultrasound DOL 2 (coronal view).*



**Fig. 4**

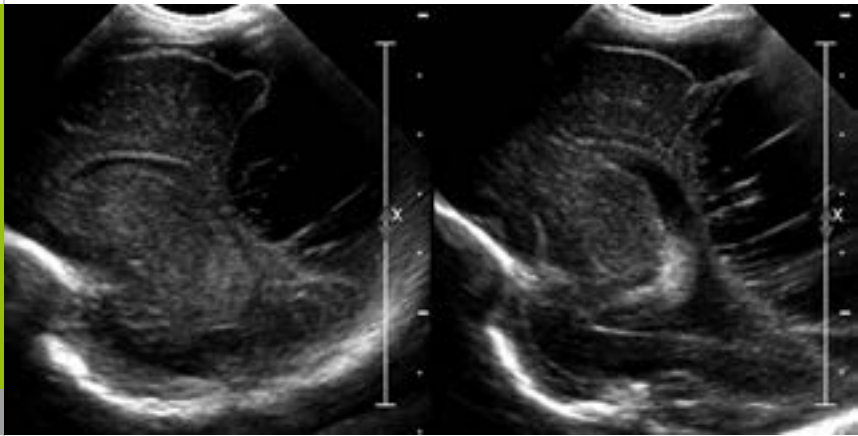
*Case 1: cranial ultrasound DOL 8 showing multiple cysts in the white matrix and the cortex of the parieto-occipital regions (coronal view).*





Fig. 5

*Case 1: cranial ultrasound DOL 23 showing bilateral porencephaly of the parieto-occipital regions (coronal view).*



**Fig. 6**

*Case 1: cranial ultrasound DOL 23 showing bilateral porencephaly of the parieto-occipital regions (sagittal view).*

## CASE REPORT 2

These female MC/MA twins were born to a 38-year-old mother at 29 2/7 weeks of gestation. Cord entanglement had been noted on prenatal ultrasound. The mother was hospitalized and daily fetal heart-rate monitoring and repeated sonograms and Doppler studies were performed. The decision to perform the caesarean section was based on a non-reassuring fetal heart-rate pattern in one twin. Examination of the placenta showed entanglement of the umbilical cords (Fig. 7).

Neonatal adaptation was excellent in both infants and their initial clinical course in the NICU was uncomplicated. They did not require intubation and were supported with nCPAP for 16 and 30 days, respectively. The

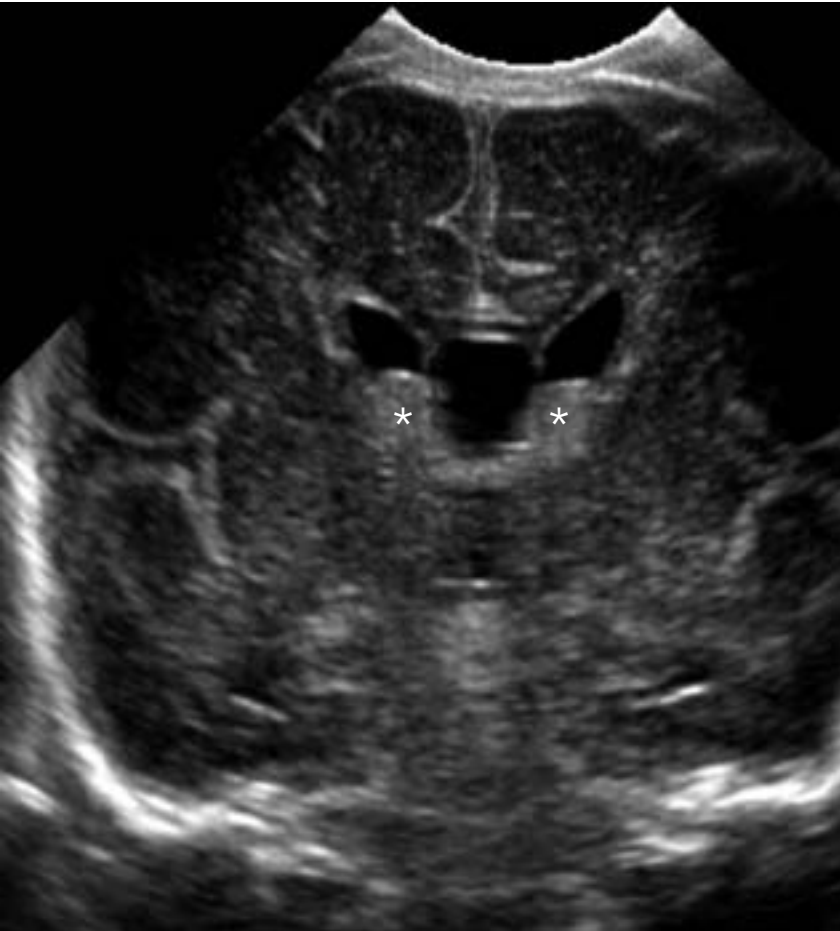
cranial ultrasound examinations in twin A were normal apart from a small right-sided subependymal hemorrhage which resolved by one month of age (Fig. 8). Twin B had bilateral subependymal hemorrhages which subsequently resolved. However, on follow-up ultrasound examinations, slightly enlarged ventricles and subarachnoid spaces were noted (Fig. 9). Twin A was discharged 10 days after her due date and was fully breast fed. Twin B was discharged home at a corrected age of 43 weeks but still required gavage feeding through an NG tube. At discharge, her neurological exam showed movement abnormalities and truncal hypotonia.

While twin A reached normal developmental milestones at a corrected age of 3 months, her sister had severe neurosensory impairment with a developmental age of 2 weeks and dystonic left-sided spastic hemiplegia. An MRI was performed at a corrected age of 4 months and revealed generalized atrophy of both cerebral hemispheres and pathological signals in the basal ganglia (Fig. 10). These findings were felt to be the result of recurrent hypoxic events during intermittent intrauterine cord occlusions.

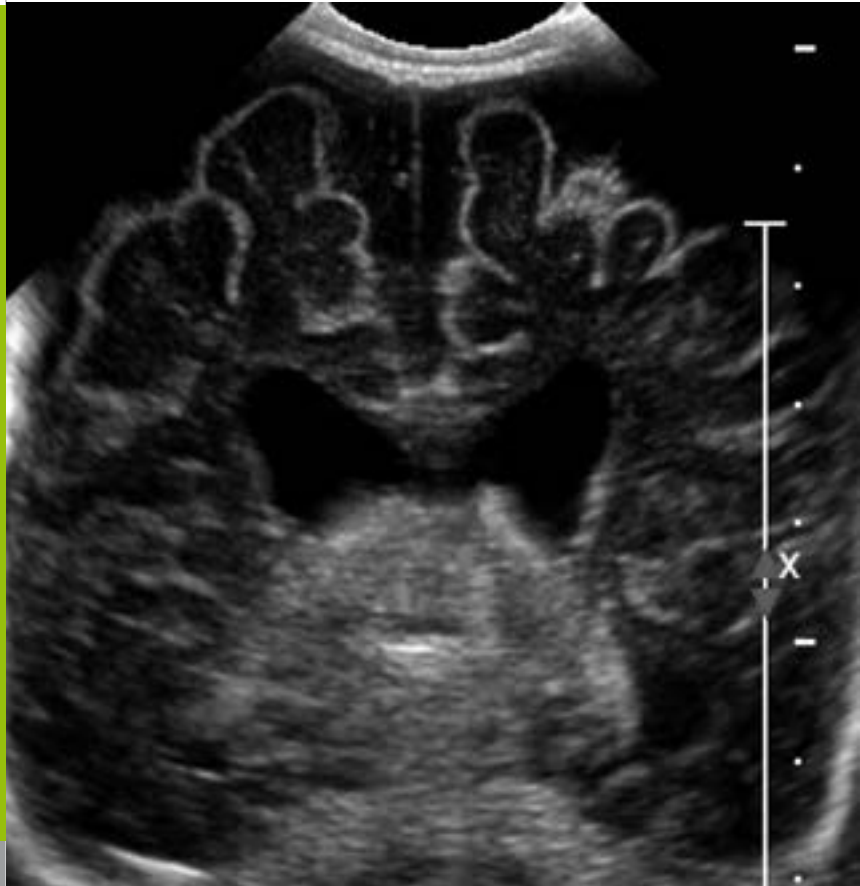


Fig. 7

*Case 2: cord entanglement.*

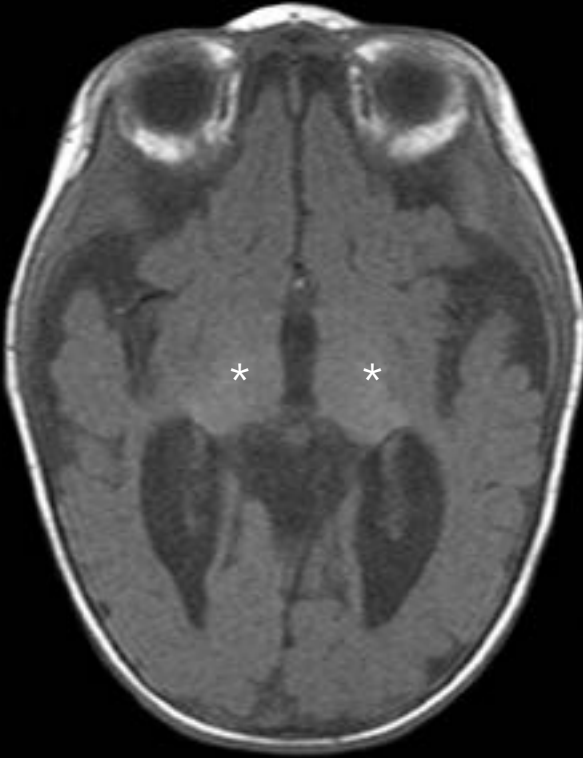
**Fig. 8**

*Case 2: cranial ultrasound DOL 2 showing bilateral subependymal hemorrhages (asterisks, coronal view).*



**Fig. 9**

*Case 2: cranial ultrasound at a corrected age of 40 weeks of gestation showing ectasia of the ventricles and the subarachnoid space (coronal view).*

**Fig. 10**

*Case 2: MR at a corrected age of 4 months showing hypotrophy of the cerebral hemispheres and pathological signal alteration of the thalami (asterisks, axial view).*

## DISCUSSION

Monozygotic twins occur in approximately 1 out of 250 births. In contrast to dizygotic twin pregnancies, the incidence is constant across populations and maternal ages but is reported to increase twofold with ovulation induction techniques and in vitro fertilisation (1). Embryonic division between day 7 and 13 results in monochorial (MC) monoamniotic (MA) twins, affecting only about 1-2% of all monozygotic twin gestations (2, 3).

MC/MA twin gestations carry a high perinatal mortality (20 weeks of gestation through 28 days of life) risk ranging from 10 to 70%. Complications include premature labor, twin-twin transfusion syndrome (TTTS), fetal anomalies and umbilical cord entanglement.

The incidence of TTTS is reported to be lower in MC/MA pregnancies (3-10%) than in monochorial diamniotic (MC/DA) pregnancies (10-15%) (4). Unidirectional arterio-venous (AV) placental anastomoses are responsible for the development of TTTS. Additional oppositely directed anastomoses may compensate for the circulatory imbalance. Intuitively, oppositely directed VA anastomoses would be expected to compensate better than arterio-arterial (AA) anastomoses because of the higher pressure gradient. But according to Ohm's law the resulting flow is proportional to the pressure gradient and indirectly proportional to the resistance (the resistance itself is proportional to the 4th power of the radius, Poiseuille's law). It has been shown in a mathematical model that due to the vascular architecture of the placenta the resistances of



AA anastomoses are significantly lower compared to VA anastomoses. This difference is a consequence of anatomical differences in VA versus AA anastomoses, because VA anastomoses occur at the cotyledon capillary level, whereas AA anastomoses occur at the placental feeding vessel level (5). Therefore, AA anastomoses have a higher ability to compensate and are more protective against the development of TTTS. This theory is consistent with the almost ubiquitous presence of AA anastomoses in MC/MC placentas (up to 98%) (4).

Following single fetal death (e.g., due to cord entanglement, see below), blood volume can rapidly shift through the AA and VV anastomoses from the surviving twin towards its deceased co-twin, causing acute exsanguination and subsequent death of the second twin (4).

Congenital anomalies, typically congenital heart disease (CHD), occur with an increased frequency in monozygotic twin pregnancies. In MC/DA twin pairs the risk is approximately 7% for at least one of a twin pair having CHD. This risk is even higher in MA twins with a significant increase in anomalies due to disturbance of laterality. The definition of the corporal left-right axis occurs around embryonal day 7 to 13. Since MC/MA twinning happens during the same time period, it is supposed to impair this process. The failure to establish left-right asymmetry may lead to heterotaxy in one twin (3).

Umbilical cord entanglement (CE) and cord knotting is the most important cause of perinatal death in MC/MA twin pregnancies with 50% or more of the deaths being attributed to this complication. CE is present in up to 70% of these pregnancies. It may be detected by prenatal ultrasound as early as in the first trimester because the initiation of CE is a phenomenon of early pregnancy, when the amniotic fluid volume is greater in relation to the fetal mass (5). Umbilical cord occlusion may occur either acutely or in a subacute or intermittent manner (6). Acute occlusion of the umbilical cord leads to the fetal death of one twin and puts the other one at high risk for either death or profound cerebral damage as illustrated in the first case report. The risk of fetal death appears to be higher if the CE or CK occurs close to the placenta as compared to close to the umbilical insertion (7).

Because of the rarity of MA twin pregnancies, accurate survival data and optimal perinatal treatment strategies are difficult to ascertain. In the past perinatal mortality rate ranged from 30 to 70 %. More recent studies reported an improved survival with perinatal mortality rates of 10 to 20% (7, 8). This is mainly attributable to an intensive prenatal monitoring. Serial fetal sonograms every 1 to 2 weeks are typically used. Inpatient admission for electronic fetal monitoring two to three times daily from 26 - 27 weeks gestation has been proposed. Finally, timing of delivery is advocated between 32 to 34 weeks gestation since late fetal deaths have been reported.

Little is known about the neonatal morbidity of MC/MA twins (8, 9). In a recent study only 8% of survivors showed cerebral abnormalities in the ultrasound (8). But no data is available about their long term outcome. Lacking signs of ischemic brain damage on cranial ultrasounds do not guarantee a normal neurodevelopmental outcome as shown in our second case report. Long-term morbidity of MC/MA twins may be higher than commonly appreciated.

**See also COTM 03/2006:** Twin-twin transfusion syndrome

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